A series published in the *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases*

Quality of Tuberculosis Care

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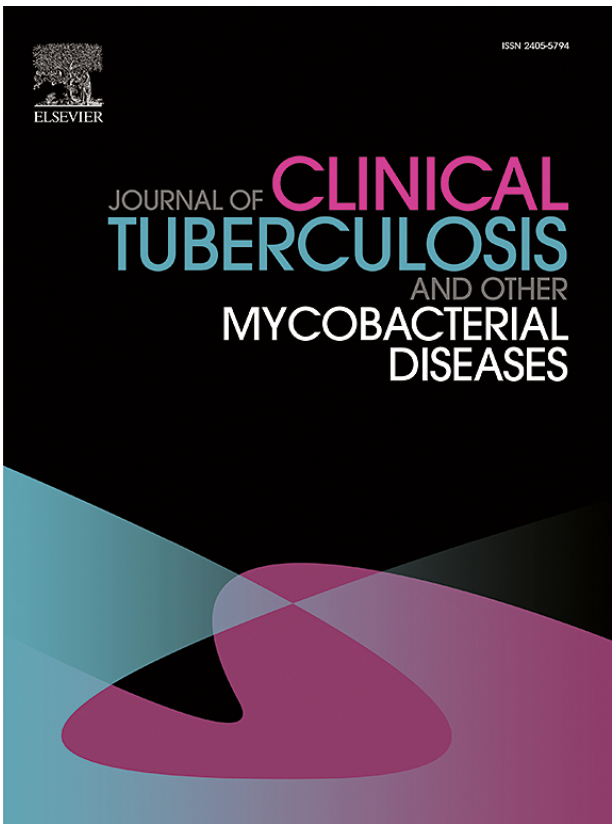

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journal homepage: www.elsevier.com/locate/jctube

Editorial

Quality: The missing ingredient in TB care and control

Good health is a function of the utilization of healthcare services and the quality of healthcare. In the field of global health, there is growing awareness of the need to go beyond coverage of services and improve the quality of care [1,2].

Recently, The *Lancet Global Health* published a landmark report entitled High-quality health systems (HQSS) in the Sustainable Development Goals era: Time for a revolution [3]. In this HQSS Commission report, the authors asserted that providing health services (i.e. coverage) without guaranteeing a minimum level of quality is ineffective, wasteful, and unethical. What is needed, the Commission argued, are high-quality health systems that optimize health care in each given context by consistently delivering care that improves or maintains health, by being valued and trusted by all people, and by responding to changing population needs [3].

Throughout the report, tuberculosis (TB) is used as a key example to illustrate the need to go beyond coverage and focus on the quality of care. According to the HQSS report, more than 8 million people per year in low- and middle-income countries die from conditions that should be treatable by the health system. Sixty-percent of deaths from conditions amenable to health care are due to poor-quality care, whereas the remaining deaths result from non-utilization of the health system [3].

The HQSS report provides a detailed analysis on TB deaths. Of the 946,003 TB deaths amenable to healthcare, the authors estimate that 469,956 (50%) are due to poor quality TB care. The remaining 476,047 deaths are due to non-utilization of healthcare services [3].

The report suggests that high-quality health systems could prevent 900,000 TB deaths each year [3]. In other words, by using already existing tools and improving the quality of care, we can avert 50% of all TB deaths.

The fact that 50% of deaths in association with TB occur despite the patient seeking medical care is a sad reflection on the current state of affairs. How is it acceptable that we cannot save patients with a curable, bacterial infection for which we have policies, tools and technologies?

Why is the quality of TB care suboptimal? Patient-pathways analyses from 13 countries show long, complex pathways to health care, private or informal sectors being the preferred first point of contact, and lack of adequate TB services at the primary care level. [4] Several studies show large gaps in the cascades of care, across types of TB and countries [5–7].

Simulated (standardized) patient studies in 4 countries (India, Kenya, China and South Africa) confirm gaps in cascades of care, and show poor quality of care in both public and private sectors, with private sector faring worse [8–12]. Across these studies, only about a third of simulated patients with presumed TB were managed correctly at the primary care level.

To end TB, we need nothing short of a quality revolution [13]. The TB field urgently needs to adopt and implement the science of quality improvement (QI). But QI alone is not sufficient, since even the foundations of TB care are weak. Countries need to invest adequate funds to control TB, and make sure TB services are of high quality and patient-centric.

In September 2018, the United Nations General Assembly hosted the first ever High-level Meeting (UNHLM) on TB, and adopted a political declaration, which recognized that "tuberculosis is both preventable and curable, yet 40 per cent of people newly affected by tuberculosis are missed by public health reporting systems, and millions do not receive quality care each year, and that tuberculosis can only be eliminated through prevention efforts and access to quality diagnosis, treatment and care, including access to affordable diagnostic tools and drug treatment, effective people-centered and community-based models of care supported by integrated care services, as well as financing innovations" [14].

The TB field must build on this emphasis on quality in the UNHLM declaration and push all stakeholders to think beyond coverage and demand high quality care for all TB patients in all countries. If we are serious about ending TB, we must put quality on the agenda, in addition to expanding coverage of critical interventions.

Given the importance of quality in TB care, *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases*, has launched a series on this topic. The series will cover papers on quality of TB care, approaches to measuring quality, and quality improvement interventions. It is our wish and hope that this series will result in a robust and sustained conversation about quality TB care, a topic that has heretofore been woefully neglected.

Conflicts of interest

None.

Ethical statement

None.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jctube.2018.12.001.

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https://doi.org/10.1016/j.jctube.2018.12.001
Received 29 November 2018; Accepted 23 December 2018

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J Clin Tuberc Other Mycobact Dis 16 (2019) 100109

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Lessons on the quality of tuberculosis diagnosis from standardized patients in China, India, Kenya, and South Africa

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ARTICLE INFO

Keywords:
Quality of care
Tuberculosis
Standardized patients
Health care providers
Low- and middle-income countries

ABSTRACT

Standardized patients (SPs) are people who are recruited locally, trained to make identical scripted clinical presentations, deployed incognito to multiple different health care providers, and debriefed using a structured reporting instrument. The use of SPs has increased dramatically as a method for assessing quality of TB care since it was first validated and used for tuberculosis in 2015. This paper summarizes common findings using 3,086 SP-provider interactions involving tuberculosis across various sampling strata in published studies from India, China, South Africa and Kenya. It then discusses the lessons learned from implementing standardized patients in these diverse settings. First, quality is low: relatively few SPs presenting to a health care provider for the first time were given an appropriate diagnostic test, and most were given unnecessary or inappropriate medication. Second, care takes a wide variety of forms – SPs did not generally receive "wait and see" or "symptomatic" care from providers, but they received a medley of care patterns that included broad-spectrum antibiotics as well as contraindicated quinolone antibiotics and steroids. Third, there is a wide range of estimated quality in each observed sampling stratum: more-qualified providers and higher-level facilities performed better than others in all settings, but in every stratum there were both high- and low-quality providers. Evidence from SP studies paired with medical vignettes has shown that providers of all knowledge levels significantly underperform their demonstrated ability with real patients. Finally, providers showed little response to differences in patient identity, but showed strong responses to differences in case presentation that give some clues as to the reasons for these behaviors.

1. Introduction

Tuberculosis (TB) remains one of the most deadly diseases in the world. It accounted for an estimated 1.6 million deaths in 2017, overtaking the mortality attributed to HIV/AIDS [1]. That TB mortality is now higher than that due to HIV/AIDS reflects, in part, the effects of massive global investment in better diagnosis and antiretroviral therapy that has drastically reduced mortality due to HIV/AIDS. But it also reflects the fact that TB is a tenacious disease that is progressively becoming harder and more expensive to treat, as strains that display drug resistance to the standard treatment regimen become increasingly prevalent around the world.

Tackling TB requires renewed investments in every step of the care cascade that leads patients to successful diagnosis and treatment. In South Africa, the TB care cascade shows that just 53% of potential cases end up being successfully treated: 5% are lost at test access, 13% at diagnosis, 12% at treatment initiation and 17% at successful treatment completion [2]. The situation is even worse in India, with about 40% of patients in the public sector lost prior to diagnosis [3]. In China, TB prevalence has declined sharply from 215 in 1990 to 108 in 2010, thanks to improved treatment access for those who were already diagnosed [4], but the fraction of people with TB who remain undiagnosed is persistently high [5]. In countries like Kenya and South Africa, the majority of patients with TB are also infected with HIV (54% in Kenya and 70% in South Africa) [6,7]. This further complicates diagnosis as high rates of HIV co-infection require that people with TB are tested for HIV and vice-versa.

Using data from these four countries, this paper summarizes recent research on the least well understood part of the care cascade-the quality of initial diagnosis and management of TB. This research is motivated by the fact that massive improvements in treating those who have already been diagnosed have not been matched with similar gains

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https://doi.org/10.1016/j.jctube.2019.100109

in the timely and accurate detection of individuals with TB in the first place [8,9]. Difficulties in directly measuring the quality of primary care and providers' diagnostic accuracy implies that we do not know how patients presenting with TB symptoms are managed at different stages of the disease. At this point, we cannot answer the simple question: "In Country X, what do the doctors do when a patient arrives, presenting with 2–3 weeks of cough, fever and night sweats?" Our relative ignorance about how TB patients are actually managed during this first critical interaction is particularly surprising, as delays at the diagnosis and treatment initiation stage allow patients to remain contagious and continue to spread the disease among their contacts. In fact, several systematic reviews show that TB is often diagnosed after about 2 months of delay, with several visits before diagnosis [10,11].

In order to address this gap, researchers have developed and applied the method of standardized patients (SPs) to measure the quality of TB diagnosis and treatment in multiple settings. With the SP method, the research team recruits and trains a team of local people to present as patients with the same set of scripted symptoms (in this case, typical symptoms of TB) to a sampled set of health care providers [12]. Health care providers do not know when they are interacting with an SP, and therefore researchers are able to obtain accurate measures of the management that real patients presenting similar symptoms would receive.

By interacting in a real-life setting with health care providers, the SP method improves on "structural" quality measures, such as the availability of equipment and medicines, which have been shown to not predict actual clinical performance [13]. The SP method also has several advantages relative to quality measures based on clinical observation and chart abstraction. Because the underlying condition of the SP is fixed and known by design, the appropriateness of clinical action (or inaction) can be assessed against predetermined checklists; by contrast, any medical records that do exist may contain incomplete information on patients and recorded diagnoses may be incorrect. Standardizing the presentation further implies that an individual SP can present the "same" case to many providers, allowing valid comparisons across providers and locations. Since the SP presents unannounced to clinics, SP studies avoid "Hawthorne effects", whereby providers change their behavior when they know they are being observed [12,14]. Finally, training SPs to accurately recall each clinical encounter allows for the use of an extensive, detailed, structured exit questionnaire for each interaction to answer specific research questions.

Following previous large SP studies using asthma and angina cases in India [15,16], our team extended the SP method to evaluate the quality of TB care in 2015 [12,17]. This study showed that data generated from using the SP method for TB was (a) valid, with low detection rates and high agreement between audio recordings and structured questionnaires; (b) reliable, with key regularities documented in the data; and (c) informative, allowing researchers to understand both the overall quality of care and variation in care across different groups of providers. Since the pilot, research groups have applied the SP method to study the quality of TB care in large-N samples across multiple settings in India [18,19], China [5], Kenya [12], and South Africa [20].

In this study, we summarize global findings using a combined sample of 3,086 SP-provider interactions using data from published studies in India [18,19], China [5], South Africa [20] and Kenya [12]. We first focus on 1,861 provider-patient interactions with an SP portraying a classic case of a person who should be investigated for TB – the "Classic" scenario of presumed or suspected TB – which was used in all these studies. In the Classic scenario, the SP presented with 2–3 weeks of cough to a health care provider for the first time, and if prompted reveals additional symptoms such as fever and night sweats. We document the overall quality of care in these settings. We assess whether SPs received appropriate diagnostics in the form of TB testing and HIV testing. We also document whether they received unnecessary or harmful medicines, including fluoroquinolone antibiotics and steroids, which can mask TB symptoms and delay future diagnosis. The results demonstrate high variability in care quality across the settings and provider strata that SPs visited.

We then investigate the responsiveness of providers to variations in patient presentation, using additional data from the India study. We address whether provider behavior (a) varies according to the personal characteristics of the patient; and (b) is responsive to the information presented by the patient, versus being fixed by external constraints or incentives. The first examines the external validity of SP results to other patients and contexts. If the results vary enormously depending on the characteristics of the SP, conclusions are valid only for the specific group of SPs used in the study. The second question offers insights into the reasons for low average quality, a key direction that future research will need to tackle.

The India study provides two key avenues to approach these questions. We first use staff records from that study to assess the impact of the personal characteristics of the presenting individuals on management decisions by providers. Second, the study also included 1,225 additional interactions among the same set of providers, in which SPs reported to (a) have already undergone a chest X-ray and carried the (abnormal) image with them; (b) to have completed a laboratory sputum test and carried the (AFB-positive) result with them; or (c) to presented a classic history of multi-drug-resistant TB (treatment non-completion and symptom recurrence). We therefore use these variations to report how providers changed their management decisions when the patient presented different forms of information to them during the interaction.

2. Methods

In each of these primary studies, conducted after ethics approvals in each country, research teams recruited healthy individuals from the local population, who were then extensively trained to present TB cases to health care providers. Every SP was trained for several weeks to portray a single case presentation. The training focused on embedding the medical details of the case within the overall character of the SP in a consistent manner and further ensured that providers would not be able to distinguish the SPs from regular patients during the interactions.

Each study developed SP scripts detailing what information the SP was to give the provider at the beginning of the interaction, typically a short sentence in the local language such as: "*Doctor, I have a cough that is not getting better and some fever too.*" The scripts further specified exact responses to anticipated follow-up history questions from providers, including a scripted personal background, family and socioeconomic situation, and health history details such as smoking and alcohol use. SPs were coached on how to avoid unsafe situations and detection. The details of each study's SP recruitment, provider selection, and fieldwork implementation can be found in the respective primary studies and their online supplements [5,18,19]. Further general details on the SP method are available in a series of pilot and full-scale studies [15,21–24].

SPs were trained to recall all aspects of the interaction including the questions that the provider asked, the examinations they performed, the tests ordered and any treatment given. These were recorded in a structured questionnaire, developed through extensive consultations with a technical advisory group composed of local and global TB experts in each country, shortly after the SP left the provider's clinic. While SP presentations can vary contextually, all studies used the "Classic" presentation, characterized as "a case of presumed tuberculosis with 2–3 weeks of cough and fever". In accordance with national and international guidelines as well as the recommendations of the studies' advisory groups, the SP was typically judged to have been correctly treated if they received either a chest X-ray, a sputum AFB test or an Xpert MTB/RIF diagnostic. In the South African study, the study guidelines additionally required the provider to request an HIV test. No study penalized providers for provision of unnecessary or potentially

harmful medications. However, since "correct" management is a complex contextual combination of offering appropriate care and avoiding inappropriate care, here we choose not to report an aggregated "correct" management for any setting, but instead report various outcomes separately for all studies. The public data that accompanies this paper allows researchers to further refine these measures in accordance with their specific requirements.

We report the management decisions observed in 1,861 Classic TB SP presentations completed between 2015 and 2018 in these four settings. For each study, we investigated: the proportion of "history checklist questions" completed (which varied by study); whether the provider ordered a chest X-ray, a sputum AFB or an Xpert MTB/RIF diagnostic; whether any medication was given or prescribed; use of any antibiotics; whether any anti-TB medication was used; the use of any contraindicated steroids or fluoroquinolone antibiotics; and whether an HIV test was ordered. This analysis reports unweighted proportions only, and the results reported here should not be considered to be nationally-representative comparisons for any of the constituent studies.

We also present separate estimates of quality of care outcomes for the Classic TB presentation by each study's primary sampling strata. In Kenya, SPs visited both public sector and private sector (for-profit and nonprofit) clinics in Nairobi; private sector providers account for a majority of all providers in the city. In South Africa, all interactions were conducted at public primary health care centres (PHCs). In India, all interactions were in the private sector and SPs visited "informal" and "formal" private sector clinics in urban Patna, and AYUSH and hospital-based private providers in Mumbai. Informal providers in Patna are those without MBBS (allopathic) degree qualifications; such providers account for 42% of all providers in Patna. AYUSH providers are those with a degree in alternative systems of medicine covering Ayurveda, Yoga, Unani, Siddhi and Homeopathy. In China, SPs visited village, township, and county-level public providers (the three levels of primary care in China) across Sichuan, Shaanxi, and Anhui provinces. Training and expertise in China increases at higher levels of care, moving from village to township to county. The exact details of the sampling strata and the sampling and visitation protocols are available in each study.

We also present additional results from the studies in urban India, where the team prepared and completed three additional case scenarios, resulting in an additional 1,225 SP interactions. SPs presented one of the following case scenarios:

- A case of presumed TB in a patient who has had 2–3 weeks of cough and fever. The patient has taken a broad-spectrum antibiotic (amoxicillin) given by another health-care provider for one week with no improvement. The SP also carries an abnormal chest X-ray suggestive of tuberculosis.
- Chronic cough with an AFB-positive sputum smear report for TB from a public health facility, highly suggestive of TB.
- Chronic cough, and, if asked, elaborates a history of previous, incomplete treatment for TB, which would raise the suspicion of multi-drug-resistant TB.

These additional case presentations were piloted in a previous study to ensure that the presentation with medical records was not considered unusual in the context [12]. These presentations were each conducted among a statistically comparable subset of the providers who also saw an SP giving the Classic TB presentation. This sampling design allows differences between the actions of the providers to be attributed to the change in case presentation rather than other confounding factors. Therefore, we compare these additional cases separately to the Classic TB case presentation on the same outcome measures.

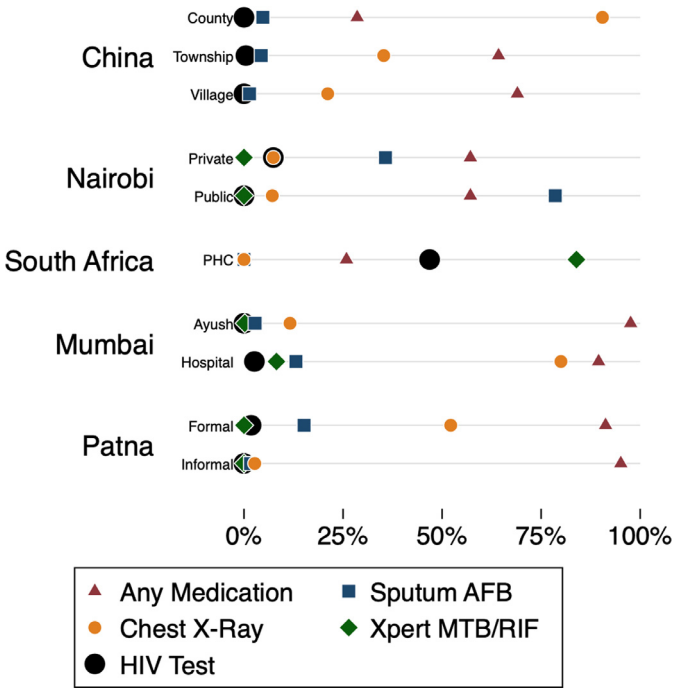

Fig. 1. Classic TB case management by study and strata
Note: This figure reports the overall proportion of SPs presenting the Classic TB case in each study who received each of the indicated management decisions by the provider. Number of observations: China County (21), Township (207), Village (71); Nairobi Private (28), Public (14); South Africa Public PHC (143); Mumbai Private Ayush (499), Private Hospital (305); Patna Private Formal (389), Private Informal (184). AFB: Acid-Fast Bacillus; MTB/RIF: Mycobacterium Tuberculosis/Rifampicin.

3. Results

3.1. Management of the classic TB case presentation

We report three main findings for the Classic case presentation. First, the use of appropriate TB testing varies widely across the study population, ranging from 4% among informal private clinics in Patna to 90% in county-level public hospitals in China. As can be seen in Fig. 1, testing frequency was substantially higher in higher-level clinics than in lower-level clinics (in China), in formal clinics and hospitals than in informal clinics and AYUSH providers (in India), and public than in private clinics (in Kenya). Chest X-rays, recommended in 36% of interactions, were the most popular TB test ordered in India and China; in Nairobi both public and private sector providers preferred sputum smears, which were ordered in 50% of interactions. At the time of these studies, Xpert MTB/RIF testing was just becoming available in most settings and was observed only among South Africa PHCs (84%) and Mumbai providers in hospitals (3%). In South Africa, test orders were not directly observed, but Xpert testing is in place nationally, so all sputum collection was recorded as Xpert. [25] HIV testing was rare in most settings – less than 5% in all study strata except South Africa PHCs, in which 47% of SPs were ordered HIV tests.

All types of providers (although not all providers) were observed to prescribe some kind of medication to the SP (83% of interactions), and these were likely to be demonstrably unnecessary or harmful. Table 1 highlights three classes of medications that are of special interest for TB treatment: broad-spectrum antibiotics, fluoroquinolone antibiotics and steroids. These medications either have adverse public health implications or are contraindicated in possible TB cases because they may mask symptoms and delay further diagnosis. We also documented the use of unlabelled, traditional, and homeopathic medicines whose provenance is unknown; the use of such medicines are problematic as they convey

Table 1.
Use of unnecessary and contraindicated medications for the Classic TB case.

	China County	China Township	China Village	Nairobi Private	Nairobi Public	South Africa PHC	Mumbai Ayush	Mumbai Hospital	Patna Formal	Patna Informal
None	15 (71%)	75 (36%)	22 (31%)			132 (92%)	13 (3%)	49 (16%)	43 (11%)	10 (5%)
Antibiotics	1 (5%)	15 (7%)	5 (7%)			11 (8%)	2 (<1%)	76 (25%)	80 (21%)	14 (8%)
Quinolones							1 (<1%)	4 (1%)	13 (3%)	3 (2%)
Steroids								5 (2%)	3 (1%)	
Unlabelled	3 (14%)	13 (6%)	18 (25%)	13 (46%)	6 (43%)		226 (45%)	33 (11%)	13 (3%)	73 (40%)
Antibiotics + Quinolones								1 (<1%)	8 (2%)	1 (1%)
Antibiotics + Steroids		1 (<1%)						28 (9%)	63 (16%)	11 (6%)
Antibiotics + Unlabelled	2 (10%)	85 (41%)	25 (35%)	13 (46%)	8 (57%)		143 (29%)	67 (22%)	62 (16%)	23 (13%)
Quinolones + Steroids		1 (<1%)						4 (1%)	18 (5%)	3 (2%)
Quinolones + Unlabelled		3 (1%)	1 (1%)	1 (4%)			15 (3%)	6 (2%)	18 (5%)	7 (4%)
Steroids + Unlabelled		1 (<1%)					34 (7%)	11 (4%)	8 (2%)	9 (5%)
Antibiotics + Quinolones + Steroids								2 (1%)	10 (3%)	
Antibiotics + Quinolones + Unlabelled		11 (5%)					4 (1%)	2 (1%)	12 (3%)	3 (2%)
Antibiotics + Steroids + Unlabelled		1 (<1%)		1 (4%)			54 (11%)	13 (4%)	27 (7%)	17 (9%)
Quinolones + Steroids + Unlabelled							7 (1%)	3 (1%)	6 (2%)	7 (4%)
Antibiotics + Quinolones + Steroids + Unlabelled		1 (<1%)						1 (<1%)	5 (1%)	3 (2%)
Number of Observations	21	207	71	28	14	143	499	305	389	184

Note: Medications from each interaction were ex-post coded by name to correspond to ATC code classifications, the WHO system for categorizing medications according to their purpose and action. This figure reports the whole number of SP interactions in which each combination of the following medicine classes were observed to have been given to the patient, and the corresponding proportion of interactions in that sampling stratum. The categories are: broad-spectrum antibiotics (other than fluoroquinolones), defined as ATC codes beginning with J01 but not J01M; fluoroquinolone antibiotics, defined as ATC codes beginning with J01M; steroids, defined as ATC codes beginning with H02, R01, or R03; and unlabelled medications, for which the field team was unable to identify generic ingredients (including homeopathic, traditional, and herbal medications, but excluding vitamin and mineral preparations). Percentages may not add to 100% due to rounding.

no information to the patient. Strikingly, cases where none of these medicines were used are in the minority everywhere. We observe every possible combination of these medications in the data at least once, with providers in every study strata except South Africa PHCs prescribing or administering antibiotics in more than half of cases.

One potential explanation for the low adherence to national and international standards of TB care is that the healthcare providers in these samples did not have the requisite training or knowledge to follow the protocols correctly. Therefore, in studies in Delhi and China, researchers have sent trained enumerators to the same providers some weeks after the completion of Classic TB SP visits and asked the providers to evaluate a hypothetical patient who presents with the exact same symptoms and scripts as the SPs did [5,12]. The use of such medical vignettes had been validated in India previously and shown to produce reliable measures of medical competence or knowledge [26]. In both these paired vignette studies, the same providers were far more likely to recommend management options consistent with standards of TB care in the vignettes as they were with identical SPs. In China, the use of chest X-rays or sputum tests was 47 percentage points higher in vignettes than in SP interactions, and in Delhi it was 62 percentage points higher. Similarly, in both studies, providers gave more unnecessary medications to the SPs than they said they would during the medical vignettes. This phenomenon, labelled the “know-do” gap, has been replicated in multiple studies and cites since it was first highlighted in studies from India and Tanzania [27,28].

We used adherence to an essential checklist of history questions to examine variation in quality of care within every setting and strata, using the checklist questions reported for the underlying study (these are not comparable across settings). **Fig. 2** illustrates this variation. While the practices of different groups in each study differ *on average*, there is a broad range of observed provider behavior within each group as well. In no study did any provider type strictly dominate all the others. Instead, these provider type and qualification classifications were weakly associated with provider behavior, and the variations are wide within each strata. Every strata group contains providers who complete many checklist items as well as providers who complete very few.

3.2. Provider response to variation in patient presentation

These results raise key questions about how providers respond to patient presentation. The first question relates to the external validity of SP studies. Since many SP studies use a small number of individual SPs drawn from specific backgrounds in order to be suitable for data collection, the findings from these studies may not be applicable to general patient populations. For instance, SPs typically have at least secondary education, whereas many TB patients may have education at the primary or less than primary level. If providers behavior varies by the personal characteristics of SPs, each of these studies is ultimately limited to the specific group of SPs that was deployed. The India study used a relatively larger number of individual SPs in order to accommodate the scale of the study, and we use this design to investigate the role that individual SP identities played in their treatment outcomes.

Fig. 3 uses the individual characteristics of the included SPs we hired in an ANOVA analysis. We added these characteristics sequentially to a regression model after controlling for the case presentation, study setting and provider type. The first panel shows that SP age, gender, height, weight, and BMI do not significantly contribute to explaining variation in TB testing. This is of independent interest, as there is a concern that doctors change their behavior if SPs do not conform with their view of what a TB patient looks like; in our data we do not find strong evidence for this view. In the second panel, we use an individual indicator variable (dummy) for every SP used in the study to fully test for differences across all specific individuals. Although we cannot rule out the hypothesis that SP identity indicators are jointly significant – they seem to have some effect – we observe that the overall

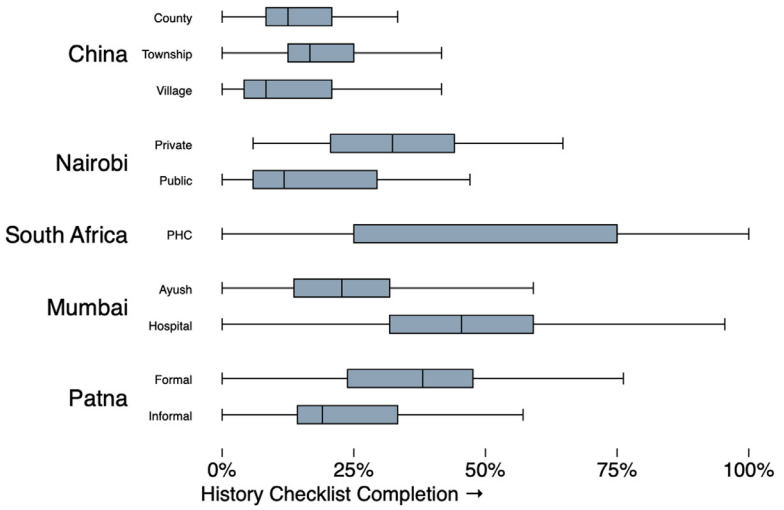

Fig. 2. History checklist completion for the Classic TB case: variation by study and strata

Note: Using the context-specific measure of history checklist items, this figure illustrates the range of item completion within each study and sampling strata. Number of observations: China County (21), Township (207), Village (71); Nairobi Private (28), Public (14); South Africa PHC (143); Mumbai Ayush (499), Hospital (305); Patna Formal (389), Informal (184). History checklist questions in each study are a subset of: Duration of Cough, Sputum, Past TB, Family TB, Blood in Sputum, Cough Throughout Day, Fever, Fever Type, Family or Family with Similar Symptoms, Chest Pain, Loss of Appetite, Lost Weight, Wheezing, Difficulty Breathing, Smoking, Alcohol History, Taken Medicines for Illness, Diabetes, HIV/AIDS, Age, TB Suspicion, MDR-TB Suspicion, High blood pressure or hypertension, Weakness, Night Sweats.

variation in outcomes due to all SP characteristics is (at most) 13% of the amount of variation explained by case presentation, city, and strata indicators.

The fact that health care providers do not alter their behavior substantially depending on the background of the SP does not necessarily imply that their behavior is invariant to the specific case presented by the SP. In the research on private providers, one question of particular interest in is the role of financial incentives. A potential explanation for poor quality is that providers do not want to disclose that the patient has TB due to the fear that the patient will then seek care elsewhere, hurting the revenue of the provider. Indeed, SP studies combined with provider knowledge surveys have repeatedly demonstrated that health care providers typically do far less for patients than they have the knowledge to do.

The India study addressed this explicitly by varying the information that the SP made available to the provider in a given interaction. The idea was that if the SPs presented diagnostic information that they were not able to interpret themselves, providers driven only by financial incentives would continue to behave in the same way as in the presentations with less available information. Alternatively, if the providers had in fact had difficulty diagnosing the SPs, their behavior should change in response to the new information. SPs presented three additional TB case scenarios to a randomized subset of the same providers, allowing direct comparability between management in those cases and in the Classic case. In each of these cases, the SP presented additional information in the form of a specific TB test such as an abnormal chest X-ray or an AFB-positive sputum smear report. The first panel in Fig. 4 summarizes TB-related management across all case presentations for each of the sample strata, highlighting the use of TB testing (chest X-ray, sputum AFB smear, or Xpert MTB/RIF); anti-TB medication; and contraindicated steroids and fluoroquinolone antibiotics.

For all types of providers, the use of TB testing was higher when the SP carried an AFB-positive sputum smear report, even though the SPs clearly indicate that they do not know what results the test implies. This is also true for the case presenting the abnormal chest X-ray in all but one strata. We also report overall rates of fluoroquinolone and steroid usage for each of the case presentations. As in the overall data for the Classic TB case, there are no clear patterns and wide variation in usage across both strata and case presentation.

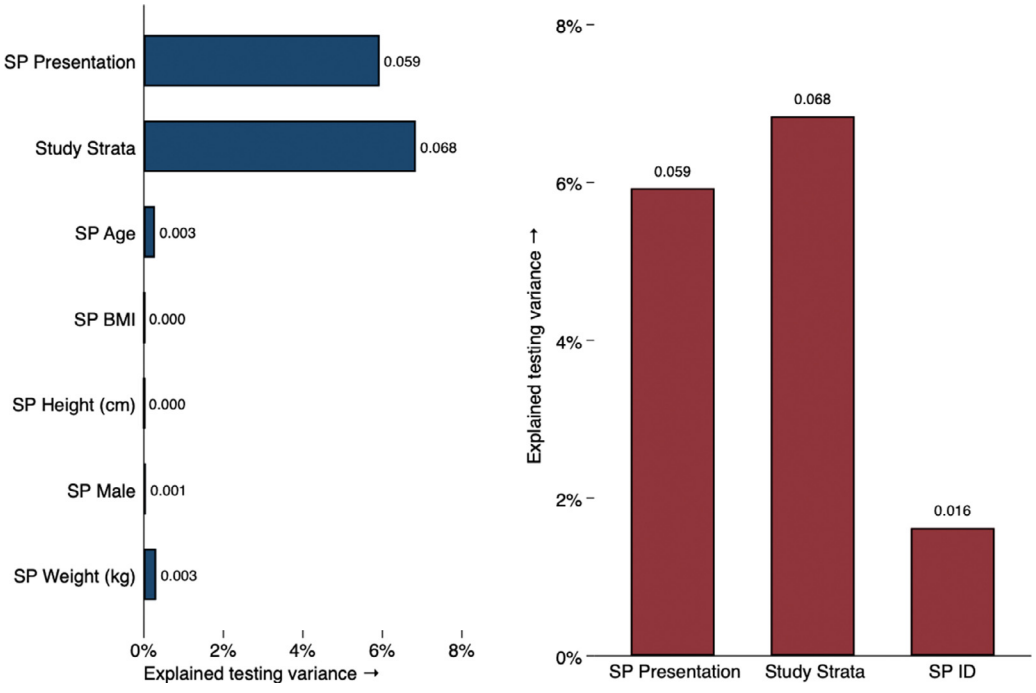

Fig. 3. ANOVA analysis of variation in TB testing explained by patient presentation

Note: This figure reports the sequential-ANOVA contribution of SP characteristics to the explained variance of receiving at least one of the following TB tests: a chest X-ray, a sputum AFB smear, or an Xpert MTB/RIF test. The binary outcome is first regressed on SP presentation and study location and strata, and in the first panel, individual characteristics are sequentially added and the improvement in explained sum of squares reported. In the second panel, the entire set of individual SP identity indicators is added to the regression and its overall contribution to explained variation in TB-testing outcomes is reported. AFB: Acid-Fast Bacillus; MTB/RIF: Mycobacterium Tuberculosis/Rifampicin.

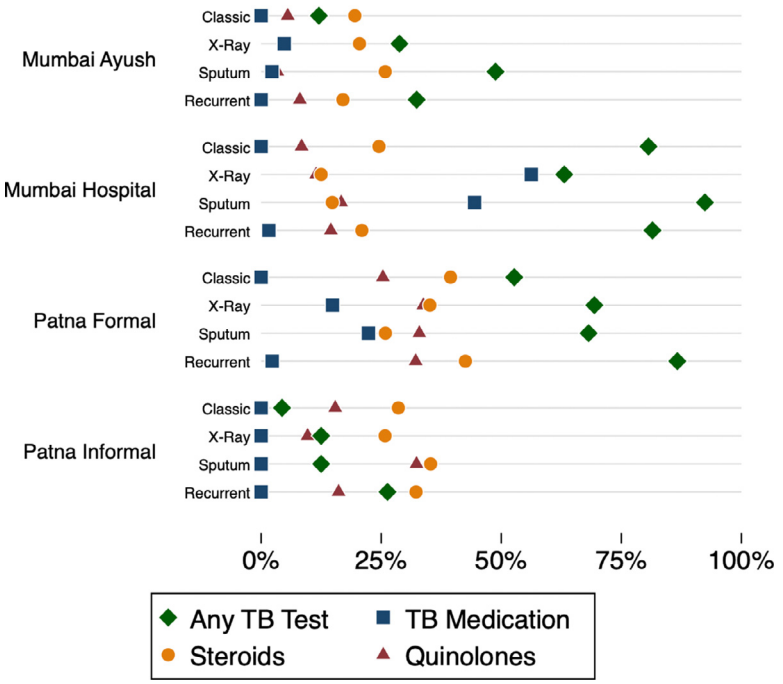

Fig. 4. TB-related testing, anti-TB medication, and contraindicated medication use by case presentation at private providers in urban India for all case presentations

Note: This figure reports the usage of laboratory testing, anti-TB medication, fluoroquinolone antibiotics, and steroids across each study strata for four case presentations. These were the Classic TB presentation; the X-ray presentation; the sputum report presentation; and the MDR/recurrence presentation. Number of observations: Mumbai Ayush Classic (499), X-ray (125), Sputum (125), MDR (247); Mumbai Hospital Classic (305), X-ray (122), Sputum (79), MDR (81); Patna Formal Classic (389), X-ray (98), Sputum (110), MDR (120); Patna Informal Classic (184), X-ray (40), Sputum (40), MDR (38). Medications from each interaction were ex-post coded by name to correspond to ATC code classifications. This figure reports the proportion of SP interactions in which each of the following medicine classes were observed to have been given to the patient: fluoroquinolone antibiotics, defined as ATC codes beginning with J01M; and steroids, defined as ATC codes beginning with H02, R01, or R03.

4. Discussion

4.1. Strengths and limitations of SPs for tuberculosis

Following our first study validating the use of SPs to measure the quality of TB care, researchers have successfully deployed SPs in large provider samples across multiple countries. These studies are tailored to the country context, and therefore differ in their sampling schemes and providers covered; consequently, we have been able to show that the SP methodology can be successfully used for a variety of providers (public, private, formal, informal, etc.) in various settings.

The methodology has proved to have a variety of strengths and weaknesses in policy-relevant applications. In terms of strengths, it remains the only method by which complete information about provider behavior can be acquired from a targeted sample for a specific case scenario. This is essential to construct measures of access to quality care at a population level; estimating the frequency of antibiotic use and misuse; supporting and improving the function of disease control programs; monitoring patient safety measures; and evaluating training programs.

With greater use, the limitations to this method have also become clearer. SPs cannot measure the quality of care received over the entire treatment phase of TB care, for example, because they are not in fact ill. SPs have not yet been used to construct standardized measures that include follow-up visits to providers. SPs also remain limited by nature in the patient presentations that are feasible in terms of identities and conditions; and utilizing SPs in more advanced medical and insurance systems poses major operational challenges to SP studies since they lack “real” identities for these systems. Currently, we also cannot construct full care cascades for SPs following a misdiagnosis in the first interaction. Suppose providers ask SPs to return if they are not improving – what happens next? In the studies summarized here, the SPs simply never went back. Our team has now carried out a small (unpublished) field pilot to investigate the ability of the SP method to be useful in such cases; the principal difficulty is that a single initial SP presentation can quickly morph into various “un-standardized” cases as each SP will likely have received a different treatment in the first interaction.

4.2. Global findings from the use of SPs for tuberculosis

Several important patterns in quality of care have become apparent from SP studies focusing on TB. First, appropriate TB testing increases as expected at higher levels of care-formal providers and hospitals in India and county doctors in China were more likely to appropriately test patients for TB when symptoms warranted. Second, even as appropriate testing increases at higher levels of care, the inappropriate use of medicines does not decline. In fact, formal providers and hospitals in India, and township clinics in China were just as likely to use antibiotics and quinolones as their less-qualified counterparts. Similarly, although care was better in the public sector in Nairobi than the private sector, medication use was identical. Third, even though higher levels of care are associated with greater use of appropriate testing, there is always wide variability in quality within every setting and strata. There were always *some* informal providers who did more than *some* formal providers in India; *some* village clinics that did more than *some* township hospitals in China; and *some* private providers that did more than public providers in Nairobi, for example.

One important question these studies raise is whether it is fair to expect health care providers to recommend TB tests on a new patient's very first visit. Cities like Patna and Mumbai in India are polluted and conditions associated with chronic coughs are therefore common. In these situations, it may be appropriate for providers to recommend cough suppressants and move to TB testing if the symptoms do not subside. We are sympathetic to this critique. However, two patterns in the data lead us away from this specific interpretation. First, providers do not follow a general “alternate” protocol where medicines are used for symptomatic relief prior to further testing. Instead, we find widespread use of all types of medicine combinations, including those that can lead to antibiotic resistance and can mask TB symptoms in the future. Second, providers at higher levels of care are always more likely to recommend appropriate treatments. This suggests that even if our benchmarks of appropriate treatment are unrealistic, they remain helpful in ranking different types of providers in a manner that is consistent with their practice setting and qualifications. Rather than limiting analysis to a binary definition of right and wrong, detailed SP data can be used to classify providers across a multidimensional quality spectrum, and these classifications can be further refined by using

auxiliary information such as the completion of checklist items.

A second question raised by these studies is the underlying reasons for frequent mismanagement. One possibility is that providers do not have the knowledge to diagnose patients appropriately. However, studies from India and China were able to directly compare performance with SPs to tests of knowledge on the same conditions and demonstrate a "know-do gap" in the data. Providers misdiagnosed and mismanaged SPs at a much higher rate than what tests of their knowledge would suggest. Additionally, in India, giving additional diagnostic information to the same providers in the alternate presentations led to higher rates of TB-related management, suggesting that there is at least some gap preventing providers from recognizing the condition in real practice. Further study in Kenya and South Africa is needed to determine whether such patterns hold in those settings as well.

Another possibility is that providers-particularly those in the private sector-deliberately misdiagnose patients to maximize their revenue when patients return. Our data from case variants where the SP provides a positive test result show that even if revenue considerations are part of the explanation they cannot be the *only* reason for frequent misdiagnosis. When SPs carry a positive test result, misdiagnosis declines even if providers take a financial loss from doing so. Since SPs indicate to the provider that they cannot interpret the test result, the providers should not have changed their behavior if their only aim was to maximize their revenues. These results suggest instead that providers face systematic (yet currently unidentified) barriers in their attempts to diagnose TB patients that are unrelated to knowledge or financial incentives. What these barriers are requires further research.

A final concern with SP studies is that the individual identity of the SPs could dramatically affect study results (and, therefore, outcomes for real patients), and many studies to date have used only a small number of individual people as SPs. In these studies, SPs were hired from a healthy working population and selected for their ability to accurately and reliably perform a very difficult job in the field. It could be that providers are being systematically misled by the appearance or behavior of these SPs, leading them away from an accurate diagnosis. However, as the same SPs were used for all providers, the higher frequency of appropriate treatment among formal providers and at higher levels of care mitigates against this possibility: "better" providers who asked more TB-relevant questions were more likely to behave as if the SPs actually had TB. In addition, by using detailed staff information from the large study in India, we are able to look directly at the correlations between quality of care and anthropometric data on SP gender, height, weight, BMI and age and by comparing individual SPs directly. The personal characteristics of SPs have little systematic effect on the quality of the care provided. Though we cannot rule out individualized effects completely, we show that they are small relative to differences across providers and cases and seem to be nothing more than the normal variation that any diverse patient population would entail – there is, after all, no perfect "Classic Case".

With these broad-based results, we believe that SP studies therefore satisfy multiple demanding requirements for the reliable measurement of diagnostic and treatment accuracy for TB. We have made substantial progress in addressing several open questions that have been raised following our initial validation study. Additionally, our fieldwork has led us to believe that while SP studies have high start-up costs in terms of initial staffing and provider mapping, when studies are geographically concentrated or maintained over time, the marginal costs of additional investigations using SPs are significantly lower than in smaller studies.

4.3. Policy relevance of SP study findings for tuberculosis

To date, the problem of tuberculosis management has been framed and researched as a post-diagnosis question. It is only now with the development of TB care cascades, studies of the delays in diagnosis, and the use of the SP methodology that we are starting to discover that the diagnosis stage itself can pose a major hurdle towards effective TB care. Since the problem has surfaced so recently, what to do about it is less clear, particularly as multiple studies have shown that changing provider behavior at this stage is quite difficult.

The main benefit of the SP method thus far has been to bring the problem of diagnosis front and center in global health discussions. We are very much in the beginning stages of understanding how the method can then be embedded in quality improvement efforts around the world, but there are emerging positive signs. As one example, our research team has worked closely with the Gates Foundation to assess a program that networked private providers and worked intensely with them over a period of several years to improve quality of care and increase TB notifications. Early results from this program suggest that significant improvements in TB diagnosis were achieved in both the cities where this program was trialed [29]. As a second example, one of us (Pai) has been involved with the World Health Organization to bring the problem of diagnosis to the forefront and this collaboration has led to the development of the first essential diagnostics list [30].

Achieving further progress in the future now requires us to urgently understand why misdiagnoses are so frequent at first contact. It also requires us to understand and why so many providers continue to use a cocktail of antibiotics, steroids, and quinolones to treat patients with 2–3 weeks of cough, when these approaches may mask TB symptoms. We must understand why providers do not typically immediately suggest a TB-sensitive test like an X-ray in these cases, if only to rule out TB. We suspect that the widespread use of incorrect medicines may be linked to financial incentives, and this is a further area to explore, especially given the rapid rise of anti-microbial resistance in countries like India. Indeed, ethnographic and qualitative research now suggests that multiple pressures drive the widespread empirical practices observed, including the use of medications as diagnostic tools, a desire to provide rapid symptom relief to patients, a desire to manage illness cost-effectively, uncertainty about the presentation of TB, and uncertainty about the accuracy of available TB tests [31].

Ethical approvals

Each study presented in this paper was granted ethical clearance from institutional review boards (China: Institutional Review Boards at Stanford University, United States (Protocol Number 25904) and Sichuan University, China (Protocol Number K2015025); India: McGill University Health Centre, Canada (REB No. 14-137-BMB) and the Subcommittee for the Ethical Approval of Projects at the Institute for Socioeconomic Research on Development and Democracy in Delhi, India; Kenya: the review board at African Medical and Research Foundation (AMREF), Reference AMREF-ESRC P94/2013, with additional clearances from the Ministry of Health, Government of Kenya and each county in which the facilities were located; South Africa: Research Ethics Committee for Human Research (Humanities) at Stellenbosch University, South Africa (HS1096/2014-REC)). Since we rely on data produced from these different studies, a separate ethical approval was not obtained for the analysis in this paper.

Declarations of interest

None

Competing interests

None of the authors have any competing interests to disclose.

Disclaimer

The findings, interpretations, and conclusions expressed here are those of the authors and do not necessarily represent the views of the World Bank, its executive directors, or the governments they represent.

Data availability statement

Individual de-identified interaction data, including data dictionaries, will be available. All variables needed to re-create the results reported in this article will be included, as will the code required to reproduce these results. Data will be available indefinitely upon publication to anyone who wishes to access the data for any purpose. The data and code can be accessed at https://github.com/qutubproject/jclintb2019.

Acknowledgements

We acknowledge the following individuals and study teams for sharing their efforts, knowledge, and data from SP studies in China, India, Kenya, and South Africa, respective: Sean Sylvia and the Rural Education Action Project (REAP) team; the Quality of Tuberculosis Care (QuTUB) study team and the Institute of Socio-Economic Research on Development and Democracy (ISERDD); Guadalupe Bedoya and the Kenya Patient Safety Impact Evaluation (KePSIE) Project team; Carmen Christian, Ronelle Burger, and the South Africa study team. Additionally, we thank Hao Xue for his contributions to harmonizing and combining SP datasets; and Giorgia Sulis for her contributions to medicine identification and classification.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jctube.2019.100109.

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J Clin Tuberc Other Mycobact Dis 16 (2019) 100101

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Quality of drug-resistant tuberculosis care: Gaps and solutions

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ARTICLE INFO

Keywords:
Tuberculosis
Quality
Drug resistance
Human rights

ABSTRACT

Drug-resistant forms of tuberculosis (DR-TB) are a significant cause of global morbidity and mortality and the treatment of DR-TB is characterized by long and toxic regimens that result in low rates of cure. There are few formal studies documenting the quality of DR-TB treatment services provided globally, but the limited data that do exist show there is a quality crisis in the field. This paper reviews current issues impacting quality of care in DR-TB, including within the areas of patient-centeredness, safety, effectiveness and equity. Specific issues affecting DR-TB quality of care include: 1) the use of regimens with limited efficacy, significant toxicity, and high pill burden; 2) standardized treatment without drug susceptibility testing; 3) non-quality assured medications and drug stock outs; 4) lack of access to newer and repurposed drugs; 5) high rates of adverse events coupled with minimal monitoring and management; 6) care provided by multiple providers in the private sector; 7) depression, anxiety, and stress; and 8) stigma and discrimination. The paper discusses potential ways to improve quality in each of these areas and concludes that many of these issues arise from the traditional "public health approach" to TB and will only transformed when a human-rights based approach is put into practice.

1. Introduction

The world is facing a crisis in antimicrobial resistance, and drug-resistant forms of tuberculosis (DR-TB) are one of the significant pathogens in this growing threat to global health [1]. Although insufficient access to diagnosis and treatment for DR-TB remain significant challenges—with only 160,684 of the 558,000 people estimated to become sick with DR-TB each year being diagnosed and only 139,114 (25%) of them started on treatment—poor quality care is rampant in the field [2]. This is reflected in the 65% treatment success rate globally but also in other insidious ways in the DR-TB treatment arena [3]. Patient centeredness—a term that has inserted itself into the vocabulary of the TB field in recent years [4] if not into its actual practices—safety, equity, and effectiveness are all quality domains [5] where there are urgent needs for improvement in DR-TB. Little is known about quality in the routine management of DR-TB, however, for a number of reasons, including the fact that measures of successful treatment are based primarily on bacteriologic outcomes [6].

Three recent "cascade" reviews highlight serious problems with the way DR-TB is diagnosed and treated [7–9] but there is limited literature reporting formal assessments of quality in the treatment of DR-TB. In fact, it is only in the last two decades that the treatment of DR-TB in resource-poor settings has been viewed as a necessary and viable strategy [10]. Prior TB control efforts focused on the prevention of the development of resistance among people who were receiving treatment for drug-susceptible TB, ignoring the fact that most DR-TB occurs via primary transmission [11] and placing the locus of blame square on the shoulders of people living with TB [12]. Even now there is still a tendency to fault people living with the disease for the life-threatening predicament in which they find themselves [13], and this could be one reason why quality of care has been drastically understudied in the field of DR-TB.

2. Experiences and perceptions of quality in DR-TB care

The few studies that have been done on DR-TB and quality show a miserable experience for those individuals who become sick with DR-TB, with a participant in one study summing it up by stating: "I cry every day"[14]. In the absence of formal quality of care assessments, studies on quality of life among persons living with DR-TB become important [15]. A recent mixed-methods study done in India found low quality of life measures among people living with DR-TB, especially in the physical and psychological domains [16]. Other qualitative studies have reported similar low quality experiences for people with DR-TB, including lack of engagement in care, paternalistic attitudes of TB providers, and staffing shortages/absences that greatly compromise DR-

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https://doi.org/10.1016/j.jctube.2019.100101

TB services [17–20].

Individual perceptions of quality of care among persons living with DR-TB are driven by multiple factors [21]. Some of these can be attributed to the treatment regimens themselves and include pill burden, routine use of injectable agents, adverse events, and a lengthy duration of therapy [22]. The treatment for DR-TB is highly problematic. Boasting a global "success rate" of around 65%, the regimens given to people living with DR-TB are complex [23]. The most commonly used regimens consist of a total of five to seven different drugs given for a period of 9 to 24 months [24]. Most problematic among these agents is the daily injection that, until recently, formed the core of most DR-TB regimens, even though there was limited scientific evidence to support the use of this category of drugs and that they are associated with permanent hearing loss in as many as one of three people who receive them [25]. Recently, the WHO updated its recommendations on the routine use of injectable agents, stating that only one of these drugs (amikacin) should only be used when there are no other treatment options and then only if there is demonstrated susceptibility to it and formal hearing assessments can be done [26]. In spite of this, many programs are continuing to use these medications and have no plans to phase them out of treatment regimens anytime in the near future, in part because they are relatively cheap.

Although significant attention has been paid to the damages associated with the injectable drugs, the oral medications that are used for treating DR-TB also lead to poor quality experiences among people with the disease. In the WHO-recommended shorter DR-TB treatment regimen, a total of 13 tablets must be taken daily just for the DR-TB regimen [27]. In addition to this, the pills are associated with multiple adverse events ranging from nausea/vomiting and skin discoloration to hypothyroidism and renal failure [28]. As many as 80% of people on treatment for DR-TB experience an adverse event during treatment, and access to monitoring for and management of these side effects is limited [29]. In fact, the lack of rigorously applied standards to evaluate and treat adverse events for people with DR-TB is one of the most glaring gaps in the provision of quality DR-TB care [30]. Also of concern is the limited counseling and treatment literacy support provided to people during their treatment, with many patients reporting that they were never informed about the possibility of side effects or offered treatment alternatives [31].

Others have to do with the experience of undergoing DR-TB treatment and include psychological distress, economic hardship, and the stigma and discrimination faced by people living with DR-TB, often at the hands of medical providers themselves. The experiential treatment journey of a person who is diagnosed with DR-TB is treacherous at best [32]. High rates of depression and anxiety have been reported among persons undergoing treatment for DR-TB, and while some of this may be due to circumstances faced prior to the DR-TB diagnosis, a substantial proportion of people report worsening of mental health during the first several months of treatment [33]. These mental health issues may be associated with worse TB treatment outcomes and require management by multi-disciplinary teams consisting of counselors, social workers, and psychiatric/psychologic specialists [34]. The important roles of patient empowerment and the support provided by people who are DR-TB survivors and activists via official and unofficial support forums must also be underlined [35].

Some of the mental health challenges faced by people living with RR-TB is due to the discrimination such individuals face, including the loss of jobs, homes, and family support [36]. Of great concern, there is evidence showing that such discrimination may frequently occur at the hands of health care providers themselves [37]. This discrimination is often internalized and can increase feelings and shame and guilt leading to a worsening of mental well-being [38]. Exacerbating many of these issues is the rampant poverty that is both associated with and caused by DR-TB itself [39]. Studies show that even though TB services are technically provided "free of charge", many individuals are driven deep into an economic crisis from which they and their families cannot emerge [40]. Multiple studies have shown that relieving these burdens can result in improved treatment outcomes [41,42]. The first target of the "End TB" strategy is to eliminate catastrophic costs for people living with TB by 2020 [43], but the international community has remained ill-equipped to address the socioeconomic needs of people with TB and will fail to achieve this bellwether target.

3. Effectiveness and equity in DR-TB care

Not only is the experience of people undergoing treatment for DR-TB of poor quality, but there are also issues regarding whether or not individuals are receiving the highest quality of care for DR-TB as well—that is the performance of DR-TB health services in the quality domains of effectiveness and equity. The global approach to TB has historically been one of "control" where there has been an emphasis on "public health" often at the detriment to individual people living with TB [44]. When programmatic management DR-TB was finally—if somewhat reluctantly—embraced, the approaches to care put forth did not focus on providing quality services. Rather, they advocated for two standards of care for people living with DR-TB, depending on the income levels of the countries and programs within which are was provided. In low resource settings, treatment recommendations eschewed the use of drug-susceptibility testing and personalized medicine that are considered the gold standard of care in wealthy countries, opting instead for standardized approaches to all patients, regardless of their individual human needs [45].

The past few years have seen promising advances in the treatment of DR-TB with both newer and re-purposed drugs demonstrating both efficacy and safety [46]. In fact, for the first time ever, the World Health Organization has strongly recommended several drugs—including bedaquiline, linezolid, and the fluoroquinolones—based on moderate quality evidence [47]. These medications have not only been associated with improved treatment outcomes in people living with DR-TB but also with lower mortality rates [48]. Access to these medications—along with clofazimine and delamanid—however, is a significant concern. An analysis done comparing estimated need with actual use found that only 15% of persons who would qualify to receive either bedaquiline or delamanid received these medications [49]. While some countries—-most notably South Africa—provide bedaquiline to a majority of their patients with DR-TB, others such as India have provided bedaquiline to just over 1600 of the estimated 30,000 people who become sick annually with DRTB [50]. While there are multiple potential barriers to using the newer DR-TB medications, including regulatory delays, diagnostic roadblocks in detecting resistance, complex health-care systems dominated by unregulated private sectors, concerns about side effects and unjustified fears about development of resistance, most of these have been successfully overcome in countries where there is political will to use these life-saving agents [51]. The prevailing policy of "protecting the drug" rather than protecting the patients whose lives depend on speedy access to bedaquiline (BDQ) is to be condemned as a violation of not only the right to health but also the right to benefit from scientific progress [52].

Other factors that significantly affect the quality of care for people with DR-TB are drug stock outs—which occur at alarmingly high rates in some settings—as well as the use of products that have not been quality assured or tested. Many countries use a two-year ordering and forecasting cycle for DR-TB drug procurement which can led to imprecise quantification and both overstocking and under-stocking of medications [53]. Although the Stop TB Partnership's Global Drug Facility is able to provide most countries with second-line drugs that have gone through rigorous evaluation to ensure they meet minimal standards, many countries forego these services to procure through local suppliers [54].

Finally, the locus of DR-TB care and whether it occurs in the public sector, the private sector, or both may have a significant impact on the quality of care received. Many countries with a high burden of DR-TB

Table 1
Barriers and solutions for quality care in DR-TB.

Barrier to quality care	Potential solutions
Limited measures of studies on quality of care in DR-TB	Undertake formal studies in key settings and adopt formal quality measures as part of routine monitoring and evaluation activities undertaken by TB programs. Additional work should also focus on quality of life after treatment completion, since some patients have persistent and ongoing health issues caused either by the DR-TB itself or by treatment for the disease.
Poor treatment outcomes seen with current regimen	Improved regimens and treatment approaches linked to access to these clinical advances
Continued use of injectable drugs	Cessation of the injectables except in rare individuals who need them, with tangible consequences for countries, programs, and providers who continue their routine use
High pill burden	Improved regimens and treatment approaches linked to access to these clinical advances
Use of standardized regimens without drug susceptibility testing	Targeted therapy based on drug susceptibility testing to allow for the use of effective drugs and avoidance of ineffective drugs which only cause toxicity.
Use of non-quality assured medications	Procurement of medications for a quality-assured supplier of via the Stop TB Partnership's Global Drug Facility.
Medications stock outs	More frequent forecasting and ordering of medications used to treat DR-TB
Lack of access to newer and repurposed medications, including bedaquiline, delamanid and linezolid	Ensure adequate supplies of these medications are procured and evaluate access to them (i.e. percentage of people needing them who receive them) as part of program monitoring and evaluation.
High rates of adverse events	Improved regimens and treatment approaches linked to access to these clinical advances
Limited access to monitoring and management of adverse events	Basic packages of services offered as an essential part DR-TB care, with reporting on access to these types of support in addition to routine TB program outcomes Pharmacovigilance programs must stress quality management of adverse events, with incentives for those who meet them Improve treatment literacy for people living with DR-TB and their support networks and utilize counselors, social workers, and peers to provide and ongoing counseling and support throughout care.
Private providers may utilize sub-standard treatment approaches, including persons trained in other types of medical practices (i.e. homeopathy, Ayurvedic medicine)	Train private providers in the optimal treatment of DR-TB and legislate clear roles for different cadres of practitioners (i.e. active case finding, screening, treatment initiation, adverse event monitoring, etc.).
Depression, anxiety and stress of DR-TB treatment	Provide supportive counseling and services as routine DR-TB care. Enlist the services of multi-disciplinary teams made up of counselors, social workers, and persons with expertise in psychiatry/psychology.
Discrimination and stigma	Use existing laws and court systems to uphold the rights of people living with DR-TB
Socioeconomic burdens	Implement programs to immediately address the socioeconomic needs of people living with DR-TB, including conditional cash transfers, nutritional support, disability grants, etc. Monitor and report on access to these types of support in addition to routine TB program outcomes
Public health approach	Implement a human-rights based approach to TB with accountability mechanisms at all levels

have health systems dominated by private practitioners—a term which encompasses a broad array of providers ranging from those trained in biomedical approaches to DR-TB as well as persons providing alternative forms of medical care, including homeopathy, faith-based healing, and Ayurvedic treatment. India is an example of such a setting, and numerous studies document the heterogeneous nature of TB services provided within such a complex health system. This is not surprising given that 68% of persons who received care in the public sector in India found treatment in the government clinics unacceptable and would prefer to buy their own drugs and access private care [55]. It was long estimated that around 40% of Indian TB patients were treated in the private sector: among persons who have been previously treated for TB—a majority of whom have DR-TB—at least 50% first attempted treatment in the private sector before reaching the Revised National TB Control Program (RNTCP) [56,57]. Even these figures have been shown to be considerable underestimates with data from sales of anti-TB drugs in the private market showing that this market provided 17.79 million patient-months of anti-tuberculosis treatment, almost twice as many as in the public sector, and three times higher than previously assumed [58]. While some studies suggest that care for TB in the private sector is of higher quality than in the public sector [59], persons living with TB often receive sub-standard care from both public and private providers.

With such vast numbers of patients accessing private providers it is crucial to assess and monitor the quality of care these patients receive in this sector. Studies show that such care is sub-optimal, with audit data of prescriptions revealing that only 5 of the 106 respondents could write what could be classified as a good quality prescriptions [60]. The variation in the quality of TB care in urban India has been more recently highlighted in studies using trained standardised patients which found that only 35% of interactions met minimum quality standards [61]. This number was only 28% when the standard patient was one who was living with DR-TB. An added factor to consider when assessing quality of care in the private sectors is that patients also contact unregulated providers of alternative faiths for advice and treatment of their TB, including homeopaths and Ayurvedic practitioners. Furthermore, pharmacies are often the first point of contact for people with signs and symptoms of TB: standardized patient studies found that pharmacists provided correct management in only 13–62% of interactions with over the counter antibiotics (often a fluoroquinolone) dispensed 16–37% of times [62].

Table 1 summarizes the barriers to receiving quality care among persons living with DR-TB as well as some potential solutions for quality improvement measures.

4. Conclusion

Although there are limited formal studies on quality of care received by persons who have been diagnosed with DR-TB, there appears to be a crisis in the field. Not only are there multiple problems with the qualitative experience of DR-TB treatment but also with the provision of care that meets minimum standards of effectiveness and equity. While global efforts have been mounted to “End TB” within the next decade, almost none of them are focused on measuring or improving the quality of care provided to people living with DR-TB [63]. Without such efforts, however, it is likely that TB will continue to remain one of the world's leading infectious killers and that the dire predictions about the impact DR-TB will have on mortality related to anti-microbial resistance are likely to be realized. While there are many factors associated with the

dismal services provided to people living with DR-TB, perhaps a driving force behind most of them is that aspirations for quality on behalf of people living with the disease seem to have been trumped by desire for simplicity among those who are serving such individuals [64,65]. There is a growing recognition that a human rights-based approach to DR-TB could lead to improvements in the field—as was seen with HIV [66,67]. The TB community seems eager to co-opt the language of human rights and health care: these words, however, must be backed with urgent and concerted actions to ensure all people living with DR-TB receive the highest standard or care, regardless of where they find themselves living when they become sick.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jctube.2019.100101.

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J Clin Tuberc Other Mycobact Dis 16 (2019) 100111

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

In the eye of the multiple beholders: Qualitative research perspectives on studying and encouraging quality of TB care in India

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ARTICLE INFO

Keywords:
Quality of care
Health services research
Patient care management
Qualitative research
Tuberculosis diagnostics

ABSTRACT

This paper outlines insights qualitative research brings to the study of quality of care. It advocates understanding care as sequential, interpersonal action aimed at improving health and documenting the networks in which care occurs. It assesses the strengths and weakness of contemporary quantitative and qualitative approaches to examining quality of care for tuberculosis (TB) before outlining three qualitative research programs aimed at understanding quality of TB in India. Three case studies focus on the diagnosis level in the cascade of TB care and use qualitative research to examine the clinical use of pharmaceuticals as diagnostics, the development of diagnostic tests, and the role of care providers in the utilization of diagnostic services. They show that 1) care must be understood as part of relationships over time, 2) the presence or absence of technologies does not always imply their expected use in care, 3) physicians' provision of care is often inflected by their perceptions of patient desires, and 4) effective care is not always perfectly aligned with global health priorities. Qualitative methods with a networked perspective on care provide novel findings that can and have been used when developing quality of care improvement interventions for TB.

1. Introduction

Qualitative research is one approach to addressing quality of care for tuberculosis (TB). A substantial body of qualitative and ethnographic research, including work we (AM, NE, AD) have led, views quality of TB care as a networked phenomenon [1,2]. These inquiries define care as interpersonal action aimed at improving or regaining health and wellbeing. Care, as repeated interpersonal action, occurs within a network of people—such as physicians, patients, pharmacists, laboratory technicians, families, and nurses—, places—such as clinics, households, and hospitals—, and things—such as technologies, money, health systems, and pharmaceuticals. Hence to meaningfully document care and interpret its quality, we must study the network of factors at play in a given care action – in our case TB – and from multiple perspectives.

In our work, we examine the form and quality of TB care as a function of the network within which it occurs. We argue that analyzing linkages and multiple interactions between networked elements of care to understand how they inform care provision is essential for understanding and improving quality of TB care. A networked approach also recognizes that quality of care is dependent on context and changes according to illness and outcomes. In TB, a networked approach allows us to document and draw on quality expectations from unique localized care networks and from global public health. Insights on diverse drivers and assessments of quality of care inside and outside health facilities provides important data for developing quality of care metrics and interventions that can integrate local and international expectations of care.

A networked approach is different from many existing studies of quality of care which measure quality by assessing possible epidemiological and public health effects of care or it's correspondence to international standards. These studies, often quantitative, utilize scales to assess a particular action's adherence or non-adherence to national and international standards like the Hippocratic oath or the US's Institute of Medicines' six aims for health care: Safe, Effective, Patient-centered, Timely, Efficient, and Equitable [3–5]. Other studies, many of which engage TB quality of care, create checklists to record the absence or presence of material objects deemed essential for quality [6,7], analyze

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https://doi.org/10.1016/j.jctube.2019.100111

stepwise models of successful or unsuccessful care cascades [8–10], or observe practices such as referral or prescription for possible effects on epidemic trends and individual health [11–14]. Quality is assessed on the basis of single interactions between a physician and patient rather than a relationship over several visits. Other methods rely on patient pathways and satisfaction surveys to document clinical action as a measure of quality [15–19]. Based on recollections of experienced care and care in sequence, these studies privilege efficient care for its effects on health outcomes like transmission or adherence. However, they struggle to capture care in real time, and often neglect to report on the contexts that could help interpret patient satisfaction or dissatisfaction.

Qualitative researchers by contrast seek to understand and describe care as a social phenomenon and interpret its effect on individuals. Rarely is care framed in terms of high or low quality in the aggregate [20–27]. Care processes are often described from the perspectives of engaged actors such as doctors, families, and patients to avoid imposing normative standards on quality assessments, foreground the complexity of care as social and moral action, and learn how global health interventions can affect caregiving at the front-line [28–34]. This approach has been used to study programmatic interventions for TB and relatedly HIV's effects on social relations between disease, care providers and patients [35–38]. For example, qualitative researchers have studied the effects of direct observation of treatment on patients' lives and described changes in care resulting from the DOTS strategy [35,39–41]. A second body of qualitative research concerning the 'knowledge, attitudes, and practices' or *KAP studies* of TB healthcare workers and patients relies on the idea that care is shaped by individuals' reported beliefs and attitudes [42–47]. These KAP studies probe contextual factors to a lesser extent. A networked approach avoids reducing quality of care through a single indicator, episode, or system of evaluating quality, as many quantitative studies do. Additionally, it moves the qualitative framework beyond focus on single interactions and individual behaviors to investigate how broader, but mutable, contextual factors shape quality, including the very definition of quality as well as its intended and inadvertent impacts.

In this article, we combine our own original research projects to outline a qualitative, networked approach to quality of care. It helps us move beyond KAP frameworks to understand contexts, pathways and processes of care, and develop multivariate tools to study and improve quality of care. By considering the multiple factors that affect quality across sequential caring actions and from multiple perspectives, a networked method illuminates the dynamism that is implicit within care, and qualitative research's struggle to locate clinical care in a public health's quality of care discussion. Finally, a networked qualitative approach identifies the ways in which context affects care, particularly when working in settings associated with less-than-optimal outcomes for patients and public health.

Using qualitative methods such as in-depth and/or serial interviews, observations, focus groups, patient narratives of care, mapping networks, and policy analysis, we investigate dynamic TB care processes. We engage values used by multiple actors to interpret care as they traverse tasks like diagnosis, treatment, palliation, adherence, or rehabilitation. One can use these methods in multiple entry points throughout the cascade of TB care for indicators of quality, but here we focus on diagnosis and diagnostic processes.

2. Qualitative research on quality of TB care in India

Clinicians and public health researchers argue that tuberculosis care in India is highly idiosyncratic, of variegated quality, and often diverges from global standards [48]. Studies of the private sector, where just under 50% of patients access care, reveal a staggering diversity of care practices [49–54]. Though few published analyses of quality of care in the public sector exist, patient pathways indicate that public sector TB care may vary across clinics, cities, and states [15–17,55]. Attention to quality of care is essential in India where drug resistance is a persistent problem [56–58] and pharmaceuticals, though rarely anti-TB drugs [13], are often dispensed without a prescription [59–62]. Interventions designed to address quality of care in India thus require flexible, dynamic solutions that can address the problem from multiple angles.

Our three cases, all based in India, engage TB diagnosis as care from different qualitative perspectives. McDowell uses medical anthropology to describe how physicians diagnose TB in urban private-sector clinics. Engel uses a science and technology studies (STS) perspective to analyze the production and use of diagnostic tools. Daftary uses an implementation science approach to understand how extra-clinical actors such as pharmacists can be partners to improve diagnosis. In each case, a networked approach helps to identify important levers for improving quality of care.

2.1. Quality of care viewed from medical anthropology and the clinic

Most medical anthropologists study clinics and hospitals to observe care [28,29,63–66]. They consider the effects of patient and physician communication about disease and the ways relationships affect care [64]. They also examine how physicians learn about and respond to disease [63,67]. Though anthropologists once understood factors related to quality of care as 'cultural,' contemporary work shows that care is influenced more strongly by economic, political, and infrastructural contexts than cultural practices or beliefs [68,69].

As part of a broader research team, McDowell conducted ethnography of TB care in Mumbai by observing clinical interactions and interviewing clinicians and patients to describe clinical care practices that combine diagnosis and treatment [70,71]. He observed 3000 clinical interactions and interviewed 300 general practitioners and patients. He documented the progression of care from first visit to TB diagnosis and treatment. He paid particular attention to the signs and symptoms that prompted physicians to ask for a diagnostic test or begin empirical TB treatment. With this real-time approach, he and colleagues compared physicians' clinical action and their self-reported behavior and found divergences in the characteristic of 'the know-do gap [72].' In practice, physicians did not implement the best practices they reported to know. McDowell and colleagues sought to understand this divergence in context and found that physicians rely on low cost pharmaceuticals as diagnostic tools and privilege symptom relief above diagnostic certainty in their assessment of quality of care.

By tracing the network of physicians, pharmaceuticals, laboratories, patients, and finance that made up medical care in the city, this approach reveals that most patients left the clinic without a clear diagnosis and very few demanded one. Instead, patients received small sachets of medicines to consume until their next visit and perhaps a prescription. On follow-up visits, physicians assessed changes in clinical signs to gauge the medicine's effects. Physicians adjusted their regimen based on physiological and etiological responses to pharmaceuticals until the patient's health improved or it became clear that the health issue would require testing. They ordered a diagnostic test only after passing through these steps, without observable improvements in the patient's health, or in the context of clear pathology like crepitation. They most often ordered complete blood counts, erythrocyte sedimentation rates, or chest x-rays. This majority of physicians observed shared this multiple-visit pattern of care-before-testing. On further interviews and analysis, McDowell's research found that non-standard practices in the context of several weeks of cough were related to the very low cost of generic pharmaceuticals, patients' prioritization of symptomatic relief over diagnostic certainty, and ambiguity of cough as a sentinel TB symptom in urban slums.

In this case ethnography was able to outline a set of considerations shared across a community that could be engaged at the collective level. It revealed important information about time and process that quantitative research rarely captures. Care was a process with several steps or layers rather than a single 'snap shot' event. The subsequent analysis does not identify a single cause of non-standard quality but

rather presents a way to understand quality that privileges a community-wide approach and situates clinical behavior in context, and from which a palette of interventions may be developed.

2.2. Quality of care viewed from science and technology studies

Tests can support provider-patient relationships and contribute to quality of care. A diagnostic test conducted at the doorstep can support community health workers in convincing patients to accompany them to the public clinic and instill trust in the healthcare system. Yet, if done inconsistently, the same test can damage care relationships [73]. In each case, the interaction between the imagined use of a clinical technology and the care setting makes for unexpected patterns of quality that could be studied by focusing on the production and use of diagnostics as technologies.

Science and technology studies scholars highlight the multiple actors, objects and steps that must be involved and coordinated to make technologies work. Even a seemingly simple technology like the Pap smear includes more than just the testing kit, swab and brush. The kit includes all the people, bodies, things, infrastructures, places and activities that produce a Pap smear result [74]. Such a networked technology-in-practice perspective has implications for how quality of care is produced and analyzed. It highlights that medical practice, and therefore its quality, is always a combination of very different elements (bodies, samples, professionals, research designs, patients, hospital or clinic organization, equipment, materials, reagents, conversations, questions, etc.) [75].

Secondly, STS scholars identify co-constructions of imagined designers and users during innovations' design and use [76]. Designers anticipate future users' interests, motives, skills and behavior, and build these ideas into the material aspects of the technology [77]. As a result, technologies contain an anticipated mode of use and anticipated type of user which influence what form and quality of care is possible. Over time, such anticipations or 'inscriptions' are stabilized, tools become entrenched in routine practice, and their use is not problematized [78]. While imagined users, inscribed in this way into innovations, guide human-machine interactions [77], real users also shape technology by attaching different meanings [79] or changing and manipulating the technology in daily practices [80,81]. That means diagnostic tests do not exist independent of health systems and practitioners, but are a central part of and transformed through their application within a network of actors and objects [82–89].

Engel mobilized these STS perspectives in her study of technology and diagnostic practices across different points of care. Her team's work helped to explain why tests are unlikely to be used in the ways developers envisioned and examined ensuing differences in quality of care. Mapping the processes and challenges of diagnosing major infectious diseases at point of care (POC) across different healthcare settings in India, her team showed how the majority of diagnostics at POC (including TB tests and tests intended to be rapid) were not being made to work within one patient encounter. The majority of (rapid) tests were conducted in overburdened laboratories, not at the bedside or consultation space. Even if test turn-around times were just a few hours or minutes, patients were told to return for test results and further management the following day, a practice that increased chances of loss to follow-up. The scarcity of human resources, material equipment and money available to providers and patients, combined with complicated referral pathways and strained relationships between patients and providers meant that, in trying to mitigate patient costs, providers more easily prescribed treatment rather than diagnostics. The resulting care favored empirical treatment over treatment guided by diagnostic test results [54,73].

In this case, technology was not used as intended and influenced how care was given. An STS perspective showed that to improve quality of care the availability of rapid and easy-to-use POC diagnostics was insufficient. Instead, existing relationships, infrastructure, networks, and resulting practices as well as the undesired or unexpected consequences of introducing such technologies must equally be taken into account. Though frequently presented and researched separately in global health, diagnostic technologies interact with, are molded by, and shape health system issues, and can produce altered constructions of quality.

2.3. Quality of care viewed from implementing interventions

Implementation science (IS) is a common framework guiding public health interventions. Social, behavioral, economical and operational factors are considered key determinants of intervention uptake and adoption. Related research uncovers 'real-world' bottlenecks to incorporating evidence-based knowledge and strategies into routine healthcare practices [90,91]. As qualitative researchers also study people's behaviors and practices in their 'real world' setting [92], qualitative inquiry fits well within IS projects by bridging gaps between intervention efficacy and impact and helping improve quality of care under an intervention [92].

Working with pharmacists in urban Patna, Daftary's team [93] adopted an IS framework to analyze the impact of a referral intervention among private pharmacies, from whom people commonly seek medical advice. Indeed, pharmacists are the preferred provider amongst people disinclined to wait in queue or pay to see a doctor [94]. Pharmacists, however, are known to sell over-the-counter (OTC) medicines to people who could benefit from immediate referral for a test or consultation [13]. The intervention team trained one hundred and five pharmacists to triage and directly refer persons with TB symptoms for a TB screening test. Referred patients would bypass OTC drugs or an initial doctor consultation, and access a consultation only after completing the test. Daftary's team hoped that quality of TB care would improve due to increased efficiency gained when removing one step from patients' diagnostic pathway.

In the preparatory phase, the researchers conducted a situation analysis observing retail pharmacies and interviewing doctors, patients, and other actors affected by the planned intervention. They identified three considerations which challenged early conceptualizations of good quality care [95]. First, persons approaching pharmacies for medical advice were assumed to benefit from referral to a testing laboratory and go directly thereafter to a doctor. However, it became apparent that this process would disrupt people's expectations for a resolution during their initial pharmacy encounter and jeopardize longstanding relationships between pharmacists and patients. Enforcing off-site referrals before pharmacists had an opportunity to provide symptom relief through the sale of an OTC medicine was thus not entirely feasible. In response, the interveners re-conceptualized good quality of care as practices that allowed providers to balance decisions to refer patients away from their own practice in ways that nurtured patient expectations. Even so, sales of unnecessary medicines, especially antibiotics needed to be curtailed. Negotiating between intervener and pharmacist priorities, the team eventually gained pharmacists' buy-in by advertising the referral as an item they could 'sell' to patients. Though the tests were free of charge to patients, pharmacists 'dispensed' a voucher to reflect that a test had been ordered. This dispensing of a service maintained patient-pharmacist trust and satisfied the demand of those who expected to leave the encounter with a tangible product in hand.

Second, it was assumed that people referred for a TB test would visit a doctor immediately after test completion. Here too, deep-set patient and provider expectations outweighed efficient practices. Using interviews and observations, Daftary's team learned that it was critical for patients to return to the initial referring provider to share their test result before considering a subsequent consultation. Patients and pharmacists valued exchanging information and stoking relationships through constant check-ins prioritized this above any public health mandate to accelerate the diagnostic pathway. Accommodating this existing networked care process in the intervention likely promoted

referral uptake and completion amongst participating pharmacists and patients which, as part of a subsequent impact evaluation, were found to be 81% and 86% respectively [93].

Finally, open-ended inquiry revealed that tedious monitoring and evaluation processes discouraged providers from participating. Referring patients was simple, but documenting it in line with a research protocol was onerous. In response, Daftary's team invited pharmacists to design instruments that could improve acceptability. Nonetheless, even these simpler forms were cumbersome, and many busy pharmacists opted to provide patients with undocumented verbal referrals.

These considerations improved acceptability and uptake of the intervention model. Efficiency, understood to denote good quality by traditional global health metrics, was found to be detrimental to attentive, personalized and affective care that was a closer marker of high quality from the perspectives of intervention implementers and users. Using the qualitative results produced by an IS model, the resulting intervention model catered to the norms, behaviors and expectations of key actors. It more aptly responded to local notions of good quality care.

3. Discussion

The cases studies and the qualitative networked approach we advocate reveal four important points about the study of quality of TB care: 1) Care must be understood as part of relationships over time, 2) The presence or absence of technologies does not always imply their expected use in care, 3) Physicians' provision of care is often inflected by their perceptions of patient desires, and 4) Effective care is not always perfectly aligned with global health priorities.

Our approach points out that quality is produced over time rather than in a single action. The clinical diagnosis case engages quality of care as the sum of actions from first visit to completed treatment. The POC case extends the drivers of quality of care even earlier to the development of a technology and its use. Finally, the pharmacy case shows that quality of care can begin outside the clinic and relate to events in illness episodes preceding it. These cases show that it is necessary to consider quality of care as a process. Our qualitative networked research approach allows this by attending to a whole cascade of steps, by analyzing linkages and multiple interactions between networked elements and actors of care inside and outside the clinic that shape the patterns through which care emerges and by capturing a dynamic view of care through iterative data collection and analysis.

Second, the cases suggest that quality of care needs to be studied through the use rather than mere presence of clinical or technical objects. The presence of a rapid test did not necessarily speed up diagnosis. A surplus of incomplete referral slips at a pharmacy did not necessarily mean that pharmacists were not referring patients or improving quality of care. In each case a focus on what people actually do in a care setting by observing their work and asking questions about the ways they give care helps shed new light on what objects might mean for quality of care.

Third, care is a negotiation between caregivers' priorities and knowledge and patients' needs and desires. Each case shows how caregivers negotiate effective medical practice and their patient's expectations, budgets, and desires to achieve quality. In the clinic and pharmacy cases caregivers went through a complicated process of providing care and meeting patients' expectations of quality of care, often providing care that their patients considered as high quality but did not match international standards. Caregivers with access to POC tests had to balance the health system workload, patient desires to leave the clinic and return to their normal life, and technology producers' ideas that a test's speed would speed up diagnosis. Attending to the negotiation between caregiver and patient is important to assess quality. Qualitative research's insistence on actors' perspectives allows it to account for multiple values in caregiving and how values are negotiated. Qualitative work also considers key interpersonal aspects of quality of care like listening, meeting patient expectations, and adjusting for context in ways that quantitative studies find difficult.

Finally, our approach shows that global public health's standards of quality of care are important but may not always align with good clinical practice. Each case suggests that assessing quality of diagnostic care retrospectively, when researchers know the diagnosis, misses the complexity of determining what quality of care might look like before diagnosis. Clinicians and pharmacists had to work toward a TB diagnosis while most often seeing patients who sick with self-limiting or other bacterial illness. They take the likelihood of TB into account before ordering a test, despite its recommendation by global standards. This led to inefficiency, diagnostic delay, and transmission when the patient had active TB, but in other cases avoided unnecessary procedures, another indicator of quality care. For instance, physicians assessed the additional stress put on the health system and patient when asking patients to wait for a rapid test that might or might not be run immediately. Qualitative research with a networked approach at core allows for the uncertainty of diagnostic and other care because it frequently observes care in action, and situates itself in the know-do gap rather than on one side of it. This can help avoid the pitfalls of assuming knowledge or attitudes necessarily affect behavior.

Our networked approach to care has some limitations. It is often time consuming and requires multiple investigation and analytic exercises. It can be affected by self-reporting bias and the Hawthorne effect as observation may affect the kinds of care given. Its commitment to studying care in context and mapping networks also makes the creation of global level comparability difficult. These obstacles, however, can be overcome by using qualitative methods alongside quantitative ones and creating collectives like ours.

4. Conclusion

Together the three cases show that quality of care, both in terms of form and degree of excellence, is not reducible to a single factor or individual. They suggest that quality of TB care improvement work that aims to put patient experience at the center of TB care and intervention cannot rely solely on measures by efficiency, technical excellence, or speed. Instead they should consider a networked approach to understand quality of care in context. Our disciplinary diversity means that we use different analytics and methods to understand care, but in each case the networked and uncertain nature of quality of care reveals itself. Moreover, qualitative results can be used to interpret patient pathways, studies of diagnostic or treatment delay, or standardized patient results. In light of these benefits we propose interdisciplinary intervention teams include social scientists from conceptualization and that quantitative studies of quality of care too will benefit from a consultation with social science colleagues.

Funding

This work was supported by the ERC [Globhealth], a VENI grant from the NWO Dutch Science Foundation, and a Junior Research Award, Fonds de Recherche Santé Quebec.

Declaration of Competing Interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jctube.2019.100111.

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J Clin Tuberc Other Mycobact Dis 16 (2019) 100112

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Measuring and improving the quality of tuberculosis care: A framework and implications from the *Lancet Global Health* Commission

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ARTICLE INFO

Keywords:
Developing countries
Health systems
Quality
Measurement
Monitoring
Improvement

ABSTRACT

In this article, we describe the framework of the *Lancet Global Health* Commission on High Quality Health Systems, propose new and undermeasured indicators of TB care quality, and discuss implications of the Commission's key conclusions for measuring and improving the quality of TB care services. The Commission contends that measurement of quality should focus on the processes of care and their impacts. In addition to monitoring treatment coverage and the availability of tools, governments should consider indicators of clinical competence (for e.g. ability of providers to correctly diagnose TB and adhere to treatment guidelines), of timely, continuous and integrated care and of respectful and patient-centered care. Indicators of impact include TB mortality and treatment success rates, but also quality of life and daily functioning among TB patients, public trust in TB services, and bypassing of the formal health system for TB care. Cascades of care, from initial care seeking to recurrence-free survival, should be built in every high-burden country to monitor quality longitudinally. In turn, improvement efforts should target the foundations of health systems and consider the Commission's four universal actions: governing for quality, redesigning service delivery, transforming the health workforce and igniting demand for quality TB services. Important work remains to validate new indicators of TB care quality, develop data collection systems for new measures, and to test new strategies for improving the delivery of competent and respectful TB care.

1. Introduction

Tuberculosis (TB) experts are increasingly acknowledging that expanding diagnosis and treatment coverage alone will not suffice for "building a TB-free world", and that high-quality health systems are essential [1]. After an individual develops active TB, they must navigate a long and complex process of care-seeking, diagnosis, linkage to care, treatment initiation, notification to national TB programs, and follow-up [2]. TB is therefore a condition that is particularly sensitive to the quality of health systems. In addition, TB is preventable, treatable and curable. Nonetheless, millions continue to die from the condition every year.

A recent study estimated that half of TB deaths in 2016 were due to poor-quality care while the other half resulted from non-utilization of the health system [3]. Poor-quality care is now an equal barrier to reducing TB mortality than insufficient access to care.

What is a high-quality health system? In 2018, three separate reports aimed to answer this questions and to identify approaches to redressing global inequalities in health care quality [4]. The *Lancet Global Health* Commission on High Quality Health Systems – a group of 30 academics, policymakers, and health system stakeholders from 18 countries – proposed a new definition and framework for high-quality health systems, described available data on quality in low- and middle-income countries (LMICs), and provided recommendations for quality measurement and improvement [5]. Improving the quality of TB services first requires that it is adequately defined, measured and monitored. The Commission's recommendations and framework were developed for understanding quality throughout the health system, for all health needs and across all health system platforms (community outreach, primary and tertiary care). In this paper, we describe the *Lancet Global Health* Commission's framework and discuss implications of the Commission's key messages in the context of TB. TB experts may use and adapt the framework and recommendations for exploring new approaches for measuring and improving TB.

2. High quality health system framework

The Commission's framework on high-quality health systems shown

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https://doi.org/10.1016/j.jctube.2019.100112

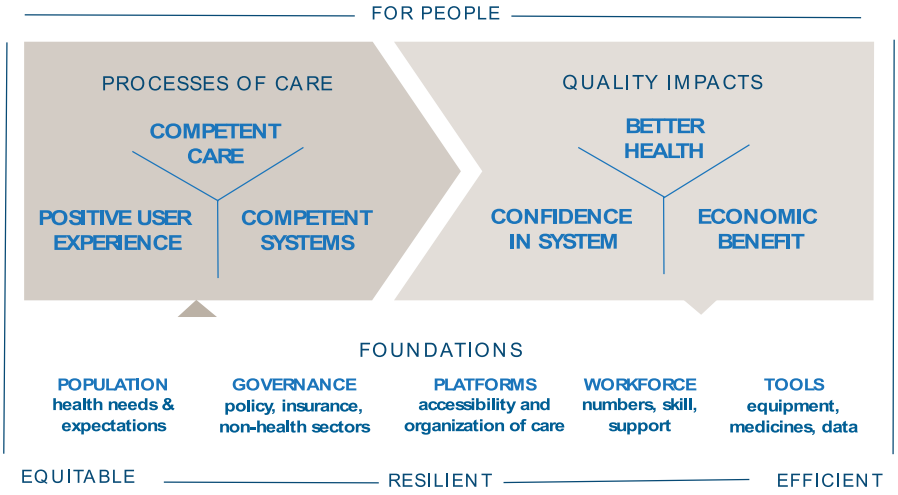

Fig. 1. High-quality health system framework.

in Fig. 1, emerged from a review of past work on health care quality and quality improvement, and from a recognition of the need to update the definition of high-quality health systems in light of today's health challenges, patient expectations and rising ambitions [5–8]. First, the framework is underpinned by four values: high-quality health systems are for people, and they are equitable, resilient, and efficient. The emphasis on people-centeredness and equity is especially crucial for a highly stigmatized conditions such as TB that predominantly affects vulnerable social groups. The framework is centered around three key domains: health system foundations, processes of care and quality impacts. The Commission argued that quality should be primarily measured based on the processes of care and their impacts. In turn, health system foundations should be targeted by improvement strategies. Below, we define these three domains and discuss their implications for measuring and improving the quality of TB services. Readers can refer to the Commission report Sections 1 and 2 for more detailed definitions of the framework dimensions, and Sections 4 and 5 for additional material on measuring and improving health care quality.

3. Quality impacts

High quality health systems should produce better health, they should garner people's confidence and trust, and should produce economic benefits for people and countries.

3.1. Health

Mortality, morbidity and patient-reported outcomes measures (PROMs) (e.g. function, symptoms, pain, wellbeing) are useful to monitor the impact of health services on health. Half of TB deaths in 2016 were among people who accessed the health system [3]. Given that 95% of TB deaths are avoidable, the number of people who die from TB is an essential indicator of health system quality [1]. Nonetheless, mortality alone does not capture the full burden of poor-quality TB care. For many people in LMICs, access to care does not result in the control of this manageable condition. Treatment success/failure rates are also reflective of the quality of TB care. TB is also a disease that can seriously undermine the quality of life (QOL) in people who suffer from it [9]. For example, TB and drug-resistant TB are associated with an important proportion of the global burden of serious health-related suffering [10]. QOL is increasingly used to evaluate patient outcomes rather than traditional criteria such as mortality and illness [9]. Improved daily functioning and QOL among TB patients should be considered to monitor quality of TB services.

3.2. Confidence

The Commission also argued that the population's confidence in the health system reflects the quality of care available to them and is an important indicator of health system performance. For example, the Commission found that few people believe their health system works well in LMICs (only 24% across 11 LMICs), while the proportion of people who trusted their health system was double in high-income countries (48% across 11 high-income countries) [5]. People who do not trust their health system will often choose to forgo care for symptoms of TB, leading to long diagnostic delays and disease transmission. They are also less likely to be retained in care and to adhere to treatments contributing to the rise in MDR/XDR TB. Poor confidence may also lead to bypassing of the public or formal health system for the private or informal sector. The recent *Lancet* Commission on TB revealed that as many as 50% – 60% of TB patients first seek care in ayurvedic or homeopathic doctors, pharmacists and private sectors [1]. The private sector often includes a heterogeneous mix of highly qualified providers (treating the richest segment of the population) and highly unqualified providers and facilities [11]. Confidence and public trust have rarely been measured in LMICs but is routinely collected in high-income countries [12]. Monitoring trust in the formal health system over time and for specific conditions such as TB, could be useful to inform policy decisions. For example, monitoring public trust among the population as a whole, across regions and over time, may help target efforts and monitor improvements in quality.

3.3. Economic benefits

The *Lancet Global Health* Commission described three types of economic consequences that could be averted by high-quality health systems: the economic effects of premature mortality, health system waste, and catastrophic or impoverishing health expenditures faced by households. A study estimated that avoidable TB deaths in twenty-two high-burden countries resulted in $3.2 trillion in welfare losses over a decade [13]. The *Lancet* Commission on TB also estimated that the value of the benefits of averting a death from TB exceeds the value of its costs by a factor of 3 to 5 [1]. Health system waste due to poor-quality TB care includes the overuse of harmful medicine such as steroids and fluoroquinolones (which can hide symptoms and delay diagnosis) and hospitalizations due to TB that could be avoided by high-quality primary care [14,15]. In the case of TB, inappropriate treatments are particularly costly as they contribute to drug resistance and continued transmission of TB, in addition to their unnecessary out-of-pocket costs for the patient [16]. The cost of treating MDR/XDR TB strains can be

9–25 times higher than treating drug-susceptible TB [17]. Finally, TB patients risk suffering from catastrophic or impoverishing expenditures when repeating visits of poor-quality services or when forced to seek care from costly providers. Ensuring that everyone can access care without risking catastrophic medical costs is an integral component of a high-quality health system.

4. Processes of care

The second domain of the framework relates to the quality of the processes of care. The quality of the processes of care is reflected by the levels of competent, respectful, patient-centered care and requires that competent systems are in place to support health care providers.

4.1. Competent care and systems

Competent care means that all TB patients should be managed according to the latest evidence-based guidance for TB care. Standardized patients' studies have shown that many providers in high-burden countries do not follow the International Standards for TB Care guidelines [18,19]. Competent care also requires diagnostic accuracy and immediate treatment. In LMICs, many providers fail to diagnose TB further delaying treatment. Across six sub-Saharan African countries, diagnostic accuracy from clinical vignettes ranged from only 52% of providers correctly identifying TB in Ethiopia, to 86% of providers in Tanzania [5].

A heavy reliance on outdated diagnostic technologies also contributes to misdiagnoses: many countries continue to rely on often inaccurate smear microscopy [20,21]. In turn, health systems must ensure patient safety, appropriate prevention and detection, case notification, timely treatment, and continuous and integrated of care. Early case detection and timely treatment is fundamental to interrupt TB progression and transmission. TB screening among high-risk groups is a recommended strategy and an essential function of high-quality health systems [22]. Continuity of care is reflected by the ability of health systems to retain people in care, coordinate care overtime and ensure adequate follow-up. Cascades of care can be particularly useful tools to monitor continuity of care (Fig. 2) [23,24]. Studies in India and South Africa have shown that patients are lost at every steps of the cascade: many TB-affected people reach facilities but are never diagnosed, some are diagnosed but never start treatment, others start treatment but never complete it [23,24]. Integration of care is the extent to which health services are delivered in a complementary manner. This means when seeking care for TB, people's other health needs (e.g. HIV, diabetes or pregnancy) should be addressed by health systems in a coherent and patient-centered manner.

4.2. User experience

An important, and vastly under-measured dimension of quality, relates to the user's (or patient's) experience with care in terms of respect and patient-centeredness. Respectful care includes respect for patient privacy, confidentiality and dignity and a caring and compassionate attitude of staff. A positive user experience also requires that TB services are user-focused i.e. that they are as easy as possible to use, accessible, affordable and in accordance with patient values. User experience is infrequently assessed in LMIC health systems and more research is needed to determine best indicators and measurement approaches to monitor user experience with TB services. TB programs should consider this crucial dimension of quality. In addition to its intrinsic value, a positive user experience can improve retention in care, adherence to treatment and overall confidence in the health system, likely leading to better health outcomes [5]. Ensuring patient-centered care is a particular challenge for TB, given the long treatment plans required for detecting and curing the condition. Nonetheless, it remains crucial to achieving good health outcomes.

5. Measuring TB quality

We reviewed the indicators currently used for global and national monitoring of the performance of TB programs [22,25,26]. Existing indicators such as TB death rates and treatment success rates reflect the impact of health system quality on health outcomes. The World Health Organization's Global TB report also includes an indicator for the proportion of TB patients facing catastrophic costs [26]. Case detection and notification rates and treatment default rates reflect the ability of health

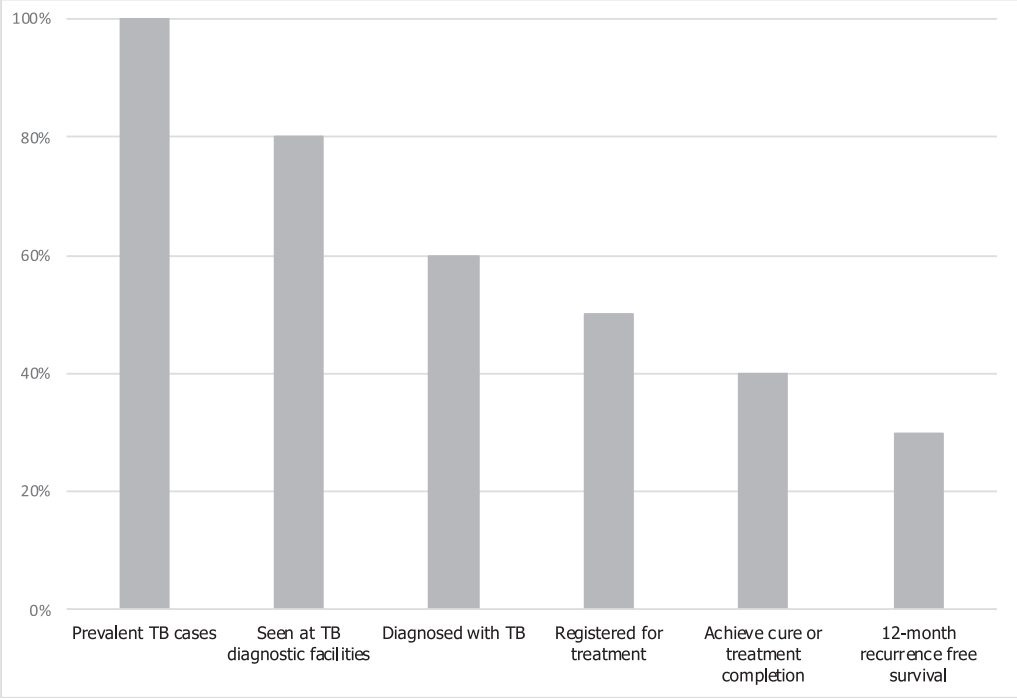

Fig. 2. Hypothetical national TB cascade of care.

Table 1
Dimensions of quality and illustrative indicators to monitor the quality of TB care at national levels.

Quality impacts	
Health	- Avertable TB deaths
	- TB treatment success rate
	- Daily functioning and quality of life among TB patients [9]*
	- Serious health-related suffering caused by TB [10]*
Confidence	- Proportion of TB patients who bypassed the public system for care*
	- Proportion of TB patients who are confident in their ability to receive the most effective treatment if they are sick [12]*
	- Proportion of TB patients who would recommend the clinic to others with the disease*
Economic	- Number of productive days lost to TB*
	- Proportion of TB patients with catastrophic care expenditures
	- Avoidable hospitalizations due to TB*
Processes of care	
Competent care	- Proportion of providers correctly diagnosing TB*
	- Proportion of patients managed according to the International Standards for TB Care guidelines*
Competent systems	- Proportion of high-risk individuals screened for TB
	- TB case detection rate
	- TB case notification rate
	- Average days between first contact with the health system and definitive TB diagnosis and treatment [31]*
	- National TB cascades of care (showing the proportion of patients lost at every step) (**Fig. 2**) [23,24]
User experience	- Proportion of TB patients with high ratings for provider's respectful attitude, communication, explanations received, respect for their privacy and confidentiality*
	- Average wait time in TB diagnostic centers*

systems to detect, follow-up and retain people in care. These are important indicators of health system quality. Most of the other indicators currently used for TB relate to treatment coverage or focus on the availability of inputs necessary for care (e.g. laboratories, drugs, human resources, presence of TB policies). Crucial dimensions of the processes and impacts of TB care fail to be captured in current measurement including the clinical competence of TB care providers (e.g. ability of providers to correctly diagnose TB and adhere to treatment guidelines), the quality of user experience, patient satisfaction and TB morbidity (e.g. PROMs, persistent symptoms, quality of life).

In Table 1, we propose new indicators of TB care quality that should be considered for national monitoring of the quality TB care. New indicators are followed by an asterisk while existing indicators are in black. Some of these new indicators remain to be tested in the context of TB. However, they have been either previously used in TB studies, or for other health conditions, largely high-income country contexts [12,27–30].

5.1. Data sources

Research is needed to carefully validate new indicators of quality and to identify data collection methods. While existing data sources such as vital registries and routine health information systems can provide some of the data needed to measure the indicators in Table 1, new data will also be needed. We describe some of the data collection methods previously employed to measure quality. For example, direct clinical observations – where a trained observer records performance during a clinical visit typically using a checklist – have been used to assess clinical practice for primary care and labor and delivery services in several countries [32,33]. Studies on the quality of TB care have also pioneered the use of the standardized-patient method to measure clinical practice [2,18,19,34,35]. Standardized patients, also known as mystery patients, involves training individuals to portray a patient with symptoms of TB, and having them record the clinical decisions while the provider is blinded to the assessment. The TB field has also relied on modeling approaches to estimate the performance of TB control programs in high-burden countries [23,36,37]. Others have used provider vignettes (knowledge tests) to assess provider knowledge as a proxy for clinical competence [38]. Other data sources for quality include client exit interviews or population surveys (for example, to measure user experience, confidence or PROMs), register abstraction or review of medical records. The different strengths and limitations of these methods are described in the Commission's appendix [5]. Cohort studies may also be needed to assess clinical quality longitudinally and build cascades of care for TB from initial care-seeking to recurrence-free survival (Fig. 2) [23]. As mentioned previously, cascades of care can be particularly useful tools to visualize quality longitudinally and across health system platforms. However, determining how to collect data from individuals at each step of the cascade at national levels remains a challenge. Further research is needed to develop data collection systems for these undermeasured indicators of quality.

6. Health system foundations

Health system foundations (Fig. 1) begin with the population, including people who suffer from TB, their health needs, knowledge and preferences. Governance includes financing, policies and accountability mechanisms. Health system platforms include the number of facilities and their distribution and organization, and the systems connecting the different levels of care. Providers, from health workers to managers, and their knowledge, skills and training, constitute another crucial foundation. Finally, health systems require physical tools such as equipment, diagnostics, vaccines, medicines, supplies and information systems. Although these foundations are crucial to the provision of high-quality TB care, their sole presence does not guarantee good health outcomes or that good quality care is provided to people [39]. For example, availability of TB diagnostic tools in a facility might not mean availability when needed, and that they are used for the right people, at the right time [32]. Measurement of health system foundations, ideally in real-time, is important to manage the health system, for example to manage drug stocks and provider numbers. However, foundation measures are not useful measures of health system quality at national levels as they may not reflect actual health system performance for patients.

That said, foundations of health systems are the most appropriate starting point for improvement. This recommendation stands in contrast to standard approaches to quality improvement which targets individual facilities or provider behavior. Recent evidence shows that in-service training and other interventions targeted at the point of care, mainstays of quality improvement, have only a modest effect on quality of services delivered [40]. The Commission contends that without reforms to strengthen health systems, facility-level quality improvement schemes are unlikely to create sustainable impact at the scale necessary to overcome large quality gaps evident in TB care in LMICs today [5].

We have seen this with TB diagnostics, where availability of new tools is difficult to translate into adoption at scale because of barriers in underlying system performance [41]. The Commission recommends investing in the foundations of health systems by considering four universal actions for improving quality: 1- governing for quality, 2- redesigning service delivery, 3- transforming the health workforce and 4- igniting people's demand for high-quality care.

6.1. Universal action 1: governing for quality

Governing for quality means refocusing the national lens on *effective* coverage of TB care, rather than treatment coverage alone. Political leaders, with the support of technical experts, must express a commitment to quality and align national policy, strategy and implementation around a vision for high-quality services. For example, countries can govern for the quality of TB care by considering losses-to-follow-up and treatment failures as core *health system* responsibilities rather than facility-level shortcomings. This high-level leadership translates into improvement through tougher regulations that keep system actors accountable for delivering high quality care. These regulations should be based on international standards for TB care that are well-supported by evidence, but should also be adapted and endorsed by national organizations. Bringing civil society organization, such as professional organizations, into the dialogue on quality can be especially important for ensuring quality in the private sector where oversight and accountability can be particularly challenging [42]. Finally, development partners have a role to play in making quality governance possible; short cycles of vertical programming for TB make critical improvements such as integration into primary care very difficult [43]. Governing for quality raises the national standard for TB care by measuring success differently; high coverage of poor-quality care is no longer an acceptable outcome.

6.2. Universal action 2: redesigning service delivery

Redesigning service delivery in the context of TB care is critical for TB, but also for making high-quality healthcare of other conditions possible. Redesign starts with a critical analysis of where and by whom TB services are being delivered, including the contribution of the private sector. Redesign also requires an understanding of patterns and barriers for individuals with TB symptoms to seek and access diagnosis and treatment. To restructure these systems and maximize quality for TB, this review cannot be limited to TB. For example, routine TB care, including active case finding, should be delivered at the primary care level where personnel are more likely to understand local social networks and practices. More complicated cases should be managed at secondary or tertiary care facilities; many countries are moving towards this model of community based care [44]. However, health systems will need to consider moving other less complex conditions, such as routine hypertension, out of secondary and tertiary facilities to decongest and make resources available for patients that need them. Redesign efforts will need to be particularly sensitive to how changes may impact access, equity and quality for vulnerable groups and will need to be informed by local data on quality and disease patterns. For example, a study in China showed that integrating TB care into primary care could actually compromise population detection and treatment in rural areas due to poor quality of care in distal health facilities. Redesigning in rural China would need to carefully address this barrier before restructuring the system [34].

6.3. Universal action 3: transform the health workforce

The Commission recommends that improvement efforts should target pre-service training such that providers enter practice with better baseline knowledge and skills. For TB, this means learning how to diagnose and manage latent and active TB, but it also means graduating with demonstrable competence in delivering TB care. Gaps between provider knowledge and the actual care that they deliver in clinical settings can be large; measuring and improving knowledge alone is unlikely to have large impacts [45]. In order to build a workforce that is able to prevent and treat a complex, socially stigmatized disease such as TB, clinical education will need to include broader (and softer) skills such as population health management, patient counseling, cultural sensitivity, and understanding bias. Providers should enter practice with a solid foundation in ethical practice and in patient-centered respectful care. These are not skills that can be gained in day-long trainings. Rather, they must be introduced early and modeled by respected clinical educators: they must be woven into the core of how providers work.

6.4. Universal action 4: ignite demand for quality

Igniting demand for quality means challenging countries and partners to raise population expectations for quality care. To do so, health systems will need to share information and educate communities about what constitute good quality care and create opportunities for meaningful participation. Appropriate expectations of healthcare quality and demand for high quality services can put pressure on systems to deliver effective care. We have seen effective advocacy around TB drug access already; for example, advocates in South Africa have played a key role in the country's adoption of bedaquiline for multi-drug resistant TB. This type of action is a health system resource that needs to be fostered and supported. Improving patient education is also critical to ensure that systems are used appropriately. Efforts to integrate TB services with primary care, especially in middle-income countries, has been challenging in part due to the perception that specialty care was *always* better for TB [46].

7. Conclusion

Further research is needed to define and validate new indicators of TB care quality and to develop data collection systems for these undermeasured dimensions in high-burden countries. New technologies should be explored to improve data accuracy, timely data collection and reduce measurement burden (e.g. phone/SMS surveys, wearable trackers etc.). Countries and global partners should invest in data systems for quality. The Commission's four universal actions should also be considered and tested for improving the delivery of competent and respectful TB care.

Funding sources

This work was supported by the Bill & Melinda Gates Foundation (Grant no. OPP1161450), Seattle, WA.

Ethical statement

The authors have no conflicts of interest

CRediT authorship contribution statement

Catherine Arsenault: Conceptualization, Writing - original draft, Validation. **Sanam Roder-DeWan:** Writing - original draft, Validation. **Margaret E. Kruk:** Conceptualization, Writing - review & editing, Validation.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jctube.2019.100112.

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J Clin Tuberc Other Mycobact Dis 17 (2019) 100116

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Implementing quality improvement in tuberculosis programming: Lessons learned from the global HIV response

ARTICLE INFO

Keywords:
Quality improvement
HIV
AIDS
Tuberculosis

ABSTRACT

The quality of care and treatment for tuberculosis (TB) is a major barrier in global efforts to end TB as a global health emergency. Despite a growing recognition of the need to measure, assure, and improve quality of TB services, implementation of quality improvement (QI) activities remains limited. Applying principles of systems thinking, continuous measurement, and root cause analysis, QI represents a proven approach for identifying and addressing performance gaps in healthcare delivery, with demonstrated success in low- and middle-income settings in the areas of HIV/AIDS, maternal, newborn, and child health, and infection control, among others. Drawing from lessons learned in the development of QI programming as part of the global response to HIV, we review key enablers to implementation that may assist NTPs in turning aspirations of high-quality service delivery into action. Under the umbrella of a formal quality management (QM) program, NTPs' attention to planning and coordination, commitment to tracking key processes of care, investment in QI capacity building, and integration of TB QI activities within efforts to advance universal health coverage provide a framework to sustainably implement QI activities.

1. Introduction

Tuberculosis (TB) is a major public health threat, claiming the lives of 1.6 million worldwide in 2017. TB is preventable, treatable, and curable, yet decreases in TB incidence and mortality remain below targets advanced as part of WHO's End TB Strategy. Despite the wide availability of TB treatment, millions of people with TB receive care that is of consistently poor quality [1,2]. According to WHO's Framework on Integrated, People-Centered Health Services, high-quality healthcare is safe, effective, people-centered, timely, efficient, equitable, and integrated [3]. Endorsing a health systems approach to quality, the recent *Lancet Global Health* Commission on High Quality Health Systems in the SDG Era has furthered this framework by articulating the call for a "revolution" to support resilient, equitable and efficient health systems that serve people, are responsive to population health needs, and support ongoing learning and improvement [1]. A rapidly expanding body of work has documented the shortcomings of current TB care when assessed according to the ideals of high-quality health systems, emphasizing a crucial need to embed quality improvement (QI) concepts and methods in national disease control programs to achieve epidemic control targets [4,5].

While this imperative to measure, assure, and improve the quality of TB services is now well recognized, systematic attempts to integrate QI within TB service delivery and national TB programs (NTP) remain sparse [6]. At its core, QI seeks to optimize outcomes by applying systems thinking, routine measurement, and data-informed tests of change to routinely diagnose and improve shortcomings in processes of healthcare delivery [7]. Lessons learned through more than two decades of implementing QI programming as part of the global HIV response in low- and middle-income country (LMIC) settings offer NTPs a framework within which to advance QI efforts that are effective and sustainable. Through the core functions of a formal quality management (QM) program—defined as the organizational infrastructure that enables routine measurement and QI activities [8,9]—NTPs in LMICs should seek to develop a public health approach to quality in which improvement is conceptualized as a continuous activity requiring dedication to centralized planning and coordination, attention to processes as well as inputs and outcomes, investment in capacity building and system strengthening, and linkage to broader quality initiatives.

2. Dedication to centralized planning and coordination

As part of early attempts to improve the quality of HIV care and treatment, national programs in LMICs witnessed the proliferation of QI initiatives spanning multiple implementing partners, methodologies, standards, and aims [10,11]. These initiatives were laudable for addressing recognized quality gaps. However, the simultaneous, loosely coordinated implementation of these initiatives created the need for national programs to address "the problem of many hands," a phenomenon in which the simultaneous implementation of multiple QI efforts can, paradoxically, produce suboptimal outcomes by dividing HCWs' attentions, placing inordinate strains on limited resources, and generating micro-level solutions for problems that require a macro-level response [12]. Accordingly, without central, Ministry-led coordination of these "many hands," well-meaning QI initiatives may yield disappointing results over time, thereby undermining the attractiveness of QI to policy makers, fomenting disillusionment among healthcare workers, and wasting already limited resources [1].

Any effort to improve the quality of healthcare services should begin with a clearly articulated vision of what quality "means" within a

https://doi.org/10.1016/j.jctube.2019.100116

Table 1
Core components of a QM plan.

Component	Description
1. Quality statement	A brief mission statement that characterizes the aims of the QM program.
2. Quality program	A characterization of the programs' leadership, systems of accountability, membership, roles and responsibilities of technical working groups and oversight committee, and expectations for communicating program updates and activities.
3. Performance measurement system	A description of which performance measures will be tracked as part of the QM program, and how, when, and by whom they will be routinely collected and reported.
4. Setting improvement goals	A set of endpoints or conditions (e.g., treatment completion rats) around which the QM program will seek to prioritize and structure QI activities.
5. Stakeholder and patient participation	A description of how staff, providers, patients, communities, and other stakeholders will be involved in the QM program.
6. Evaluation	A plan for evaluating the performance of the QM program, including progress in meeting stated improvement goals, organizational effectiveness of current QM program committees, and robustness of existing QM plan.
7. Annual QI work plan	A detailed roadmap of implementation, which changes annually, that specifies improvement priorities and QI activities that will be advanced as part of the QM program's activities.

particular context and a common roadmap for bringing that vision to fruition in a coordinated fashion [13]. Early attempts to coordinate quality at national level included approaches, like HIVQUAL, that supported a core set of national indicators, development of a standardized national QI training curriculum and building QI coaching capacity. Further recognition of the need to situate facility-level QI activities within a cohesive policy framework led to the development of HIV QM plans in LMICs derived from lessons learned from HIV programs in the United States (Table 1) [14]. HIV QM Programs have developed and implemented these plans over the past decade that provide this organizational framework for ongoing support of quality. For example, in Zimbabwe, the National AIDS Program convened key stakeholders from local governments, donors, implementing partners, universities and civil society to develop its common plan and policy for quality that embraced QI and developed a plan for its spread throughout the country [15]. Through this participatory process, stakeholders agreed upon a common measurement framework, and developed a national approach to quality aimed at aligning diverse QI initiatives under a shared framework of accountability.

Namibia undertook a similar process through a technical working group on quality, led by its Quality Assurance Division [16]. With support from capacity-building initiatives like HEALTHQUAL (formerly HIVQUAL International) and the USAID Applying Sciences to Strengthen and Improve Systems (ASSIST) Project, similar plans have been developed in Uganda, Tanzania and Kenya [17–19]. Acknowledging the importance of planning and coordination in implementation of QI, the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) adopted several indicators as part of its site- and national-level assessment tools that evaluate programs on the presence and stewardship of QM plans [20,21].

Like all policies, QM plans face the risk of collecting dust on a shelf rather than driving change as intended. These plans are important for imparting specifics to national programs' strategic visions of quality, but their implementation must be supported by structures, processes, and functions that establish accountability and empower local health systems to deliver care that is of consistently high quality [9]. In the context of TB, national programs can begin by developing QM plans that situate the generic calls for quality of care within their programs' strategic action plans by generating a step-by-step guide on how to translate available human and material resources into QI activities that target locally relevant performance gaps. To be successful, progress in implementation of these plans must be measured using time-bound goals and continuously monitored to adapt the plans as needed. Standardized tools such as the national organizational assessment may be useful to NTPs to assess the robustness of their QM plans [9]. Furthermore, lessons learned from the development and evaluation of QM plans in Zimbabwe and Namibia underscore the importance of having Ministry-led—rather than donor-driven—organizational support to oversee the development and administration of the QM program, and an inclusive approach to stakeholder engagement that solicits input and buy-in from across the health sector to co-develop it and reinforce its implementation. Donor support of QM programs, through assessment tools and dedicated funding, are useful levers for stimulating initial action, but may fall short in achieving sustainability [11]. Without the organizational support of a QM program, political leadership from Ministries of Health, and commitment of national governments to allocate domestic funds, the visions articulated in QM plans or strategies are unlikely to be realized and sustained.

3. Attention to processes of care

Like early applications of QM methodologies to healthcare, preliminary attempts by national programs to address quality in the setting of HIV care focused largely on a quality assurance (QA) approach of standards-based inspection and supervision. The earliest assessments of programmatic performance in LMIC settings relied exclusively on findings of population-level analyses in which "success" was approximated according to inputs, "coverage," and outcomes alone [22]. To be sure, these analyses were useful for developing accountability for resource allocation and estimating the gap between disease burden and the national program's corresponding response, but they were too infrequent and insufficiently granular to drive action and system-wide learning. Importantly, the narrow selection of inputs and outcomes neglected the key importance of assessing the cascade of processes, such as testing, diagnosis, and treatment initiation, that mediate the translation of inputs (e.g., life-saving antiretroviral therapy) into outcomes (e.g., viral suppression, long-term survival and declining disease burden) [23].

Growing recognition of the central importance of examining healthcare processes in assessments of quality spawned the intensive efforts of national HIV programs to identify, measure, and improve these processes in individual facilities. Following the lead of Thailand [24], in 2007 Namibia joined Uganda and Mozambique to become one of the first LMICs to systematically address these processes as part of its national HIV QM program. After 10 consecutive rounds of measurement, by 2013 these efforts had yielded marked improvements in 10 of the program's 11 quality indicators (Table 2) [25]. In Haiti, commitment to performance measurement led to the evolution of a centralized, comprehensive electronic platform, *Système Intégré de Gestion d'Healthqual d'Haiti* (SIGHH), for monitoring HIV QI programming (**Fig. 1**), which fused the country's pioneering electronic medical record, *iSanté*, and its monitoring and evaluation system [26]. SIGHH has allowed the national HIV program to automatically capture patient-level data, produce real-time quality reports linked to quality program organizational assessments and geographically target its response to low-performing sites or high-burden areas. Moreover, SIGHH tracks key enablers of QI implementation, such as QI coaching and ongoing QI projects, providing national program staff with further detail on site-level progress. As of 2019, data are transmitted to SIGHH from all facilities that provide HIV care in Haiti.

Table 2
HIVQUAL measures – Namibia.

Indicator	Definition
1. Clinic visits and retention	Percentage of patients on ART with a clinical visit during the last 3 months
2. Pre-ART monitoring	The proportion of Pre-ART patients with CD4 monitoring completed in the past 6 months.
3. Viral load monitoring on ART	The proportion of patients with a viral load test completed in the past 6 months.
4. New ART initiation	The proportion of eligible patients who were initiated on ART within the past 6 months.
5. TB screening	The proportion of patients with documented TB screening result at each clinic visit within the past 6 months.
6. Isoniazid prophylactic therapy	Proportion of eligible patients currently on isoniazid prophylactic therapy during the past 6 months.
7. Cotrimoxazole prophylactic therapy	Proportion of patients with CD4 ≤ 250 or WHO clinical stages 3 or 4 prescribed cotrimoxazole prophylactic therapy during the past six months.
8. ART adherence assessment	Proportion of patients who received an adherence assessment at each of their clinic visits during the past 6 months.
9. Nutritional assessment	Proportion of patients who were administered a nutrition assessment during their last clinic visit
10. Alcohol screening	Proportion of patients screened for alcohol use in the last 6 months.
11. Family planning assessment	Proportion of patients aged 15–49 who were assessed for their family planning status.
12. STI screening	Proportion of patients aged 15–49 years screened for genital ulcers and urethral/vaginal discharge in the past 6 months.
13. Cervical cancer screening	Proportion of female patients older than 15 years who had a documented cervical cancer screening result not older than 15 months.

Like HIV, delivery of high-quality care for TB can be conceptualized according to a cascade of key processes that directly translate into achieving epidemic control [27]. Lessons learned from implementation of HIV QI programming in countries like Namibia and Haiti underscore the importance of building robust measurement platforms that track facility-level performance in these key clinical processes. To stimulate action among providers, performance measurement data must be continuously collected, sufficiently local, and conceptualized as the basis for improvement rather than fodder for blame [28]. While many TB programs collect these data elements as part of routine service delivery and program monitoring [29], the purpose and method of collection for each data point may vary, creating a data ecosystem that is fragmentary and ill-suited for use in improvement. Consolidation of these data sources into a centralized system with defined indicators offer NTPs a common rubric with which to evaluate performance and develop evidence-informed policy responses. While some processes are, and ought to be, commonly measured across settings (e.g., receipt of drug susceptibility testing), decisions to track others may be informed by local policies and priorities. HIVQUAL-Namibia's decision to track screening for food insecurity, for example, underscores the utility of selecting measures that reflect both internationally defined standards of treatment and locally relevant priorities and social determinants of health.

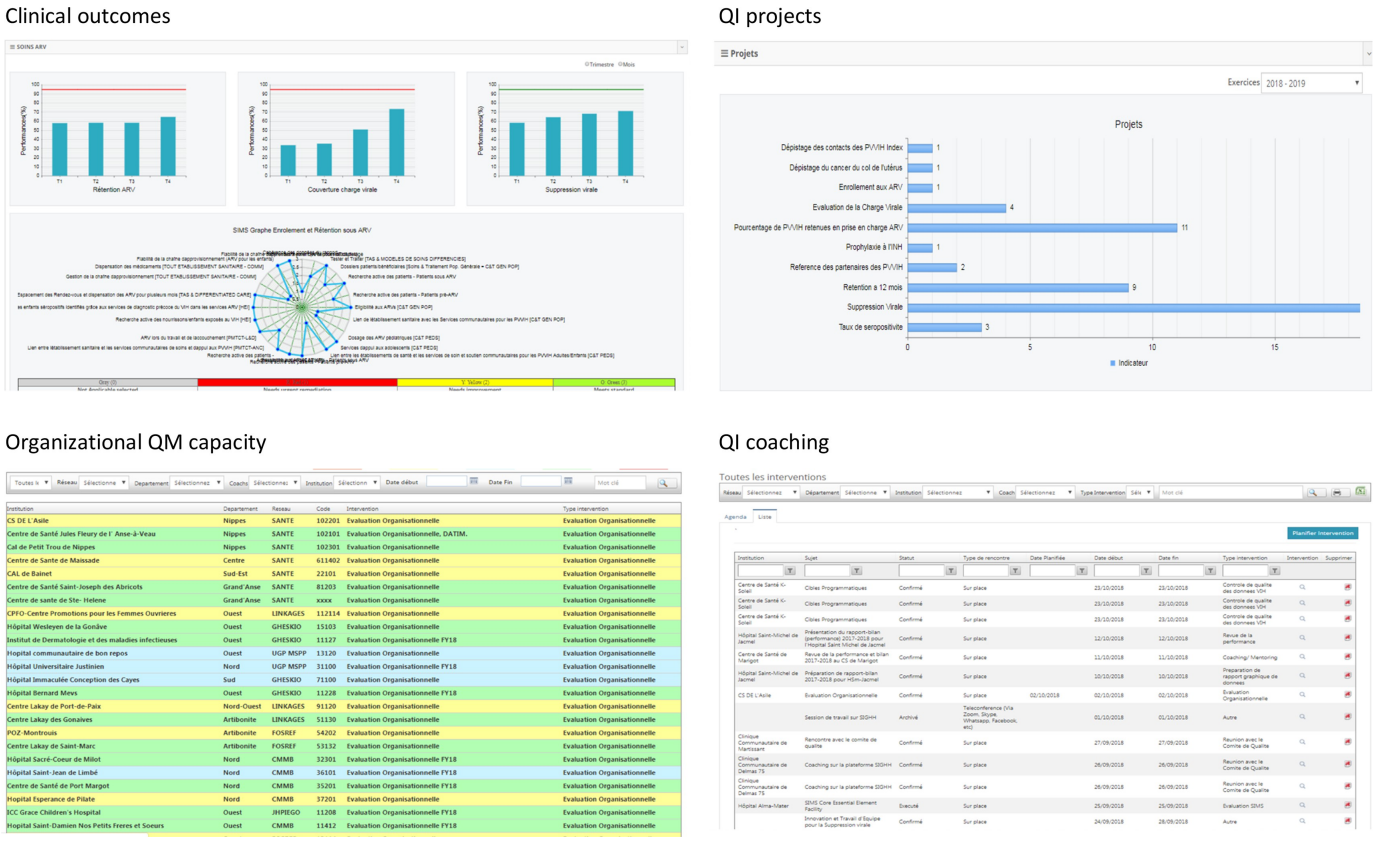

Fig. 1. SIGHH dashboards – Haiti
In Haiti, SIGHH dashboards are used to track the site-level progress of QI implementation according to several factors, including clinical outcomes (a), QI projects (b), organizational QM capacity (c), and QI coaching visits (d) [60]. Progress is monitored centrally and further coaching and support is tailored to low-performing sites. The juxtaposition of the different components also allows a retrospective evaluation of the role coaching played in advancing implementation of QI activities and quality programs, and whether a cascading effect on performance was achieved.

4. Investment in capacity building and system strengthening

The global response to HIV, like TB, has relied heavily on disease-specific, donor-driven initiatives which have often valued short-term achievements in key indicators over attention to long-term capacity-building [10]. PEPFAR, in particular, has been enormously successful in stemming the tide of new infections and preventing associated morbidity and mortality [30], but evidence supporting its benefit in strengthening underlying health systems to address other population health concerns remains mixed [31,32]. As an emergent phenomenon, high-quality healthcare service delivery requires a foundation that enables vigilance, enforcement of clearly defined policies, procedures, roles, and expectations, and development of a well-prepared facility, district, and national cadres who don't simply "know" QI concepts and methods. Crucially, these cadres must be able to continuously and dynamically support QI implementation and system-wide learning to respond to evolving patient, clinical, and population health priorities in their facilities and communities [33].

The availability of an adequate, capable, and compassionate health workforce pervades any discussion of sustainable delivery of high-quality healthcare in LMICs [1], and is of particular concern in countries transitioning away from donor financing [34]. Appreciation of the challenge of sustainability in a climate of declining donor funding led many programs to pivot toward pursuit of long-term capacity-building and health systems strengthening that include quality management as part of continuing efforts to reach epidemic control targets. With this formal coordination and support, HIV programs began to embed QI capacity within national and sub-national health systems. In Vietnam, a provincial coaching model was implemented in which existing cadres from the Provincial Peoples' AIDS Committees were capacitated by the National AIDS Program to provide mentorship to facilities in QI implementation as part of routine supervisory activities. For example, in Son La Province, QI activities were successfully spread to 7 of the province's 9 HIV clinics and improving the quality of HIV care in a majority of core indicators [35]. In Ho Chi Minh City, all district health centers were coached to implement improvement activities. With the guidance of national and provincial HIV quality technical working groups, the model has been adopted as a strategy to sustainably decentralize QI implementation and expertise with limited need for additional staffing. In Namibia, the national program has developed a comprehensive framework for QI capacity building, which specifies standards, curricula, and evaluation of QI trainings for healthcare workers, trainers, improvement coaches, and consumers both within and beyond the HIV program.

Although some notable work has been accomplished to apply QI concepts and methods to TB care [36–42], these efforts have remained limited in scale and with minimal attention paid to capacity building for ongoing QI implementation, leaving their sustainability beyond the few facilities or districts in which they are implemented an open question. Experiences from HIV QI implementation in settings with workforce shortages and frequent staff rotations point to the importance of developing models, curricula, and standards whose scalability is planned from the outset, and whose intended targets for QI capacity building span facility, district, and national cadres, as well as the public and private sectors [43]. Mentorship and coaching can speed site-level implementation of QI, but their implementation remains a challenge in LMICs, in part due to a lack of consistent QI coaching standards. QI coaching certification standards, such as those implemented in Haiti and Zimbabwe, can assist in overcoming this barrier (Table 3) [44]. In addition to standards and curricula, large-scale improvement initiatives, such as collaboratives, can be useful in developing capacity of participating national-, district- and facility-level teams to implement QI and generating a package of scalable improvement interventions [45–50]. Ministry-led collaboratives to address HIV care processes and outcomes, build platforms for peer learning and exchange, and complement other QI capacity building efforts that have been implemented with notable success in Kenya, Namibia, Zimbabwe, and Malawi. These initiatives should be considered as part of TB programs' capacity-building "toolkit," especially in high-burden areas, to accelerate improvements and achieve results.

Beyond capacity building of healthcare workers, establishing consumers as active players in system-wide QI efforts represents an essential, albeit underutilized approach to build demand for high-quality health services. In Namibia, a QI curriculum for consumers, which was piloted across 6 sites in 2016, is currently being scaled as part of broader national activities aimed at promoting people-centered care delivery, including revisions of patient charters and curricula on consumer rights [51]. Other approaches for involving consumers in QI efforts, such as experience-based co-design, patient feedback systems, consumer advisory committees, and community-based monitoring programs have been used with considerable success in resource-rich settings, but have, to date, seen disappointing uptake in LMICs [1]. Systematic incorporation of these approaches into QI capacity-building agendas remains an aspiration in HIV and TB QI programming in LMICs, and warrants further attention and development [52,53]. Finally, given the damaging effects of stigma on the success of both HIV and TB control [54], urgent work is needed to leverage continuous measurement, patient involvement and QI methods to address its root causes and act to mitigate their effects, particularly in healthcare settings [55].

5. Linkage to broader quality initiatives

HIV QM programs, like other disease-specific quality programs, are typically discrete and siloed initiatives within Ministries of Health. When these programs were developed, national quality programs in LMICs were often non-existent or small outposts of QA initiatives. As national quality programs have evolved, the separation of disease-specific quality initiatives, often fueled by categorical funding requirements, has resulted in parallel systems of measurement and capacity-building that can result in confusing messages for providers and subnational units about priorities. Moreover, the jurisdiction of these disease-specific programs is often limited to quasi-independent clinics housed within larger healthcare facilities. The quality of services for people living with HIV presenting to care at other service units within these institutions, medical clinics, and those external to the public sector (private, military and prison clinics) often remains unaddressed and characterized by substandard care.

These concerns have prompted the call for integration of QM programs within a broader national health system quality framework [13]. Under the expanding push for universal health coverage, primary care providers will assume the mantle for diagnosis and primary care of people with HIV and TB, among other conditions. Some promising early examples of collaboration and alignment have been observed in several countries. In Zimbabwe, the HIV QI training curricula and coaching model has been adopted by the maternal, newborn and child health (MNCH) and malaria programs through capacity-building of provincial and district health management teams that provide support to health facilities in their jurisdictions [56]. In Thailand, the Hospital Accreditation Program [57] has developed a disease-specific certification program for HIV that includes HIV-specific measures and QM programs. In Lao People's Democratic Republic, measures to assess patient experience and stigma and discrimination in HIV clinics are endorsed under "Five Goods, One Satisfaction," the national policy on healthcare quality [58], and in Vietnam, HIV measures have been integrated into the national health sector reporting system. In some countries, conversely, HIV programs and platforms have been used to address other diseases. In Namibia, indicators to measure the quality of care for non-communicable diseases (NCD) and TB have been integrated into large-scale HIV quality initiatives, and in Haiti, *iSanté* has evolved to capture measures for NCDs, MNCH, and TB which are gradually being adopted in primary care clinics. Notably, 63TB surveillance indicators are

Table 3
Basic competencies for QI coaches.

Competency	Description
1. Knowledge of QI theory	Through completion of a formal national curriculum or internationally recognize QI training program, demonstrates knowledge of Qi theories and methods.
2. Experience as a coach	Demonstrates experience mentoring at least one facility QI team through documented completion of a QI project and organizational assessment with recommendations.
3. Understanding of patient involvement in quality	Exhibits an understanding of how to involve patients in QI activities, including methods for recruitment of patients for QI teams, approaches for including patients in priority setting, and evaluation of facilities' support for patient involvement.
4. Ability to use national program data reporting tools	Demonstrates competence in using national program data reporting tools to analyze and report performance measurement data, and provide support to facilities in data-driven QI decision making.
5. Reporting	Shows an ability to maintain a thorough record of coaching activities—Including tested interventions, implementation barriers, and improvement recommendations—for review by the national program.

available in *iSanté*, of which 24 are used for routine NTP reporting.

NTPs face the same challenges that dedicated HIV QM programs have encountered with respect to their role in the broader national health sector quality program. Too often, systems for measuring the quality of TB services are applied only within established TB clinics, an approach that may neglect patients presenting to general hospitals and health centers that lack requisite diagnostic and treatment capacity [59]. With the experience gained from nearly two decades of HIV QM initiatives that have spanned HIV prevention, testing, care and treatment, TB programs can avoid the pitfalls of separate programs by careful planning and coordination with their respective national quality programs. Practically speaking, the coordination and integration of these programs needs to strike a critical balance between the unified measurement platforms and QI methodologies with the preservation of disease-specific quality measures and expertise in clinical management. Resources can be leveraged by sharing QI training, capacity-building methods, and reporting systems. Shared measurement platforms can eliminate duplicate reporting systems for providers and facilitate inclusion of TB-specific metrics on national quality dashboards. Representation of clinical TB experts on national and subnational quality technical working groups will foster bidirectional sharing of knowledge and harmonization of policies and practices. Finally, the unification of coaching at district level will avoid duplication of activities and promote efficient use of resources. This alignment will also benefit providers and patients by assuring consistency of information and methods guiding the application of standards of care.

6. Conclusion

The quality of TB care in LMICs remains inadequate, with major shortcomings in detection, diagnosis, treatment, and recurrence-free survival. NTPs wield the mandate of addressing and improving quality across all sectors and for all affected populations, yet often have oversight over only dedicated TB clinics. To effectively tackle the substantial gaps throughout the cascade of TB care—and realize the potential role that QI plays to close them—NTPs need to apply careful planning, measurement, robust process improvement and capacity building across the entire health sector. Although HIV programs have reaped the benefits of donor largesse, the sustainability of their quality initiatives remains in peril as donor funding for associated staff and activities dwindles. NTPs now face the challenge of leveraging resources to support QI activities through effective coordination and commitment to capacity building, and the harnessing of existing measurement platforms and district health management teams. In doing so, they may realize long-term benefit and sustainability, especially as they seek to balance the growth of integrated primary care models and universal health coverage with the preservation of clinical expertise in TB. The burden of inaction is great. Aims to reduce TB deaths by 95% and incidence by 90% within the next 15 years demand the rapid implementation of strong, coordinated quality programs to achieve these ambitious improvements in population health. Lessons learned from the successes and failures of HIV programs in addressing quality offer a starting point from which NTB programs must leap.

Declaration of Competing Interest

None.

Funding

This work did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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J Clin Tuberc Other Mycobact Dis 17 (2019) 100117

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Quality of TB services assessment: The unique contribution of patient and provider perspectives in identifying and addressing gaps in the quality of TB services

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ARTICLE INFO

Keywords:
Tuberculosis
Quality
Facility
Patient
Provider
Knowledge

ABSTRACT

Ambitious efforts to detect and treat tuberculosis (TB) are required to reduce the burden of disease in low resource settings, and the provision of high quality TB services is critical to reaching global TB targets. The quality of TB services assessment (QTSA) is a facility-based approach aimed at identifying gaps in TB services and prioritizing interventions to improve care across multiple countries with high TB burden. Randomly sampled facilities are assessed with standardized instruments to collect data on structures, processes, and outcomes of TB care, with adaption for local diagnostic and treatment algorithms. The sampling strategy is modified to ensure representation of all levels of the health system where TB services are provided, as well as inclusion of private sector or other facility types relevant to the context. Instruments include a facility audit, provider and patient interviews, and a review of TB registers. A recent QTSA in the Philippines generated important data on provider and patient perspectives on quality of care, showing that providers are more likely to report that they counseled current TB patients on key aspects of TB diagnosis and treatment than patients are to report having received the information. These comparisons highlight areas where refresher training or interpersonal communication and counseling skills may be needed.

1. Introduction

Tuberculosis (TB) is the world's leading cause of death due to infectious disease. The World Health Organization (WHO) reports that 64% of an estimated 10 million TB cases are detected and treated each year, leaving 3.6 million cases with either no care at all, sub-optimal care for which the quality of services is unknown, or adequate care but not reported to National TB Programs (NTP). [1] Following the first United Nations High-Level Meeting on the Fight to End TB (UN HLM), held in September 2018, there is renewed emphasis on improving TB case detection, TB prevention, and ensuring timely care for all people with active TB disease. High burden countries have committed to ambitious treatment targets intended to reduce morbidity and mortality due to TB and interrupt the chain of transmission; the ultimate goal of the UN HLM commitments is to accelerate progress towards the elimination of TB as a public health challenge. [2] The UN HLM commitments include treatment targets for drug sensitive TB and drug resistant TB (DR-TB), as well as specific targets for pediatric case finding and TB preventive therapy among contacts of confirmed TB cases and people living with HIV/AIDS.

As the largest bilateral donor to TB programs throughout the world, the United States Agency for International Development (USAID) has an important role in supporting NTP in their efforts to achieve the UN HLM targets. Investments in high quality TB diagnosis and treatment services at all levels of the health system are an essential component of USAID's support to high burden countries. The first of four pillars underlying the US Government TB strategy is “improve access to high quality, patient centered TB, TB/HIV and DR-TB services.” [3] In order to ensure this pillar is in place as a foundation for the UN HLM targets, USAID recognized the need for detailed data on quality of TB services.

Thus, there is a need to measure quality of TB services in a systematic way across high burden countries where USAID provides

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https://doi.org/10.1016/j.jctube.2019.100117

financial and technical support to NTP. The approach to measuring quality of TB services is conceptualized according to Donabedian's framework of structure, process, and outcome. [4] Structure refers to the resources available at a health facility, for example, equipment, reagents, and other materials needed to provide services. Process is defined as the interaction between patients and providers. Finally, outcomes are the consequences of the services provided, for example, a confirmed TB diagnosis or treatment initiation and completion. The quality of TB services assessment (QTSA) was developed to provide detailed data aimed at identifying gaps in quality of care that should be prioritized by NTP and donors such as USAID, so that investments are targeted for maximum effect. Additionally, QTSA includes the perspective of current TB patients and providers, which are critical to ensuring quality of care. The objective of this paper is to describe the QTSA methodology and provide an example of how it can be used to identify and prioritize gaps in the quality of care through a case study in the Philippines.

2. Overview of TB quality of care measurement methods

There are a variety of methods which have been used to measure quality of health services in settings with high TB burden. Most are broad analyses and are not specific to TB. Methods generally include one or a combination of a facility audit, direct observations, provider interviews, and patient exit interviews.

The Service Provision Assessment (SPA), which is part of the USAID-funded Demographic and Health Surveys Program, assesses health facilities to measure healthcare availability and readiness. [5] Provider and patient interviews are also conducted. However, even though providers are asked about their training on and provision of TB services, patient exit interviews are only conducted with those visiting the antenatal care clinic, family planning services, or with a sick child. Therefore, no comparisons can be made between patient and provider perceptions of their interactions regarding TB.

The Service Availability and Readiness Assessment (SARA) [6] was developed jointly by USAID and the WHO to build upon the SPA, and is facilitated by the WHO. The SARA focuses on service availability and service readiness of specific domains, including TB. The measures related to TB are assessments of whether specific services such as diagnostics and drug regimens are available or not and training of healthcare providers. These are assessed using an in-charge interview and direct observations. There are no patient interviews conducted and so a key component, the patient perspective of quality of care, is missing.

A third methodology is the Quality of Care Through the Eyes of the Patient (QUOTE), which was developed by the USAID-funded TB Control Assistance Program to TB. [7] As the name implies, this tool includes a strong focus on the patient's perspective of quality of care. Quality is measured using nine dimensions: communication and information, professional competence, availability of TB services, affordability, patient provider interaction and counseling, support, TB/HIV relationship, infrastructure, and stigma. Patients are involved from the beginning of the process including priority rankings of the dimensions of quality and as interviewees. The strength of the QUOTE method is its focus on the patient perspective, however, without a simultaneous facility audit or provider interview, there is no context available for the patient perspective and no comparisons with provider perspectives can be made.

Finally, standardized patients have been used to assess quality of clinical practices related to TB care in urban settings in India. A validation study by Das et al. describes the process by which 17 individuals were trained to present with specific symptoms and treatment seeking scenarios at private providers with different professional qualifications in Mumbai and Patna [8]. The standardized patients reported data on 250 interactions with providers, with only 21% of reporting correct procedures for the scenario they presented to the clinician, demonstrating a wide gap between training and practice. The authors concluded that use of standardized patients is feasible, successful and that this approach yields useful insights about the quality of TB services and allows for comparisons between different types of providers.

3. Why QTSA? Methods and analysis

The QTSA is a survey of a random sample of health facilities providing TB services using standardized data collection instruments to gather information on key aspects of screening, diagnosis, and treatment services as well as supporting environmental or contextual factors. The multi-stage sampling procedure is adapted to provide a representative sample of facilities from various levels of the health system for the desired geographic area covered by the survey, which depends on the preferences of key stakeholders and the availability of funding. The survey team invites a sample of three to five TB patients per facility who are 15 years and older, who have been on treatment for more than two weeks, and who are present on the day of the survey to participate in an interview. For facilities with a low volume of TB diagnosis and treatment services, this sampling approach may include all patients who present on the day of the survey. Facility in-charges and staff with responsibility for providing TB screening, diagnosis, and treatment services are also included in the survey.

The data collection instruments include a facility audit, register review, and patient and provider interview guides. The QTSA methodology and instruments were initially piloted in a subset of local government areas (LGAs) in Nigeria in collaboration with the USAID mission and NTP. The materials were revised after this pilot in preparation for implementation at national level in the Philippines and there are multiple QTSA surveys planned for high burden countries. The survey is designed and implemented by MEASURE Evaluation, a USAID-funded project, in partnership with a local research organization (LRO) and with the NTP, USAID mission and other local TB stakeholders involved in the planning and analysis stages.

During the planning stage, the generic data collection instruments are adapted to the local context by aligning items related to TB services to NTP algorithms. Additionally, some countries request more detail on specific elements of TB care, for example, detection and treatment of childhood TB, contact investigation practices and clients' experiences of stigma. While the generic set of QTSA tools includes a standard set of variables collected across countries, with a corresponding data analysis plan, they are flexible enough to accommodate country specific needs. Fig. 1 is a visualization of the QTSA tools with linkage to the key elements of quality of services. Supplementary Tables 2 and 3 provide the questions included in the provider and patient questionnaires, respectively.

The multiple facility-based data sources provide a unique opportunity to identify specific gaps in the quality of care, for example, by

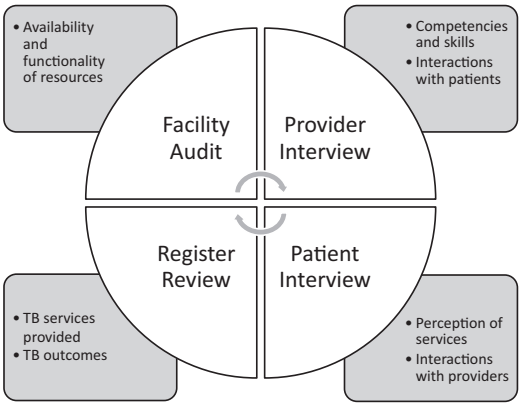

Fig. 1. Overview of assessment tools.
Overview of the four tools used during a QTSA assessment and the information collected by each one.

Table 1
Provider characteristics.

	Overall 435	Hospitals 59 (14%)	Non-hospitals 376 (86%)	Urban facilities 140 (32%)	Rural facilities 295 (68%)
Sex					
Female	85%	76%	86%	83%	85%
Male	15%	24%	14%	17%	15%
Highest Level of Schooling					
Diploma/associate degree/other	16%	2%	19%	9%	20%
Bachelor's degree	68%	83%	65%	66%	68%
Master's degree	10%	12%	10%	19%	6%
Doctorate	6%	3%	6%	6%	6%
Occupation					
Registered Nurse	49%	73%	46%	62%	43%
Rural Health Midwife	25%	2%	29%	15%	30%
Medical Technologist	12%	15%	11%	6%	14%
Medical Doctor	9%	7%	9%	10%	8%
Barangay Health Worker	2%	0%	2%	2%	1%
Other	3%	3%	3%	4%	3%
TB Focal Person	70%	73%	69%	72%	69%

comparing client and provider perspectives on the quality of care and triangulating with availability of commodities and equipment. Data analysis consists of a standard set of calculations based on agreed-upon indicators to identify gaps in service delivery, including the percentage of each facility type with specific equipment, commodities, and services needed to screen, diagnose, and treat TB, as well as perceptions of providers and clients on the quality of services. Similar to the sampling strategy, the analysis plan can be adapted to the needs of each NTP, depending on existing concerns regarding quality of care or specific questions they have about client and provider perspectives. Overall, QTSA data analysis is aimed at identifying and prioritizing gaps in quality of care; the results are presented at stakeholder workshops to engage all partners in interpretation of the data and prioritization of next steps. Although originally designed to support USAID missions, implementing partners, and host NTPs, the vision for QTSA is for broader adaptation and use through high burden settings or in any setting where quality of TB services is of concern to stakeholders. For example, the tools have been shared with research and implementing partners in non-USAID supported countries to support data collection on quality of TB services.

4. QTSA in Philippines: a case study

According to the WHO, Philippines is a high burden country for TB with an estimated 581,000 incident cases in 2017. It is also considered a high burden country for DR-TB, with 27,000 estimated rifampicin-resistant cases. [1] Historically, the Philippines has been a priority country for the USAID TB Program, receiving approximately $12 million per year for the past 6 years; the range of annual investment during the same time period is $1.5 to 13 million per year. On April 24, 2019, the Philippines Department of Health and the WHO declared an “all out war” on TB, recommitting the country to treating 2.5 million people with active TB by the end of 2022 in line with the UN HLM target set in September 2018. [9] One of the three key strategies for reaching this target is massive screening, diagnosis, and treatment, which will provide access to improved technologies and treatment regimens for all forms of TB.

Currently, the NTP is implementing the Philippine Strategic TB Elimination Plan (PhilSTEP) from 2017 to 2022 [10]. PhilSTEP emphasizes access to quality services, for example, with certification of health facilities for compliance with national standards for TB care, implementation of quality assurance procedures in laboratories, and eliminating stockouts of anti-TB medication and supplies needed for TB services. The plan reiterates the importance of integrated, patient-centered care throughout the health system and generation of support for TB services across all sectors and at the regional and local levels. Given the ambitious scope of PhilSTEP, the NTP supported the implementation of the QTSA to provide baseline data on the availability and quality of TB services, which can be used to identify gaps and prioritize interventions needed to ensure screening, diagnosis, and treatment are in place and support implementation of the plan. Additionally, the private sector is an important provider of TB diagnosis and treatment services in the Philippines, and the USAID TB Division wanted to use QTSA among private sector providers. Finally, the NTP was in agreement with QTSA objectives and wanted to use the data to inform their strategy for meeting HLM targets.

The ethics review for this QTSA was conducted and approved by the John Snow, Incorporated Institutional Review Board (IRB) in the United States and the Asian Eye Ethics Review Board in the Philippines. Additional IRB submissions were required for two hospitals included in the study and the Philippines Statistics Authority cleared the QTSA design. All clients and providers were read an informed consent statement describing their rights as participants and guarantee of confidentiality; no personal identifying information was collected and neither providers nor clients can be linked back to specific facilities.

4.1. Sampling

A total of 202 health facilities (public and private) from the NTP network providing TB and TB-related services such as diagnosis, care, and treatment were randomly selected using a multistage sampling procedure. The first stage involved stratifying the 17 regions into high, medium, and low categories based on the incidence and prevalence of TB and then randomly selecting six regions with two regions selected from each of the high, medium, and low categories. At the second stage, three provinces or highly urbanized cities were selected from each region and lastly, a sample of about 10 facilities per province/highly urbanized city within the network of NTP facilities was selected. Supplemental Table 1 in the appendix provides details on facility types and characteristics.

Table 1 provides summary data on provider characteristics. The assessment included 435 TB service providers of which the majority were female (85%). Most of the providers were attached to non-hospitals (86%) and worked in rural facilities (68%). About two thirds had a Bachelor's degree (68%) and 16% had an educational level lower than a Bachelor's degree. Providers with a higher educational level were found to be working at the hospital while those with a lower level of education work at non-hospital facilities. Almost half of the providers were registered nurses (49%) who predominantly work in hospitals, and a quarter were rural health midwives (25%). Only 9% were medical doctors. Overall, 70% of those interviewed were the TB focal person at the facility.

A total of 560 patients were interviewed as part of the assessment; however, five patients did not complete the survey. On average, slightly

Table 2
Patient characteristics.

	Overall 560	Hospital 86 (15%)	Non-hospital 474 (85%)	Urban facilities 219 (39%)	Rural facilities 341 (61%)
Sex					
Male	61%	62%	61%	57%	64%
Female	39%	38%	39%	43%	36%
Age					
15–24	12%	12%	12%	14%	10%
25–34	17%	17%	16%	23%	13%
35–44	18%	27%	17%	19%	18%
45–54	18%	17%	19%	13%	22%
55–64	19%	17%	20%	21%	18%
65+	16%	9%	17%	10%	20%
Average age in years (range: 15–88)	46	44	47	43	49
Marital Status					
Married	54%	53%	54%	43%	62%
Never married	24%	24%	24%	33%	19%
Widowed/divorced/separated	13%	13%	14%	12%	14%
Currently living with a partner (unmarried)	8%	9%	8%	12%	6%
Residence (NR = 1)					
Rural	52%	52%	52%	16%	75%
Urban	48%	48%	47%	84%	24%
Highest level of completed education (NR = 1)					
Primary/elementary or less	27%	15%	29%	21%	31%
Secondary/high School	44%	38%	45%	42%	45%
Post-secondary/technical/vocational	29%	45%	26%	37%	23%
Employment status (NR = 8)					
Unemployed	44%	43%	44%	43%	45%
Employed (full or part time)	26%	27%	26%	32%	22%
Self-employed	21%	20%	21%	12%	27%
Retired	5%	6%	5%	6%	4%
Student	3%	5%	2%	5%	1%
Average monthly household income (PHP) (NR = 35)					
0–5000	49%	45%	50%	40%	55%
5001–10,000	27%	27%	27%	21%	30%
10,001 and above	18%	24%	17%	28%	11%
Current smoker	7%	6%	8%	15%	3%
TB diagnosis self-reported (imputed)					
Drug susceptible	53% (77%)	76%	77%	60%	88%
Drug resistant	10% (13%)	24%	10%	25%	5%
Unknown	37% (10%)	0%	12%	16%	7%
Phase of treatment					
Intensive	40%	34%	41%	41%	40%
Continuation	28%	27%	28%	29%	26%
Unknown	32%	40%	31%	29%	34%

Abbreviations: NR = No response; PHP = Philippine Pisos.

less than three patients were interviewed per facility, almost two-thirds of whom were male (61%) while a little more than half of the sample was married (54%); the mean age was 46 years (Table 2). Respondents were almost equally distributed across all age groups and 52% lived in rural areas. Not surprisingly, urban dwellers were more frequently treated at urban facilities and rural dwellers treated at rural facilities. Nonetheless, 16% of the patients treated in urban facilities came from rural areas and almost a quarter of the patients attending rural facilities were urban dwellers.

Almost three fourths of the patients were educated beyond the primary school level and 44% had a secondary school degree. Patients with the highest level of education were more often seen at a hospital while those with the least education were seen at non-hospital facilities. When asked about their employment status, the percentage of patients who responded that they were employed (47%) was roughly the same as the percentage of those who were unemployed (44%). About half of the patients had an average monthly household income below 5000 PHP (equivalent to 95 USD). Those with the highest monthly income were frequently seen at urban facilities.

4.2. Analysis

Although the QTSA includes many variables related to quality of care, the Philippines case study focuses on patient and provider perspectives on quality of care, as this aspect of the methods differentiates the approach from other surveys. Observing the differences in response in these two groups provides unique insights into gaps in the quality of services and can be used to identify training and supervision needs. For example, if providers consistently score themselves much higher on the type of information provided to clients than the clients report, this points to the need for additional training or supervision to ensure correct information on TB treatment, infection control, and other topics is consistently provided to clients.

Fig. 2 shows the percentage of providers and clients who responded that they provided or – in the case of the client, were provided – information on specific topics regarding TB treatment, side effects, infection control, and contact tracing. These are key topics that providers are expected to cover in detail as part of counseling for confirmed TB patients undergoing treatment at their facility. The percentage of providers responding that they covered the topics is displayed on the left side, while the percentage of clients responding (unprompted) that they heard information about the topic is displayed on the right side. The line between the two columns shows the differences in percentage reporting the topics covered in counseling. For example, while 77% of providers reported that they discussed duration of TB treatment, only 33% of clients reported knowing how long treatment would last. Likewise, 76% of providers reported that they discussed the importance of taking medications regularly for the full course of treatment, while

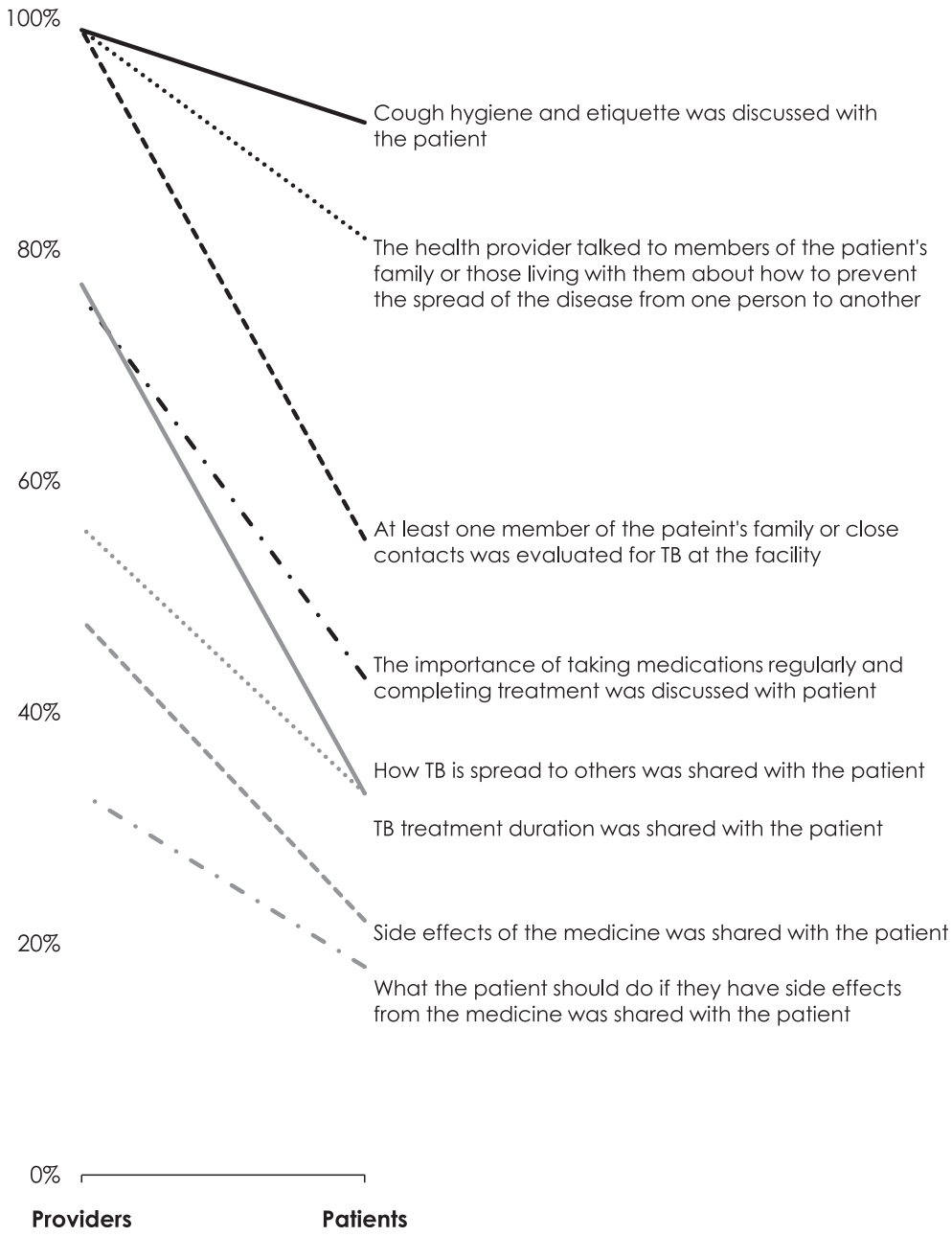

Fig. 2. Comparison of patient vs. provider responses related to patient-provider interactions.
Percent of providers (n = 330) or DS-TB patients (n = 428) who stated that the following topics were shared during patient-provider interaction.

only 43% of clients said they had received this information. The analysis shows that providers consistently reported having covered basic TB information more often than patients reported receiving the information during counseling.

To further explore the reasons why providers and clients may report differences in information covered during counseling, a series of items related to interpersonal counseling and communication (IPCC) skills were analyzed. The hypothesis is that when providers demonstrate use of IPCC skills, the client may be more receptive to the information provided during counseling and more likely to remember details. For example, clients were asked whether or not they talk to the same providers at every follow-up visit and if the providers usually explain things to them in a way they can understand. We compared recall of topics to specific elements of IPCC to determine if there were any statistically significant relationships, using Chi-square analysis. Generally, where clients reported lower levels of IPCC, their recall of key topics covered in counseling was lower. Table 3 provides a summary of findings related to this analysis.

5. Discussion

The QTSA is a comprehensive yet flexible approach to assessing the availability and quality of TB services at different levels of the healthcare system. The methodology yields actionable information that can be used to prioritize interventions needed to ensure that TB screening, diagnosis, and treatment services are available. The value-added of the QTSA is the inclusion of both provider and client perspectives on quality, which can be used to identify the need for specific interventions.

The findings from the Philippines point to a need for improved communication and counseling skills, both in terms of the quality of information provided to clients and the way the information is

Table 3
Bivariate statistical analysis of patient responses.

	The patient was more likely to state that information on the following was shared with them by a health worker						
	How the disease is spread	Taking medicines regularly	Completing treatment	Side effects	What to do if they have side effects		Treatment duration
The patient talks to the same health provider every time they visit the facility	*			**	*		**
Health providers usually explain things in a way the patient can understand	**	***	***	**	***		***
Health providers give the patient a chance to ask questions about anything that concerns them	*			***	***		***
The health providers listen carefully to the patient	***	***	***	*			***
The patient has enough time to discuss their health needs with the health providers				***	***		*

*$p < 0.1$, **$p < 0.01$, ***$p < 0.001$.

delivered. Possible interventions to address this gap include pre-service, in-service, or on-the-job training to introduce or refresh providers on IPCC, as well as integration of IPCC in the general curriculum used to train providers on TB diagnosis and treatment, and what information should be provided to patients. Future data collection could include repeat QTSA or a standardized patient approach to identify any persistent information gaps on the part of providers and clients. Additionally, more detailed data on the duration of assignment and day to day availability of the TB service provider in facilities may be required to identify where IPCC or additional supervision is a promising intervention, as staff rotation and turnover affect the availability of the TB focal point on a day to day basis.

The planning and implementation of the QTSA require a high level of buy-in from all stakeholders and commitment of financial and human resources in order to proceed smoothly. The exercise itself can provide opportunities for capacity building of the NTP and its partners and lead to future investments in quality assessments, as planned in the Philippines. One success story from this case study is the engagement of the LRO and their partnership with the NTP; a follow-up QTSA is planned after quality improvement activities have been implemented. Additionally, the NTP is using the results to update standard operating procedures that will be issued to all facilities that provide TB services. To date, QTSAs have been implemented in Nigeria and the Philippines, and planning is underway to conduct the exercise in Uganda, Ethiopia, and Afghanistan. Each country will generate lessons learned and insights that can be used to refine the methodology and tools.

6. Limitations

The QTSA provides detailed data on quality of services in a standardized way; at the same time the approach has several limitations to consider. First, although the flexibility of the approach is a strength in terms of responsiveness to NTP needs, differences in sampling across countries to address the context of health structures limit opportunities for multi-country analysis and comparison. Related, the inclusion of private sector facilities can be challenging due to lack of interest or a complete sampling frame, which limits comparisons between public and private sector facilities. Second, QTSA includes the perspectives of clients who are already on treatment, which biases the conclusions towards those with access to services; the insights of those who are not seeking services at all (perhaps due to perceptions about quality or how they will be treated at a health facility), are not represented. Third, the phrasing of two questions did not allow for direct comparison of provider and client perspectives on issues related to quality of care. For example, providers were asked if they discussed “TB and TB treatment, including duration and dosage” while patients were asked if the provider discussed “how long your treatment would last and how to take your medicines.” Although intended to capture the same concept, it is possible that patients interpreted “how to take your medicines” to refer to taking medicine with food or water or another aspect of administration other than dosage. A second item asked of providers emphasizing the “importance of taking medicine regularly for the full course of treatment” was phrased “importance of taking medicine regularly and completing treatment” in the patient questionnaire. The questionnaire will be revised in future QTSAs to ensure that these questions are consistently phrased to avoid possible misinterpretation.

7. Conclusion

The QTSA is a standardized yet flexible approach for measurement of quality of TB services at different levels of the health system. It provides important information on provider and client perspectives, as well as a broad range of other data, which can be used to inform NTP strategies and prioritization of actions to improve services.

Acknowledgments

The authors wish to thank the following individuals for their support in developing and implementing this study and reviewing the manuscript: Alexander Golubkov, Kenneth Castro, and Amy Piatek (USAID/Washington); Ernesto Bontuyan (USAID/Philippines); Briccio Echo, Junior (NTP/Philippines), Epimetrics Inc for support in training and supervising data collection, all health facilities, providers and patients who participated or were interviewed for the QTSA, and Stephanie Mullen (John Snow International).

Funding sources

This publication was produced with the support of the United States Agency for International Development (USAID) under the terms of the MEASURE Evaluation cooperative agreement AID-OAA-L-14-00004. MEASURE Evaluation is implemented by the Carolina Population Center, University of North Carolina at Chapel Hill in partnership with ICF International; John Snow, Inc.; Management Sciences for Health; Palladium; and Tulane University. Views expressed are not necessarily those of USAID or the United States government.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jctube.2019.100117.

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J Clin Tuberc Other Mycobact Dis 17 (2019) 100118

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

The high-quality health system 'revolution': Re-imagining tuberculosis infection prevention and control

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ARTICLE INFO

Keywords:
Tuberculosis infection prevention and control
Person-centred care
Health system strengthening

ABSTRACT

The Lancet Commission on High-Quality Health Systems called for a 'revolution' in the quality of care provided in low- and middle-income countries. We argue that this provides a helpful framework to demonstrate how effective tuberculosis infection prevention and control (TB IPC) implementation should be linked with health system strengthening, moving it from the silo of the national TB programmes. Using this framework, we identify and discuss links between TB IPC implementation and patient safety, human resources for health, prioritising person-centred care, building trust in health systems and refining the tools used to measure TB IPC implementation.

Prioritising patient experience has been a recent addition to the definition of high-quality care. In high TB burden settings, the encounter with TB IPC measures may be a TB patient's initial contact with the healthcare system and may cause feelings of stigmatisation. We advocate for re-imagining the way we implement TB IPC, by drawing on the principles of person-centred care through incorporating the experiences of people using healthcare services. Health workers who developed occupational TB also offer a unique perspective: they have both experienced TB IPC and have played a role in implementing it in their workplace. They can be powerful advocates for person-centred TB IPC implementation. Through framing TB IPC as part of health system strengthening and consciously including person-centred perspectives in TB IPC design, measurement and guidelines, we hope to influence future TB IPC research and practice.

1. Introduction

The Lancet Global Health Commission on High-Quality Health Systems (HQHS) has called for a 'revolution' in the quality of care provided in healthcare systems in low- and middle-income countries [1]. This call to define, measure and pursue healthcare quality has been taken forward by leaders in tuberculosis (TB) research and reiterated in the Lancet Commission on Tuberculosis report [2,3]. TB is particularly prevalent in countries with vulnerable health systems, and disproportionally affects vulnerable communities [4]. Similarly, the transmission of TB occurs in healthcare facilities with many other underlying health system weaknesses. These include facilities with staff shortages, long waiting times, uninvolved facility managers, lack of organisational safety culture, inadequate continuing education and training support and poor occupational health and safety practices. Given these constraints, TB infection prevention and control (IPC) implementation may be accorded a lower priority in facilities struggling to deliver basic services. However, we argue that focusing on TB IPC implementation in weak health systems might not only contribute to reducing transmission of TB in facilities but can also be an entry point for broader health system strengthening [5].

In this article we start by examining the evolution of approaches to TB IPC, then argue that TB IPC can embedded within components of a high-quality health system as identified in the Lancet Commission re-

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
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https://doi.org/10.1016/j.jctube.2019.100118

port. We also explain why we call for the “re-imagining” of TB IPC with a person-centred approach.

2. Historical and current context of TB IPC guidelines

Following a series of hospital-based outbreaks of drug-resistant TB (DR-TB) in the United States, one of the first TB IPC guidelines to be used globally was in 1994 by the US Centers for Disease Control [6]. The World Health Organization (WHO) produced its first TB IPC guidelines in 1999 and focused it on healthcare facilities in resource limited settings [7]. These guidelines organised TB IPC interventions according to administrative controls, environmental controls and personal respiratory protection.

The 2019 WHO TB IPC guidelines have similar content to that of the 1999 guidelines. In the guidelines, TB prevention and control are defined as a combination of measures designed to minimise the risk of TB transmission within populations [8]. The update reiterates the limitations of the existing evidence base for most TB IPC sub-components. Proving the effectiveness of TB IPC interventions is challenging due to the infrequency of measurable outcomes like development of TB disease and potential confounders such as high rates of community transmission. The guidelines recommend that TB IPC should be implemented as a package, as the combination of interventions has consistently been shown to be associated with a reduction in the rates of latent TB infection in health workers, although it emphasises the hierarchy of intervention with administrative controls as the most effective [8]. In balancing the costs of TB IPC implementation and the current limited quality of evidence against the risk and impact of nosocomial transmission and occupational TB in health workers, the committee maintained conditional to strong recommendations for implementation of the established guidelines [8,9]. There is also emphasis on integrating TB IPC with broader IPC strategies within countries, thus drawing on an ‘interdisciplinary, multisectoral and multilevel’ approach to implementation.

3. TB infection prevention and control in the context of health systems strengthening

The Lancet Global Health Commission on HQHS set out to answer the question: ‘What should a high-quality health system look like in countries with resource constraints and competing health priorities that aspire to reach the Sustainable Development Goals?’ They developed a HQHS framework that identifies the foundations, processes of care and key outcomes of high-quality care. We used this framework to explore the links between TB IPC and health system strengthening, looking to locate TB IPC within the high-quality health system ‘revolution’ rather than as part of a vertical TB programme. (See Fig. 1).

This expands upon previous arguments made by Harries et al. about the potential that TB IPC initiatives have to link vertical disease-specific programmes with broader health systems strengthening efforts [5]. It also accords with the recommendation in the 2019 WHO TB IPC guidelines to link TB IPC with universal IPC efforts. Similarly, it incorporates the call to integrate TB IPC with occupational health and safety programmes [10,11].

We explore TB IPC as a patient safety initiative which is a process of care of a competent health system and as part of a comprehensive occupational health and safety programme aimed at promoting health worker well-being. Lastly, we look at how we can promote positive user experience in facilities where TB IPC is implemented, specifically as part of person-centred care. We reflect on how we can use a person-centred approach in developing guidelines and in the measurements we use for TB IPC.

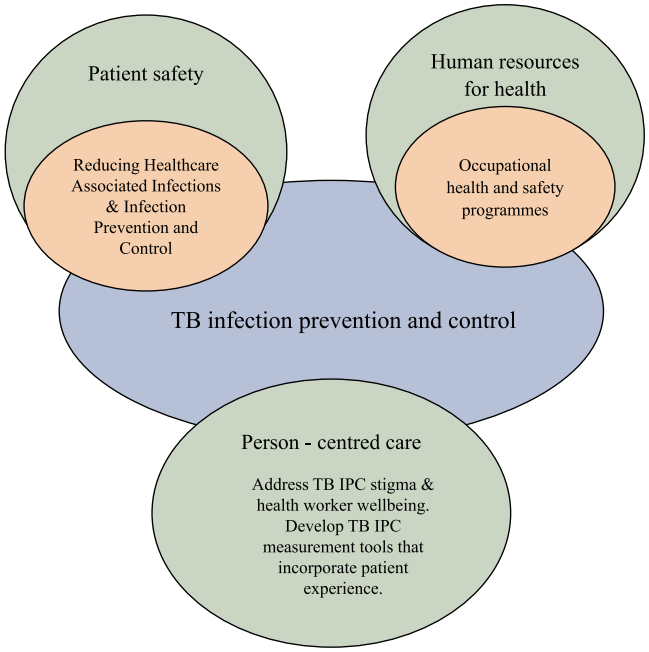

Fig. 1. Embedding TB IPC within broader health system initiatives that link with components of a high-quality health system.

3.1. Human resources for health

There is strong evidence that health workers are at increased risk of developing TB compared to the general population due to occupational exposure [12]. The rates of latent TB conversion and active TB disease in health workers have been used as a proxy to measure the effects of TB IPC implementation [9,13]. This indicator is reported in the WHO Global TB Report, but missing data from high burden countries yields a limited perspective [9].

Programmatically, there has been little integration of TB IPC and occupational health and safety programmes [14] despite joint International Labour Organisation and WHO guidelines promoting such integration [11]. The importance of worker's compensation for health workers who develop occupational TB has also been neglected [14].

Health workers are affected by the nosocomial spread of TB in devastating ways – loss of health, of income, of physical abilities due to side effects of treatment, and in some cases also their health and their lives [13]. TB not only threatens the human right of health workers to a safe and healthy workplace [15] but also the health system's ability to provide care when the health workforce falls ill [16]. There is a growing body of evidence on the relationship between patient safety and health worker burnout [17]. The well-being of overburdened health workers in high TB incidence settings is further threatened by an institutional culture that fails to prioritise TB IPC. We assert that TB IPC should form part of broader strategies to promote human resources for health [18], particularly in low-and middle-income countries where health workers are a scarce and valuable resource [1].

In some settings, TB IPC implementation may be incorrectly seen as a simple delegation to a member of staff, who may not even have received specific TB IPC training [19]. Consequently, poor IPC implementation, just as with poor quality care, may be incorrectly viewed as a failure by health workers at the individual level, attributable to deficits in their knowledge, motivation and behaviour [1]. It is important to acknowledge that health workers are part of teams within organisations that operate within a broader health system. An interplay between these factors will determine whether individual health workers

are likely to implement TB IPC. A renewed focus on the safety of health workers is an opportunity to create organisational support for TB IPC implementation, while affirming to health workers that they are valued as part of the health system.

3.2. Patient safety

"The very first requirement in a hospital is that it should do the sick no harm." - Florence Nightingale, 1863 [20]. An outbreak of extensively drug-resistant TB (XDR-TB) in a rural hospital in South Africa demonstrated that person-to-person transmission was the major driver of drug-resistant TB, rather than acquired resistance through poor adherence [21]. It showed the critical importance of TB IPC for patient safety and preventing antimicrobial resistance.

Globally, there has been renewed focus on preventing healthcare associated infections as part of combatting antimicrobial resistance [22,23]. TB infection control should be linked with such infection prevention strategies, both in preventing transmission of airborne infectious illnesses and developing skills for dealing with outbreaks [8,24].

TB IPC implementation research could similarly draw on work in the patient safety field. This could help to move away from a linear, cause-and-effect pipeline model, to viewing healthcare facilities as complex adaptive systems that function like an ecosystem, with many role players operating within a specific organisational culture [25]. Using a patient safety lens could also enable TB IPC to contribute to public trust in healthcare facilities. Building this trust is, in turn, important for linking people to care, currently identified as a major gap in TB care with the 'missing millions' campaign [2].

3.3. Using a person-centred approach to re-imagine TB IPC

The Lancet Commission on HQHS identified positive user experience as an important feature of high-quality care, drawing on evidence that indicates it is as important as patient safety and clinical effectiveness [26]. Person-centred has been defined as an approach that incorporates four key attributes: a shift from disease-orientated care to a holistic approach that focuses on the person and their context. It involves understanding the individual's experience of illness. It is based on sharing power between health workers and patients and encourages informed decision making and self-determination [27,28]. If we want to reimagine TB IPC using a person-centred approach, we need to understand the experiences patients have in visiting a facility where TB infection control is being implemented and incorporate their perspectives and needs in its re-design. Similarly, health workers who have had occupational TB offer a unique perspective - they have experience of how TB IPC measures are implemented and what makes implementation difficult. They have also been on the "receiving" end of TB IPC as patients. In this article, two co-authors contribute their experiences of occupational TB as health workers and add personal reflections on how this relates to high-quality care. (Box 1 and 2)

3.3.1. Inviting patient perspectives on TB IPC

In high TB burden settings, the encounter with TB IPC measures could be a TB patient's initial contact with the healthcare system. Even if TB IPC is implemented according to the guidelines, there is the risk of patients experiencing shame, stigmatisation and emotional isolation [29]. This compromise of patient dignity in the name of public health, can create an environment where persons with TB are disempowered. Militaristic terms like 'TB suspects', 'defaulters', the need for 'surveillance' and 'cough officers' suggest that preventing TB transmission is a conflict between people with TB and health workers, with the responsibility for achieving 'control' resting on health workers. The Stop TB Partnership's guide against the use of stigmatising language [30] recommends a shift from using the term 'controlling' TB globally to using 'integrated, patient-centred care and prevention' as a central pillar of the WHO's End TB strategy.

Box 1
How it feels to be the 'infection risk'.

> 'I think it is important for health workers to remember the patient in front of you with TB is having a new and frightening experience. When I was diagnosed with XDR-TB I was placed in an isolation room in the intensive care unit. I went from being a dietician to a patient and being free to bedridden in a matter of days. Some of the health workers and cleaning staff were scared of me and did not want to come close to me. They were even scared of objects that were close to me, like my linen or the cutlery I used when eating. The isolation room was lonely and depressing. I remember the day I was discharged from ICU to a new room, where my doctor moved my bed to the window so that I can see the trees outside. That small change, the bit of nature, made me feel hopeful. It made me believe that I could beat this disease. I'm grateful that the doctor initiated this and I think that showed person-centred care. Sensitising health workers to see the person behind the mask can play a big role in making TB IPC less stigmatising.'
>
> -Ingrid Schoeman, dietician and XDR TB survivor

However, merely changing the wording we use to describe facility-based activities that may be stigmatising or discriminatory is insufficient. We need to map a patient's journey through a healthcare facility and look at the impact of TB IPC implementation on their overall experience. In some facilities undergoing TB triage and testing may paradoxically lead to spending a longer time in facilities, as patients wait for TB test results. Patient counselling regarding the rationale for TB testing is often absent. Surgical masks, which patients being investigated for pulmonary TB are asked to wear, have been described as a public TB label that leads to shame [29].

We should explore these experiences with patients and seek ways in which they might be modified. This could include distributing masks to all patients visiting a healthcare facility or developing guidelines on how to explain the use of masks in healthcare facilities. We can think creatively about ways in which the appearance of masks can modify perceptions through redesign. These strategies should form part of the overall aim of sensitising health workers to the importance of person-centred TB care [Box 1].

3.3.2. Inviting perspectives from health workers who had occupational TB

Health workers who have had occupational TB are often hesitant to disclose this to their colleagues, due to the stigma associated with the disease [31]. Their reported experiences include delays in diagnosis, struggle to access treatment and compensation, and life-long physical and emotional sequelae [14,32]. However, health workers who have developed TB who decide to return to the clinical environment are faced with an enhanced realisation of the importance and difficulties of TB infection control implementation [Box 2]. Inviting health workers to share their experiences with occupational TB has been successfully combined with TB IPC training, changing the perception of risk of other health workers while providing the tools to create a safe working environment [33,34]. Although the responsibility lies in the first instance with managers of healthcare organisations to protect and support health workers, health workers should not underestimate their collective advocacy power. Health workers who have had occupational TB can play an important role in motivating for TB IPC implementation, both on a local facility-, national- and global-level [35].

Box 2
Occupational TB changed my perspective.

> 'When I was diagnosed with TB, I was shocked. It was during my busy final year at medical school and everything came to a standstill. There were many difficulties, including being hospitalised with a drug induced liver injury. Having TB completely changed the way I looked at infection control in the hospital environment. I became very aware of the risks we were all exposed to and the need to take precautions. I always wore a mask when I was working in wards and areas of potential risk. But it was very hard. I was ignored by my seniors and ridiculed by my peers as the person who always, "unnecessarily" wore "that mask". They simply did not see it as a priority. There was a general attitude that doctors are invincible. And as junior you take the lead from how your seniors are behaving. We need to pay attention to training students in TB infection control, and also look for good role models when they do their clinical training. We also need to promote an organisational culture where health workers are encouraged to look after their own health. Providing platforms where health workers who have had TB can share their stories is one way in which we can start this change.'
>
> -Clio Pillay, medical doctor and TB survivor

3.3.3. Person centred TB IPC guidelines

Person-centred TB IPC might suggest tensions between health worker and patient needs or priorities. For example, when using drama techniques in a research exercise to act out TB IPC implementation, health workers expressed anxieties about 'difficult patients' as an obstacle to TB IPC [36]. However, the two should not be contradictory: health workers who feel safe and valued are more likely to be retained in the field, and also able to provide empathic, person-centred care [18]. Similarly, for patients there is intrinsic value in receiving a service that has a positive user experience, which influences intention to return for follow up visits, adherence to treatment, and, ultimately, trust in health systems [1,37]. A key message that should be part of TB IPC training and communication between health workers and patients is that TB IPC aims to ensure individual and communal safety in all health facilities.

The duration of infectiousness of a person with pulmonary TB on effective therapy is important for TB IPC, as this has implications for how long patient-focused TB IPC measures should be implemented in healthcare or congregate facilities once someone has started TB treatment. Country-based guidelines often state that for drug-sensitive TB, adequate treatment for two weeks or more is associated with non-infectiousness [38] although the evidence for this duration is not grounded in robust data [39]. Data using the human to guinea pig transmission model suggest that patients on effective therapy are less infectious to guinea pigs than those who are not receiving effective therapy and that these effects may be rapid (days rather than weeks) and precede smear conversion [40]. The 2019 WHO TB IPC guidelines omit recomendations on how long patient-focused TB IPC should be implementated, stating limited data as reason. We assert that although data are limited, this should not preclude having guidelines. The absence of guidance transfers this decision onto individual health workers who are then expected to make decisions for each individual patient, which may be poorly founded. It also risks TB IPC efforts being focused on areas where they may have little impact, for example, patients with DR-TB on effective therapy who have had negative sputum cultures. It is disempowering for someone diagnosed with TB, as they do not have a reference for duration of infectiousness to use when interacting with health workers, employers, or family members. $U = U$ is an example of an HIV campaign that focuses on empowering patients with knowledge about HIV transmission, emphasising that an Undetectable viral load equals Untransmittable HIV [41] This demonstrates the shift in power from health workers to patients that is a key part of person-centred care, and should be a future goal for TB IPC guideline translation and public health campaigns.

The 2019 WHO TB IPC guidelines primarily provide guidance for transmission in health facilities but mentions applicability to other high-risk congregate settings and the role of community health workers in facilitating early diagnosis [8]. Interventions for household settings were not addressed due to the lack of directly applicable data that could be systematically evaluated. Although it is mentioned that patients and family members providing care should receive clear guidance and indications on IPC, no recommendations are provided in the guidelines. Person-centred care requires consideration of the support that is needed to navigate each step of their TB care journey. This includes clear recommendations on duration of IPC implementation at healthcare facilities, home and about return to work, as well as helping patients to address the stigma associated with TB transmission.

3.4. Measuring what matters

The Lancet Global Health Commission on HQHS placed emphasis on developing measurement tools that 'measure what matters' to patients and health workers, is simple to use and provides real-time information [1]. Currently we have two broad strategies to measure TB IPC implementation: indicators that measure risk of current or recent exposure to TB, and indicators that measure infection status or disease as outcome. Process indicators such as time-to-diagnosis and time-to-treatment initiation are helpful to indicate whether a facility is able to minimise transmission risk through accelerating rapid access to treatment. This is encompassed in the FAST strategy, which entails Find cases Actively by cough surveillance and rapid molecular sputum testing, Separate safely, and Treat effectively [42]. Periodic evaluation tools, including the WHO TB IPC checklist [43], cover all of the components of TB IPC implementation, and provide an overall view of gaps in implementation which can be re-evaluated in subsequent reviews. Continuous evaluation tools like carbon dioxide monitoring use proxy measures to assess ventilation [44]. Levels above a certain target could trigger a response from managers to intervene and improve conditions.

Outcome indicators can be quantified by the rate of latent TB conversion in health workers, measured with tuberculin skin tests (TST) or Interferon-Gamma Release Assay (IGRA) tests, which should be performed at the start of a health worker's employment in a given facility and then serially repeated. These tests present different challenges, notably TST confounding by Bacillus Calmette–Guérin vaccination and unexplained IGRA reversions [45]. Although not a proxy for recent infection, the rate of occupational TB disease in health workers is necessary information for action to protect health workers and patients [14]. In high incidence TB settings where infection may be community acquired, special effort is needed to acquire information on occupational risk given the impracticability of laboratory matching of MTB strains [46]. TB in health workers should be recorded to allow an epidemiological analysis of group risk and trends, and outbreak analysis of specific risk settings where indicated.

Currently, there is a gap in our measurement toolbox for a strategy that captures patient and health worker experience. This gap could be closed through qualitative evaluation of patient perceptions of TB IPC implementation, although people could be hesitant to criticise care they receive. Another option would be to include participant observation techniques, where TB IPC implementation is observed over a longer period of time. Standardised patients (also called 'mystery patients') have been used to evaluate quality of TB care in many high TB burden countries [47]. Actors are trained to present with symptoms of TB, which is then used to compare diagnostic investigations and management plans across different facilities, in different countries. While the experiences of actors would differ to those seeking care for illness, this technique offers a way to incorporate patient experience in IPC measurement. We could consider using standardised patient facility visits to measure TB IPC, combining process measures (such as queue time),

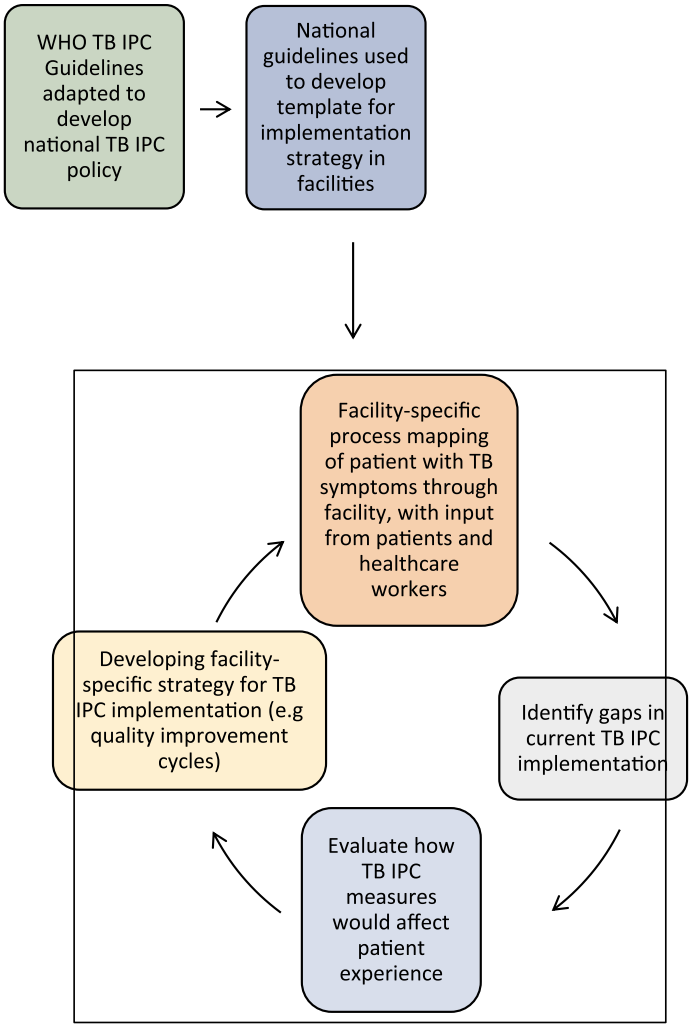

Fig. 2. Incorporating person-centred principles in TB IPC implementation.

with periodic evaluation tools (like the use of masks by patients, respirators by staff, and subjective reports of air quality) with reflections on overall experience of utilising care, including potentially stigmatising experiences.

4. Mapping the path towards re-imagining TB IPC

Re-imagining TB IPC using a person-centred approach can be a helpful tool when developing implementation strategies for national TB IPC policies (Fig. 2). The process could involve inviting health workers and patients to contribute to facility-specific implementation strategies as has been done in Romania [48]. Research methodologies that embrace this approach include human centred design and participatory action research.

5. Conclusions

The neglect of TB IPC remains an important gap in the provision of high-quality care in high TB burden countries. While there are limitations in our understanding of the effectiveness of different components of the TB IPC package, there is consensus about the risks faced by health workers and patients in facilities. There is an opportunity to shift TB IPC from the silo of national TB programmes and embed it within health systems strengthening efforts. We have used components of the Lancet Commission on HQHS framework to explore those links. This includes viewing TB IPC as part of patient safety initiatives, including those focused more broadly on general IPC and combating antimicrobial resistance. TB IPC should also be seen as a component of a comprehensive occupational health approach to promoting the well-being of health workers as part of the foundation of a strong health system.

The HQHS framework emphasises the importance of prioritising health user experience as component of high-quality care. We argue that this requires making person-centred care an essential part of re-imagining TB IPC implementation. This will only be achieved if we invite patients and health workers who have been affected by TB to contribute their perspectives. We need to keep the experiences of those seeking care for TB at the core when developing TB IPC guidelines and implementation strategies. This will enable us to create safe and compassionate healthcare environments that provide high quality care.

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J Clin Tuberc Other Mycobact Dis 17 (2019) 100121

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Quality of life with tuberculosis

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ARTICLE INFO

Keywords:
Quality of life
Questionnaire
Stigma
Tuberculosis

ABSTRACT

Tuberculosis diagnosis and treatment currently revolves around clinical features and microbiology. The disease however adversely affects patients' psychological, economic, and social well-being as well, and therefore our focus also additionally needs to shift towards quality of life (QOL). The disease influences all QOL domains and substantially adds to patient morbidity, and these complex and multidimensional interactions pose challenges in accurately quantifying impairment in QOL. For this review, PubMed database was queried using keywords like quality of life, health status and tuberculosis, and additional publications identified by a bibliographic review of shortlisted articles. Both generic and specific QOL scales show a wide variety of derangements in scores, and results vary across countries and patient groups. In particular, diminished capacity to work, social stigmatization, and psychological issues worsen QOL in patients with tuberculosis. Although QOL has been consistently shown to improve during standard anti-tubercular therapy, many patients continue to show residual impairment. It is also not clear if specific situations like presence of comorbid illnesses, drug resistance, or co-infection with human immunodeficiency virus additionally worsen QOL in these patients. There is a definite need to incorporate QOL assessment as adjunct outcome measures in tuberculosis control programs. Governments and program managers need to step up socio-cultural reforms and health education, and provide additional incentives to patients, to counter impairment in QOL.

1. Background

Worldwide, tuberculosis (TB) continues to be an important public health issue, and a major cause of morbidity and mortality. Despite advances in diagnosis and therapy nearly ten million incident TB cases were reported, and an estimated 1.6 million deaths occurred due to TB, globally in 2017 [1]. Almost a quarter of the world's population is latently infected with TB, and therefore at risk of progressing to active disease sometime during their lifetime [1].

According to the World Health Organization, health is defined as a state of complete physical, mental, and social well-being and not a mere absence of disease or infirmity. The impact of any disease, especially a chronic illness like tuberculosis, on an individual patient is therefore often all-encompassing, affecting not only his physical health but also his psychological, economic, and social well-being.

At present, the TB control services are geared towards optimizing microbiological cure, and using this parameter as an indicator for successful treatment. Although this is extremely important from a public health perspective, such an approach does not adequately address the physical, mental and social suffering of patients due to TB [2]. Patients suffer not only because of the symptoms of the disease, but also because of the resultant general deterioration in their quality of life (QOL). Despite this, patient perceptions about disease and their health have remained largely unknown.

QOL is a broad and complex multidimensional concept that incorporates physical, social, psychological, economic, spiritual and other domains. It is therefore difficult to define and measure, but may be broadly described as individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns [3]. QOL therefore is an expression of patient preferences and values rather than clinician's assessment. For the latter, one simply needs to ask the patient "How high is your fever?", while for the former, patient response to the question "How much are you bothered by your fever?" or "To what extent do you feel that fever prevents you from doing what you need to do?" can be recorded. Self-reported health-related QOL is therefore an important adjunct measure in understanding and quantifying the actual impact of TB on patients.

This review was conducted to summarize the various issues related to QOL among patients with all forms of TB. A broad search was conducted through the PubMed platform using keywords like quality of life, health status and tuberculosis. Relevant publications for detailed evaluation were identified through an abstract review of the search results. Additional key references were identified from bibliography of

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https://doi.org/10.1016/j.jctube.2019.100121

shortlisted publications during their full-text review. Data from large and well-conducted studies was preferentially used to summarize and tabulate important findings.

2. Instruments for describing and quantifying QOL in TB

An objective assessment of patient's QOL attempts to quantify the functional effects of an illness and its consequent therapy on a patient, as perceived by that patient. A wide variety of questionnaires and scales have been employed to evaluate self-rated QOL in patients with active TB [4–7]. Some of these evaluate QOL holistically, whereas others focus on specific domains like physical health or psychological morbidity.

The simplest approach to QOL assessment is using only one summary item as a global descriptor of QOL. This can take the form of a single question, a visual analogue scale (VAS), or a standard gamble approach [8–13]. However, this is likely to miss important information on several important facets of QOL that may be important to TB patients. More and more investigators therefore rely on standardized multidimensional scales to obtain a more comprehensive picture of the relevant facets and domains. Several of these instruments are generic, which means that they can be used across a wide spectrum of disorders (and even among healthy individuals). A commonly used scale in TB research is Short Form 36 (SF-36) [13–31]. This gives scaled scores across eight domains – Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, and Mental Health, and two summary scores – Physical Component Score and Mental Component Score. The EQ-5D, developed by the European QOL Group, is another commonly used instrument [10,30–34]. It has two components – health state description and evaluation. In the description part, health status is measured through five dimensions (5D) – mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. VAS is used to assess overall health status in the evaluation part. The abbreviated World Health Organization Quality of Life scale (WHOQOL-Bref) is another popular generic instrument [35–42]. This 26-item instrument evaluates QOL across four domains – Physical, Psychological, Social relationships, and Environment. Some other generic scales used include Medical Outcome Survey (MOS) [9] Social Functioning 12 (SF-12) [32,43], variants of the WHOQOL scale family [19,44,45], and other uncommon or in-house instruments [46–48].

Although generic measures permit comparisons across interventions and diagnostic categories, they fail to adequately capture facets particularly important to a particular disease. More specific instruments may prove better in this regard, and these can be either system-specific or disease-specific. Since lungs are the predominant organ involved in TB, it is intuitive that respiratory-system specific questionnaires may be appropriate in pulmonary TB. The St. George's Respiratory questionnaire (SGRQ) has been used in some studies [32,49,50]. It has 76 items, whose responses can be aggregated into an overall score and three domain scores for Symptoms, Activity and Impact. Another approach is to use disease specific instruments. Unfortunately, TB-specific QOL instruments have not been widely used. Dhingra and Rajpal proposed a disease-specific QOL instrument (DR-12) from data on TB patients treated under programmatic conditions in India [51]. This scale has 12 items over two domains – Symptoms, and Sociopsychological/exercise adaptation. However, scale development was not scientifically rigorous, and phrasing of items suggests it to be more of a health status rather than QOL instrument. It has been sparsely used [52,53]. Another disease specific instrument FACIT-TB (Functional Assessment of Chronic Illness Therapy – Tuberculosis) has been developed, and psychometrically validated in Arabic, for quantifying QOL in TB patients in Iraq [54,55]. This questionnaire, which is a part of the FACIT measurement system, consists of 45 items across five domains – Physical well-being, Social and economic well-being, Emotional well-being/Stigma of having TB, Functional well-being, and Spiritual well-being. More recently, the generic module of the Chinese Quality of Life Instruments for Chronic Diseases (QLICD) has been modified by addition of a pulmonary TB scale. The resultant QLICD-PT instrument has three domains (with 28 items) for general QOL and one pulmonary TB specific domain (with 12 items) [56]. The scale has been shown to have acceptable degree of validity, reliability and responsiveness. To the best of our knowledge, both these new QOL instruments have not been used by other independent researchers.

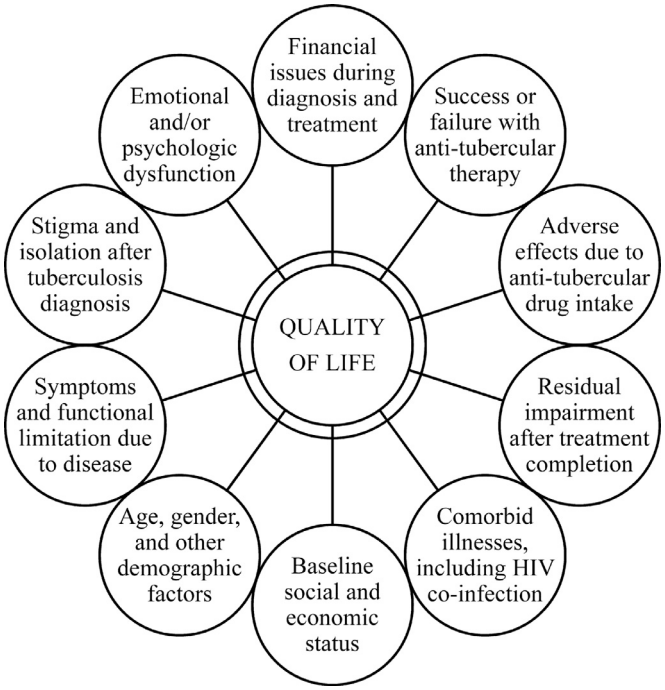

Fig. 1. Important determinants of quality of life with tuberculosis.

In addition, more specific instruments have been used to explore individual QOL domains in TB. This is most evident in evaluation of psychological morbidity, where several tools such as General Health Questionnaire 12 (GHQ12) [57], Patient Health Questionnaire (PHQ-9) [12,58–60], Centre for Epidemiologic Studies Depression Scale (CES-D) [31], State-trait Anxiety Short-Form (STAI-6) [31], Kessler-10 item scale (K-10) [45,61], Hospital Anxiety and Depression Scale (HADS) [25,32], and others have been used.

3. QOL evaluation in TB patients

QOL can be influenced by several patient, disease, and treatment-related factors in TB patients (Fig. 1). Few investigators have evaluated QOL in adult patients through cross-sectional studies (Table 1). In general, QOL of TB patients is poorer as compared to healthy individuals across most domains, with physical functioning domain affected more severely than others [5,14,19,25,31,35–38,62]. Patients with active TB generally also perceive their health status to be worse as compared to people with latent TB or previously cured TB [5,8,13,16,17,21]. However, the relative contribution of TB towards impairment of QOL can sometimes be problematic as several patients have other comorbid illnesses or socio-economic problems [63]. Overall, QOL seems largely independent of age and gender [48,64]. However, some studies report advancing age to be negatively correlated with QOL [10,13,38]. Others report worse QOL among women [17,36,38]. One Indian study has shown higher QOL scores for physical and psychological domains among women, probably suggestive of better coping strength [36]. Also, lower education level and poor socio-economic status may be associated with greater impairment of QOL [17,48]. Patients with relapse or retreatment tend to show the greatest impairment in QOL [36].

Table 1
Characteristics of selected recent studies in tuberculosis patients reporting cross-sectional data from multi-dimensional quality of life scales.

Investigator	Study setting	Study subjects	HIV+	Comorbid disorders	Non-TB comparator groups	QOL measures	Timing of QOL assessment
Dion et al. [30]	Public hospital in Canada	17 culture confirmed pulmonary TB patients	None	Excluded	25 latent TB, 8 previously treated TB	SF-36, EQ-5D, VAS, Standard gamble	Before or during treatment
Duyan et al. [48]	Hospital in Turkey	120 inpatients with pulmonary TB	None	Excluded	None	In-house instrument	At least one month after hospitalization
Dhuria et al. [35]	DOT centres in India	90 patients with pulmonary TB (20% retreatment cases)	NR	Excluded	90 age and gender matched healthy persons	WHOQOL-Bref	Within 3 days of initiating TB treatment
Guo et al. [13]	TB clinic in Canada	84 patients on TB treatment	NR	45%	78 persons on treatment for latent TB	SF-36, VAS, Health Utilities Index	Within 2 months of diagnosis of active/latent TB
Unalan et al. [17]	TB dispensary in Turkey	196 patients with TB	NR	26.5%	196 healthy persons, and 108 with latent/healed TB	SF-36	During treatment
Deribew et al. [44]	Hospitals in Ethiopia	124TB/HIV co-infected patients	100%	Excluded	467 HIV+ patients	WHOQOL-HIV	During intensive phase of TB treatment
Babikako et al. [9]	TB clinics in Uganda	133TB patients	50%	NR	None	Medical Outcome Survey, VAS	Variable – before, during, or end of treatment
Chung et al. [37]	Hospitals in Taiwan	140 patients with pulmonary TB	NR	NR	130 age and gender matched healthy persons	WHOQOL-Bref	Within 2 weeks of initiating treatment
Kittikraisak et al. [10]	Hospitals in Thailand	92TB patients	53.3%	NR	49 HIV+ patients, 81 patients with treated TB	EQ-5D	Variable
Louw et al. [46]	Primary care clinics in South Africa	4900TB patients	59.9%	NR	None	Social functioning 12	Within one month of treatment initiation
Unalan et al. [19]	TB sanitorium in Turkey	92TB patients	NR	NR	None	SF-36, WHOQOL-100	Early during treatment
Sharma et al. [39]	TB clinic in India	60 MDR TB and 60 retreatment TB patients	None	Excluded	60 persons (details NR)	WHOQOL-Bref	Variable during treatment
Kisaka et al. [24]	Hospital in Uganda	210 smear positive pulmonary TB patients (one third each at diagnosis, end of intensive phase, and treatment completion)	59%	NR	None	SF-36	Variable during treatment
Dos Santos et al. [25]	Hospital in Brazil	86 inpatients with pulmonary TB	37.2%	3.5%	None	SF-36	NR
Roba et al. [27]	Hospitals, health centres in Ethiopia	300TB, and 100 MDR TB, patients	13.8%	NR	None	SF-36	At least one month after treatment initiation
Shahdadi et al. [28]	Diabetes clinic in Iran	62 diabetic patients with pulmonary TB	NR	100%	None	SF-36	NR
Laxmeshwar et al. [42]	TB clinics in India	95 MDR TB patients	4.2%	NR	None	WHOQOL-Bref	Variable during treatment
Sineke et al. [29]	TB treatment site in South Africa	149 patients with drug-resistant TB	77.9%	4.4%	None	SF-36	NR

DOT Directly observed treatment, EQ European Quality of Life, HIV Human immunodeficiency virus, MDR Multi-drug resistant, NR Not reported, QOL Quality of life, SF-36 Short Form 36, TB Tuberculosis, VAS Visual analogue scale, WHOQOL World Health Organization Quality of Life.

4. Physical functioning and role limitation

Physical functioning is a reflection of an individual patient's capacity to carry out basic day-to-day activities, and role functioning encompasses a person's ability to function in designated roles at work, society, and home. The physical effects of TB are highly variable, and depend on patient's premorbid health status, severity of symptoms, and duration of illness. Debilitating somatic symptoms are often the hallmark of active TB, and patients are often specially concerned about generalized weakness and weight loss [63]. Poor performance status has been shown to be a strong predictor of mortality in Japanese patients with active pulmonary TB [65]. The diagnosis of tuberculosis in the family increases the workload on the family primary caregivers (wives and mothers), and diminishes the caregiver's ability to generate income and care for the remainder of the family [66].

5. Social functioning

One of the most important facets affecting QOL is the stigma associated with TB, both at the family and the community level [63,67]. In a study from urban Zambia, 82% TB patients reported stigma [68]. In another study from southern India, 51.2% TB patients felt stigmatized, and stigma was greater among sputum smear positive patients [69]. In a study using an improvised scale to quantify stigma, mean TB-related stigma score in Chinese patients was 9.33 (maximum scale score of 27) [70].

TB is most commonly stigmatized due to the perceived risk of transmission from patients to other susceptible community members [71]. In other instances, the reasons could relate to the association of TB with HIV infection or low socio-economic status, and traditional myths about TB [68]. Patients often report issues such as loss of friends, lack of respect among colleagues, and social isolation at workplace [72,73]. The stigma associated with disease may be greater among women and inability to get married, and divorce, have both been commonly reported in developing countries [74–76]. Contrary to popular belief, stigmatization of TB patients is not just confined to developing countries, but may be also be widely prevalent in low-TB burden countries as well [77].

6. Emotional and psychological health

A wide range of psychological reactions are observed once TB is diagnosed. Worry is a common feeling after disclosure of diagnosis [15,78]. The diagnosis may come as a shock to the patient, and there are instances of denial of diagnosis [63,78,79]. Another common feeling at diagnosis is fear of seclusion and social boycott, and sometimes even death [63,75]. In particular, hospitalization and isolation of patients (a common practice in several low-burden countries) can have important emotional and psychological ramifications [63,80].

Depressive symptoms such as low mood, tiredness, reduced sexual desire, sleep disturbances, anorexia, loss of weight, etc. are commonly seen [57]. Cross-sectional, community-based data from the World Health Survey on nearly 250,000 adults from low- and middle-income countries has shown a much higher prevalence of depressive episodes in patients with TB (23.7% vs. 6.8% among those without TB) [81]. The odds for subsyndromal depression and brief depressive episodes were also higher among TB patients. Interaction analysis showed that depression amplified difficulties in self-care in TB patients but did not affect other health status domains. Using PHQ as a screening tool, a Nigerian study identified 27.7% patients with depression [58]. In another study on patients attending public primary care clinics in South Africa, 32.9% showed psychological distress and 8.3% were receiving anti-depressant therapy [61]. On multivariable analysis older age, lower formal education, and poverty were independently associated with psychological distress. A cross-sectional study in Brazil on hospitalized TB patients found that 31.4% had depression, 38.4% had anxiety, and 23.3% suffered from low self-esteem [25]. Patients with depression or anxiety also had lower overall QOL scores as compared to patients without. In a study from Ethiopia, 53.9% patients were categorized as having probable depression at start of treatment, and QOL impairment, loss to follow-up, and mortality were significantly higher among this subset [12]. A study from southern India reported depression in 40.8% TB patients receiving anti-tubercular therapy (ATT) [60]. Most patients had mild or moderate depression, with a higher prevalence in pulmonary as compared to extrapulmonary disease (80.4% vs. 19.6%).

Adequate treatment can ameliorate some of these psychological issues. A South African study using HADS showed that both anxiety and depression domains changed by +95% from a state of 'moderate problems' to a state of reporting 'no problems' [32].

7. Economic well-being

Patients of TB are most commonly in the economically productive age group, and hence the resultant economic cost is rather substantial. Several patients and families feel the financial burden of disease, resulting both from cost of treatment as well as indirectly from loss of wages [79,82]. A study in Thailand noted that adult TB patients spent more than 15% of their income on out-of-pocket expenses for diagnosis and therapy of TB, and often needed to take loans or sell property [66]. Another study on southern India reported expenditure up to 40% of patients' income, with non-medical expenses (such as travel costs), and diagnosis/treatment in the private sector, also imposing a disproportionate burden on poor households [82].

8. Effect of treatment

Few investigators have longitudinally evaluated QOL in cohorts of adult patients on ATT, mostly from endemic or high-burden countries (Table 2). The greatest improvement in QOL seems to occur within the initial 2–3 months of therapy [5]. A study from South India reported improvement in patient perceptions about physical and mental well-being after treatment [15]. In a study from northern India, QOL improved significantly at end of intensive phase, and further at end of treatment [41]. Similar results were reported from another north Indian study, where overall QOL, and all domains except social, improved after treatment for three months, and all domains improved further at treatment completion at six months [36]. Another study from north India showed that QOL improved across all domains among patients showing microbiological conversion on sputum examination, but not among those with persistent sputum positivity at end of intensive phase of treatment [38]. In a study from Pakistan, mean QOL scores more than doubled in TB patients after completing ATT [34]. A study from China reported gradual improvement in QOL with TB treatment, with physical function, role-motional, bodily pain, and general health domain scores comparable to healthy individuals after treatment [14]. In one study from Iraq that longitudinally used a TB-specific QOL questionnaire, physical well-being, functional well-being, and the total QOL scores were significantly increased after two months of ATT [55]. All QOL subscales, except social and economic well-being and spiritual well-being, improved at end of treatment, and the total QOL score had a statistically significant contribution towards predicting likelihood of favourable response to ATT. In a study from Yemen, both physical and mental summary scores improved at end of intensive phase of treatment [23]. While the former improved further at treatment completion, the latter remained largely static, with mean scores still below population norms. In a study from Indonesia, 94% patients showed a clinically significant improvement in SGRQ scores after two months of treatment, and 80% achieved additional significant improvement by end of treatment at six months [50]. Progressive improvement across all QOL domains was also reported among Malaysian patients receiving ATT [20]. This suggests that QOL correlates with other objectives measures

Table 2
Characteristics of selected recent longitudinal studies reporting data from multi-dimensional quality of life scales among patients receiving treatment for tuberculosis.

Investigator	Study setting	Study subjects	HIV+	Comorbid disorders	Non-TB comparator groups	QOL measures	Timing of serial QOL assessment
Chamla, 2004 [14]	TB center in China	102 patients with pulmonary TB	NR	NR	103 age and gender matched healthy persons	SF-36	ST, EIP, ET
Rajeswari et al. [15]	TB units in India	610 patients with TB	NR	NR	None	SF-36	ST, EIP, ET
Marra et al. [16]	TB clinic in Canada		7.7%	10.6%	102 persons with latent TB	SF-36	Baseline, 3 months, 6 months
Dhuria et al. [36]	DOT centres in India	90 patients with pulmonary TB	NR	Excluded	90 persons (details NR)	WHOQOL-Bref	Baseline, 3 months, 6 months
Maguire et al. [50]	TB clinic in Indonesia	115 patients with pulmonary TB	4.5%	NR	None	SGRQ	Baseline, 2 months, 6 months
Guo et al. [18]	TB control clinics in Canada	89 patients with TB	NR	46%	None	SF-36	Baseline, 3 months, 6 months
Kruijshaar et al. [31]	Clinics in UK	61 patients with TB (20 had extrapulmonary disease)	NR	NR	None	SF-36, EQ-5D	Baseline, 2 months
Aggarwal et al. [38]	DOT centres in India	1034 patients with pulmonary TB	NR	NR	None	WHOQOL-Bref	ST, EIP, ET
Deribew et al. [45]	Hospitals in Ethiopia	124TB/HIV coinfected patients	100%	Excluded	465 HIV+ patients	WHOQOL HIV-Bref	During intensive phase, 6 months later
Atif et al. [20]	Chest clinic in Malaysia	216 patients with pulmonary TB	None	Excluded	None	SF-36	ST, EIP, ET
Bauer et al. [21]	Hospitals in Canada	48 patients with pulmonary TB (8 had extrapulmonary disease)	NR	Excluded	105 persons with latent TB, 110 healthy persons	SF-36	1, 2, 4, 6, 9 and 12 months
Dujaili et al. [55]	Specialist Respiratory Centre in Iraq	305 patients with pulmonary TB	None	Excluded	None	FACIT-TB	ST, EIP, ET
Ahmad et al. [22]	Hospital in Pakistan	81 patients with MDR TB	NR	12.3%	None	SF-36	Baseline, 12 months, ET (>20 months)
Jaber et al. [23]	TB centres in Yemen	243 patients with TB	NR	16.5%	None	SF-36	ST, EIP, ET
Louw et al. [43]	Primary care clinics in South Africa	1196 patients with TB	NR	36.8%	None	SF-12	Baseline, 6 months
Mthiyane et al. [47]	Hospitals in South Africa	62TB/HIV coinfected patients	100%	Excluded	20 HIV+ patients	FAHI	Baseline, 3 months, 6 months, 12 months
Kastien-Hilka et al. [32]	Primary care clinics in South Africa	131 patients with pulmonary TB	None	20.6%	None	SF-12, EQ-5D, SGRQ	ST, 4, 8, 16 weeks, ET
Ramkumar et al. [26]	DOT centres in India	92 patients with TB	NR	NR	83 age and gender matched healthy persons	SF-36	ST, 3 months, ET
Siddiqui et al. [53]	DOT centres in India	316 patients with TB (50 had diabetes)	NR	15.8%	None	DR..−12	ST, EIP, ET
Singh et al. [40]	Hospital in India	50 patients with pulmonary TB	NR	NR	50 age and gender matched healthy persons	WHOQOL-Bref	Baseline, 2 months, 6 months
Jorstad et al. [33]	Hospital in Tanzania	69 patients with extrapulmonary TB	23.2%	NR	63 patients without TB	EQ-5D	ST, 2–3 months, ET
Saleem et al. [34]	TB clinic in Pakistan	226 patients with pulmonary TB	NR	Excluded	None	EQ-5D	ST, EIP, ET
Dar et al. [41]	Hospital in India	198 patients with pulmonary TB	NR	NR	None	WHOQOL-Bref	ST, EIP
Jaber and Ibrahim [89]	TB centres in Yemen	80 patients with MDR TB	NR	28.8%	None	SF-36	Baseline, ET, 12 months after ET

DOT Directly observed treatment, DR−12 Dhingra and Rajpal scale, EIP End of intensive phase, EQ European Quality of Life, ET End of treatment, FACIT Functional Assessment of Chronic Illness Therapy, FAHI Functional Assessment of HIV Infection, HIV Human immunodeficiency virus, MDR Multi-drug resistant, NR Not reported, QOL Quality of life, SF-12 Social Functioning 12, SF-36 Short Form 36, SGRQ St George's Respiratory Questionnaire, St Start of treatment, TB Tuberculosis, WHOQOL World Health Organization Quality of Life.

of response to therapy. In a study from Uganda, QOL progressively improved as the patients' duration of TB treatment increased [9]. In a study from Uganda, both physical and mental component summary scores significantly improved at end of intensive phase, and further by end of treatment completion [24]. In two studies from South Africa, QOL improved significantly during treatment and at treatment completion, with biggest gains in the physical health scores [32,43]. No socio-demographic traits were significantly associated with this improvement, suggesting that TB treatment was the principal determinant of change in QOL. Maximum improvements were seen in physical, followed by psychological domain.

Relatively little information is available from low TB burden countries. In a study from Canada, QOL was better in most domains after TB treatment, with most significant improvements observed in vitality, physical functioning, role physical, social functioning, and role emotional domains [16]. In contrast, another study on Canadian patients showed that while mental component summary scores improved throughout treatment, the physical component summary score improved only slightly during the 2–4 month period and then slightly declined again [21].

On the other hand, adverse effects from ATT may sometimes paradoxically worsen QOL. For instance, gastrointestinal disturbances, visual impairment or peripheral neuropathy may hamper physical functioning [63]. A Canadian study reported that major, but not minor, adverse drug reactions were associated with significant reductions in a few mental and physical subscales of SF-36 [18]. This study also showed that patients with low pre-treatment QOL scores were more likely to experience adverse drug reactions. A study from UK suggested that while the psychological burden from depression improved with treatment, that with anxiety did not [31].

Although most patients report normal or near-normal QOL after successful TB treatment, a small proportion can still show residual impairment of QOL [15,16,20,23,31,38,49,83]. In particular, a recent systematic review suggests that psychological well-being and social functioning continue to remained impaired even after successful microbiological cure with treatment [62]. In addition to persistent physical changes, patients also report continued emotional distress or impaired mental health even after completion of ATT [20,84].

The long term impact of successful TB treatment on QOL is not clear. Few studies show that the overall QOL in patients previously treated 1–2 years back was largely similar to that in the general population [21,30,83,85]. Other investigators report substantial impairment in QOL, even several years after completing treatment, although it was still better when compared to other chronic respiratory disorders [86]. Apart from the global assessment, individual QOL facets may be important for patients. For instance, overcoming stigma and resuming normal social life (including joining work, resuming interactions with friends and colleagues, etc.) may be difficult for some patients. Others may have significant organ damage (such as extensive lung fibrosis or destruction) that can result in persistent symptoms and inability to resume normal daily activities. Other events (such as loss of job or divorce) due to TB diagnosis may also have long-lasting social, psychological and financial implications.

9. Extrapulmonary disease

There is only sparse data on how extrapulmonary TB (EPTB) influences QOL. A study from China reported similar QOL scores between pulmonary and extrapulmonary TB, though site distribution or numbers for the latter were not provided [14]. In general, QOL is likely to be related to the anatomic location of disease, and some forms are more likely to be associated with substantial morbidity and long-term disability. Therefore, the impact of skeletal tuberculosis or tuberculous meningitis is likely to be much different in comparison to tuberculous lymphadenitis or pleural tuberculosis. A study from UK found that patients with lymph node disease appeared to report better QOL than patients with pulmonary TB at time of diagnosis [31]. Another prospective study in Zanzibar followed up patients with presumptive EPTB, and reduction in working capacity was reported in a lower proportion of patients with lymphadenitis as compared to other patients [33]. These patients had better self-rated QOL at baseline as compared to EPTB at other sites. Overall, QOL improved in all patients with adequate treatment, but residual impairment was not reported for any site.

10. Drug resistance

In general, patients with multi-drug resistant (MDR) TB have endured disease and treatment in the past as well, and hence face additional difficulties related to family life, social stigmatization, and financial hardships. Treatment for MDR TB is also longer, more complex, associated with frequent adverse effects, and associated with suboptimal outcomes. It is therefore not hard to imagine that QOL among patients with MDR TB is likely to be much more impaired [87,88]. A study from north India showed that patients with MDR TB had worse QOL as compared to drug-susceptible patients receiving retreatment with ATT [39]. In contrast, an Ethiopian study found that QOL was similarly reduced among MDR and gender-matched drug-susceptible patients with TB [27]. However, MDR patients reported worse general health scores and extensive stigmatization. In a retrospective study on 61 HIV/MDR-TB patients in India, 16% had depression at baseline, and all except one improved with ATT and psychological support [59]. In a follow-up study of MDR TB patients programmatically managed in Pakistan, QOL was severely impaired across all domains before starting treatment [22]. At one year of treatment, there was minimal and clinically insignificant improvement in QOL scores. At completion of treatment, there was significant improvement in QOL domain scores and summary component measures, but the scores still remained below standard population norms, suggesting significant residual impairment of QOL. A study from western India found that psychological and physical health domains were the most affected among patients receiving treatment for MDR TB, and that loss of work adversely affected the social relationships and environmental domains [42]. However, QOL in this study was not as low as reported in some other studies, and was not influenced by drug-resistance pattern. Qualitatively, pill burden significantly affected QOL. A study from Yemen showed clinically important improvement in QOL scores at end of treatment for MDR TB, but there was no further improvement over next one year. Duration of illness before diagnosis of MDR TB was an important predictor of improvement in both physical and mental domain scores [89].

A cross-sectional study in Namibia attempted to correlate adverse drug events with QOL around the time of completion of MDR TB treatment [90]. QOL ratings were moderately low in these patients and were not correlated with adverse reactions (which were most commonly mild). In another study from South Africa, patients on drug-resistant TB treatment who reported an adverse event had poorer QOL (principally mental health and well-being) as compared to patients who did not, especially those on intensive phase treatment for six months or less [29]. However, in both studies, most adverse events had already occurred much before quantification of QOL, while some were persistent for variable length of time.

A recent systematic review and meta-analysis obtained a summary prevalence of 25% for depression across 15 studies, and 24% for anxiety across three studies [87].

11. TB and human immunodeficiency virus (HIV) co-infection

Nearly 9% of TB patients are co-infected with HIV, and TB/HIV co-infection seems to be driving the resurgence of TB in the developed world [1]. In a study from Ethiopia, TB/HIV co-infected patients were documented to have poorer QOL across all domains when compared to HIV seronegative TB patients, even after adjusting for potential confounders like age, gender, occupation, social support, WHO staging, and

CD4 lymphocyte count [44]. Similarly, another study from Ethiopia showed that QOL in TB/HIV co-infected patients was more impaired as compared to that in HIV seropositive patients without TB, and treatment led to greater improvement in QOL in the former group [45]. Similar observations were also reported from a cross-sectional study from India [91]. In contrast, a study from Brazil found that QOL was similarly impaired among patients receiving treatment for HIV infection, active TB, and TB/HIV con-infection, with the maximal decrease being observed in the physical domain in the last group [11]. Substantial impairment of physical and mental health was documented in a study on HIV-infected TB patients treated in Thailand [92]. Physical symptoms were largely relieved with treatment, but mental health remained unchanged or worsened in nearly two-third patients. In contrast, a study from South Africa reported greater impairment in physical functioning, but better mental health, among TB/HIV co-infected patients [46]. Another study from South Africa showed overall improvement in QOL with therapy in TB/HIV coinfected patients [47]. This improvement appeared similar among those receiving, and not receiving concomitant anti-retroviral therapy. However, patients with CD4 counts below 200/μL had a poorer QOL, both pre-treatment and during and after completion of treatment.

12. Impact of other comorbidities

Several TB patients have other concurrent comorbid illnesses that can themselves influence QOL. In particular, diabetes is a common association [1]. It is possible that QOL in such patients may be worse. However, most QOL studies conducted in specific disease states tend to either exclude patients with comorbid illnesses that can confound quantification of QOL, or ignore the associated clinical conditions while describing QOL (Tables 1 and 2). Hence data in this area is rather sparse. In one study from northern India, TB patients having diabetes shower poorer QOL at start of treatment, as compared to patients without diabetes [53]. In another study on diabetic patients in Iran, a significant inverse association was noted between QOL and hemoglobin A1c levels, suggesting that poor glycemic control may worsen QOL in TB patients [28].

13. Quality of TB care

As per the International Standards of Tuberculosis Care, a patient-centered approach to therapy needs to be developed for all patients in order to promote adherence, improve QOL, and relieve suffering [93]. Unfortunately, quality of TB care is still far from optimal, especially in high burden countries [94]. There are still considerable delays in TB diagnosis and, and several patients are lost even before treatment can be initiated; this contributes to prolonged patient suffering [95,96]. Several patients find the current mechanisms of directly observed ATT to be inflexible and intrusive, and prefer the less effective unsupervised treatment [97]. The quality of drugs supplied through TB programs, and their guaranteed availability, are also important issues. Most TB programs still do not address the non-medical aspects of tuberculosis with enough seriousness. All these factors directly influence QOL in TB patients. These issues may adversely affect speed of recovery as well as treatment outcomes, and thereby indirectly contribute to impairment of QOL.

14. What can be done to improve QOL in TB patients

From a programmatic perspective, one must deviate from the traditional indicators of disease severity and treatment response to capture the overall health status, with a greater emphasis on patient's, rather than clinician's, perspective of disease [2]. TB control programs need to look beyond clinical and microbiological aspects, and try and include socio-cultural and psychological dimensions that impact the disease and its treatment as part of evaluation and monitoring tools. QOL and related measures can therefore be used more frequently as an adjunct to routine disease outcome indices, and perhaps included into forthcoming guidelines. This can assist health care providers to target specific mental and physical health components that are adversely affected by the disease or treatment [98]. For this, there is also a need for developing psychometrically robust and ethnically appropriate TB-specific QOL measures in different countries. We were unable to locate any quality data that described QOL in children with TB, and this is one area where information needs to be generated. Given that the interaction between healthcare providers and patients, as well as the services rendered by the clinical team, can heavily impact a patient's QOL, there is urgent need improve the overall quality of TB care [99]. TB control programs should also try and implement patient friendly regimens that reduce pill burden, and keep hospitalization and isolation at a minimum. Metrics such as quality-adjusted life years (QALYs) can be used for economic assessment of interventions, and choosing those that provide the greatest health effects [100].

The other major target should be to promote awareness and try and bring about relevant social reforms. There is a need to understand the roots of misconceptions about TB and to address the lack of knowledge about disease. Good communication, especially at time of diagnosis and initiating treatment, is necessary, and psychological counseling should be an integral part of TB management [101]. TB patients receiving adequate social support from family, friends and community are likely to have better QOL [102]. Hence, there may be a case of implementing wellness interventions at family and/or community level to improve QOL. There is also a potential role for targeted, culturally relevant psychosocial support interventions for persons treated for TB disease, especially during the early months of treatment that integrate patients back into their communities as quickly as possible. At a higher level, policymakers should promote social protection and livelihood-strengthening interventions, such as poverty alleviation, food security, cash transfers, etc. [103]. Another major set of interventions are required to reduce TB stigma. Education and support programs aimed at healthcare providers, TB patients, and at-risk community members may prove useful [71]. Other important measures to combat stigmatization include advocacy, communication, social mobilization, and personal empowerment of marginalized groups and women who disproportionally bear the burden of TB stigma. TB clubs or social networks could be created for patients to improve patient interaction with other stakeholders [104].

Funding

None.

Declaration of Competing Interest

None.

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J Clin Tuberc Other Mycobact Dis 17 (2019) 100122

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Quality of TB care among people living with HIV: Gaps and solutions

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ARTICLE INFO

Keywords:
Tuberculosis
TB
Quality of Care
Gaps
Solutions

ABSTRACT

Tuberculosis (TB) is the leading infectious cause of death among people living with HIV, causing one third of AIDS-related deaths globally. The concerning number of missing TB cases, ongoing high TB mortality, slow reduction in TB incidence, and limited uptake of TB preventive treatment among people living with HIV, all indicate the urgent need to improve quality of TB services within HIV programs. In this mini-review we discuss major gaps in quality of TB care that impede achieving prevention and treatment targets within the TB-HIV care cascades, show approaches of assessing gaps in TB service provision, and describe outcomes from innovative quality improvement projects among HIV and TB programs. We also offer recommendations for measuring quality of TB care.

1. Background

Tuberculosis (TB) is the leading infectious cause of death among people living with HIV (PLWH), causing one third of AIDS-related deaths globally. In 2017, 1.6 million people died from TB, including an estimated 300,000 people living with HIV [1]. Only 64% of the worldwide incident TB cases were reported to have been linked to care, the remainder were either undiagnosed, untreated or unreported [1]. TB is preventable and curable, and proven interventions such as early ART and TB preventive treatment reduce TB incidence and mortality. However, gaps remain along the cascade of TB care and prevention with only 36% of new enrolees in HIV care reporting TB Prevention Therapy (TPT) initiation [2]. In 2017, among the 47 countries providing data for the Global TB Report, approximately 51% of TB-HIV co-infected patients were linked to TB treatment, with only 41% receiving ART.

In 2014, the World Health Assembly approved the End TB Strategy, which proposes the ambitious target of ending the global TB epidemic by 2035 [3]. In 2016, the United Nations Political Declaration on Ending AIDS aimed for a 75% reduction of TB-related AIDS deaths by 2020 [4]. Additionally, the WHO End TB strategy aims to initiate TB therapy in 90% of all people who require it, including those at higher risk, and achieve at least 90% treatment success by 2030 [5]. While TB incidence has been declining, incidence rates will still be 1000 times greater than the desired elimination threshold if current rates of decline remain unchanged [6].

This slow progress has in part been due to quality gaps in TB and HIV services across the cascade of care, with suboptimal uptake of interventions such as urine lipoarabinomannan (LAM) for TB diagnosis in patients with advanced HIV disease and molecular diagnostic platforms such as Xpert MTB/RIF, lack of access to optimal TB prevention and treatment regimens, infrastructure, supply of drugs, diagnostics and BCG vaccines, and information systems challenges, as a few examples. In this mini-review we discuss major gaps in quality of TB care among PLWH focusing mainly on two high burden settings, India and South Africa. These gaps impede achieving prevention and treatment targets within the TB-HIV care cascades, show approaches of assessing gaps in TB service provision, and offer recommendations for measuring quality of TB care [7,8]. TB elimination targets may be achievable through robust implementation strategies aimed at improved quality along the continuum of TB care, and through use of new technologies in TB prevention, diagnosis and treatment [9].

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https://doi.org/10.1016/j.jctube.2019.100122

2. Gaps along TB and HIV care cascades impeding achievement of global targets

2.1. TB case detection and diagnostics

TB case-finding and diagnosis continues to be a challenge overall and among PLWH. Systematic reviews evaluating the TB care cascade in India estimated that over 25% of prevalent TB cases did not access government TB facilities, never sought TB care or were evaluated at private health facilities [10]. Of the 1.9 million cases that utilized public health facilities, approximately 500,000 cases were either not diagnosed or initiated onto treatment [10]. A review of studies in India found a strong association between the type of health care provider (HCP) first consulted for TB symptoms and patient delay in TB diagnosis [11] The median reported treatment delay in TB diagnosis was 31days (IQR: 24.5–35.4, 48% of patients first consulted private providers, and had spent time consulting up to three healthcare providers prior to TB diagnosis. Hence initially seeking care from a private or informal HCP was a significant risk factor for prolonged health systems delay in diagnosis of TB. Authors recommend engaging with first-contact healthcare providers as a strategy to ensure rapid diagnosis and linkage to treatment [11]. Since then, India's national strategic plan now recommends private and informal health sector engagement in TB education activities, enhanced access to TB molecular diagnostic tests, and innovative TB care delivery approaches [11].

Novel diagnostics offer an opportunity to address these diagnostic gaps, as studies have found that TB smear microscopy fails to detect TB in 40–60% of patients, especially those with advanced HIV [12]; yet it is still the only available TB test in many primary-care resource limited settings (Table 1). Molecular diagnostic platforms such as Xpert MTB/RIF, endorsed by WHO since 2011, have been introduced in many resource-limited settings [13]. While community-based studies have shown that use of Xpert MTB/RIF has resulted in substantial improvements in time to TB treatment start, numbers of patients starting same-day TB treatment, and the number of culture-positive patients starting TB treatment. However, randomized trials (some conducted in South Africa), have not shown a reduction in TB related morbidity or mortality with Xpert MTB/RIF implementation [14,15]. Reasons posited for this lack of mortality benefit in these randomized studies include poor linkage to treatment once TB is diagnosed, high rates of empiric treatment in both intervention and control arms, and other health systems challenges leading to poor quality follow-up and linkage to treatment for patients with a positive TB test result [15,16].

Recently published TB care cascade data from HIV and TB endemic South Africa, where up to two-thirds of TB patients are co-infected with HIV, estimated that 47% of the total identified TB cases were missed and not linked to care [17]. Additionally, this study found that HIV infected patients often present asymptomatically with TB, are under-evaluated with routinely available diagnostics, leading to under-diagnosis of TB. This study recommends targeted universal TB screening for HIV infected patients [17]. Current WHO recommendations suggest Xpert MTB/RIF test be used for early diagnostic testing for those with symptoms and signs of TB, including testing of both pulmonary and extrapulmonary samples. A meta-analysis of 27 unique studies involving 9558 participants showed a Xpert MTB/RIF pooled sensitivity 79% (95% CI:70–86%) compared to 86% (95% CI: 76–92) among HIV infected vs uninfected patients, when used as a diagnostic test replacing AFB smear [3]. It is important to note that despite availability of GXP tests, data shows that the proportion of symptomatic patients that received a TB test at primary health care facilities did not change indicating the need to improve health care worker practice in investigating patients [18]. The impact of this innovative diagnostic is therefore only realisable if quality of TB screening and care improves. Despite availability of new technology, implementation and integration of new TB diagnostics into health services remains limited, with poor uptake by primary practitioners (Table 1). One major gap in implementing TB screening among HIV infected patients is failure to conduct additional sputum testing among symptomatic TB patients that have a negative or an unsuccessful GXP test results [17]. In South Africa, while the Xpert MTB/RIF testing is readily available through the national health laboratory system, health systems challenges in quality of screening and use of results persists [18]. Data from an urban health facility found that TB diagnostic delay using smear microscopy compared to Xpert MTB/RIF was 3.3 days vs 6.4 days, respectively. Authors recommend proper roll-out, interpretation, and implementation of Xpert MTB/RIF testing for improvements in treatment initiation and clinical outcomes (Table 1) [19].

Urine LAM tests such as the Alere Determine®-TB LAM Ag lateral flow assay detect urine lipoarabinomannan, an *M.tb* cell wall-associated glycolipid, in people with advanced HIV disease. While urine LAM sensitivity remains sub-optimal (40–60% in HIV co-infected patients with a CD4 count < 100 cells/mm^3) [7], a LAM-guided treatment strategy was associated with reduced mortality in hospitalized HIV-infected patients with suspected TB [14], and combined use of Xpert MTB/RIF and LAM improved identification of TB from 20% to 50% in patients with CD4 < 50 cells/mm^3, compared to standard of care [8].

South Africa has enjoyed some measure of success in TB case detection through the national roll-out of Xpert MTB/RIF testing. This coupled with additional measures such as universal TB symptom screening for all patients at all health facilities, and urine LAM testing among known HIV infected patients with CD4 counts < 100 cells/mm^3 has assisted with early TB detection. Early detection has likely contributed to the decline in national TB incidence rates and time to treatment initiation, observed recently among both HIV infected and uninfected patients [20,21]. Ongoing evaluation of the impact of novel TB diagnostics on TB transmission and case detection remains warranted in South Africa and elsewhere.

2.2. Linkage to TB treatment

Gaps in linkage to TB care are similar among HIV infected and uninfected patients and include gaps in both the number of diagnosed TB patients linked to appropriate care as well as the time to TB treatment initiation. Gaps in linkage of diagnosed TB patients to care spans inefficiencies across multiple levels of the health system including: lack of laboratory systems e.g. lack of unique patient identification that link results from laboratories with patients and providers, delays in laboratory turn-around time; patient related factors creating delays or interruptions in patients accessing clinical services due to migration or competing priorities, health facility inefficiencies such as poor record keeping, lack of appropriate patient referral, inadequate systems for patient registration and lack of resources to trace patients. Interestingly, method of TB diagnosis i.e. GXP vs sputum microscopy was found to halve time to linkage to TB treatment [16,22]. A review of individual patient factors accounting for delays in TB patients accessing TB treatment across sub-Saharan Africa found that higher education level and better knowledge of TB was associated with a reduced time to TB treatment start, whereas prolonged travel time, use of traditional healers, daily alcohol use and concurrent HIV infection was associated with delays in TB treatment start [23,24].

2.3. Gaps in successful TB outcome

Factors contributing to gaps in TB treatment completion exist at the patient and health systems level. Failure to complete a course of anti-tuberculosis therapy contribute to rising rates of drug resistant TB and impede efforts aimed at reducing TB transmission, and TB elimination. Patient centred gaps negatively impacting TB treatment outcomes include: financial expenses associated with accessing health services - especially in HIV-TB co-infected persons who require multiple health visits; sub-optimal treatment adherence from poor patient understanding and motivation, or unmanageable side effects - the latter

Table 1
Suggested approaches to measure quality of TB care in resource limited settings.

Author and year	Measurement problem identified	Proposed approach to measuring quality in TB care	Recommended measures of quality in TB Care
Cazabon (2017) [51]	- Bias in specific measures of TB care quality (e.g. observational bias, patient and healthcare worker recall bias) - Coverage of TB services not an accurate measure of quality of TB services	- TB diagnostic delays provide a good surrogate marker for quality of TB care - Simulated/standardized patients (SP) assesses application of TB screening and diagnostic approaches - TB care cascades help identify gaps in care - Knowledge assessments among HCWs - Chart abstraction and prescription audits identify gaps in use of guidelines and algorithms in patient diagnosis and management - Recall-based surveys from patient exit interviews - Direct observation of providers - Real-time performance monitoring using the QI-models (PDSAs)	- Time to TB diagnosis from first screening visit - TB recurrence-free survival - Case detection rates among simulated patients - Indicators of TB care quality using ISTC (International Standards of TB Care)
Naidoo (2017) [52]	- No accurate data on TB disease burden in South Africa, as the TB prevalence surveys have not been conducted. - Constructing care cascades limited in South Africa by the lack of unique patient identifiers linking patient laboratory and clinic data (that is key to generating a care cascade) to local, regional and national TB databases - Care cascades enumerates losses at each step, it does not reflect the delays that occur between - Successive steps.	- Constructing care cascades to identify gaps in TB care and quantify losses at: access to TB diagnostic tests, diagnosis, treatment initiation, and treatment completion - National TB data, published studies and TB registers	- Construct continuum of TB care for defined periods using TB data from national laboratories, registers, and published studies: those that accessed tests, those diagnosed with TB, those notified and treated, those that successfully completed Rx - Enhanced focus on: understanding reasons and duration for TB diagnostic delays and patient waiting times for TB specific services - Patient feedback on perceptions of quality services - Assess health care worker attitudes that drive initial loss-to follow-up
Satyanarayana (2015) [53]	- Quality in TB care as stipulated by the International Standards of TB care is not well known or followed, hence, many TB programs/ TB research studies do not benchmark TB care standards appropriately	- Qualitative assessments, self-report surveys and direct observation to: assess healthcare workers knowledge, evaluate practices and standards in delivering TB care services against an internationally accepted benchmark	- Derive indicators of quality TB care from ISTC (International Standards of TB Care): - a. Awareness/use of sputum smear for persons with presumptive pulmonary tuberculosis - b. Awareness/use of correct treatment regimen for new tuberculosis case - c. Patient support to improve adherence and treatment completion - Use of simulated standardized patients to assess provider knowledge including use of guidelines and practice - Use case vignettes in assessing providers knowledge and practice - Ongoing monitoring of Health care worker knowledge and practice will direct education and training, and track progress in delivery of quality care - Patient exit interviews to assess provider practices
Jannati (2018) [54]	- Crude coverage rates of services not a true reflection of healthcare performance	- Addressed healthcare performance in general and recommends that each healthcare intervention must define its own quality standards and measures using a suggested formula	Authors proposed a general formula: EC= U/N * Q Where EC = Effective coverage N = population in need of an intervention, U = utilization/use of intervention among population in need Q= quality of intervention defined as "the ratio of health gain delivered through an intervention relative to the maximum possible health gain given the ideal quality"

observed more frequently with concomitant TB therapy and ART [25,26]. Health system level gaps include: interrupted supply chain management of TB drugs and diagnostics often resulting from increased demand in high HIV and TB incidence settings. Other gaps include poor implementation of the treatment guidelines, and poor quality of care especially in endemic settings that have overburdened staff and facilities [23,26,27]. Integration of TB-HIV care, strong management and leadership at the health district and facility level have been shown to be predictors of good TB and HIV treatment outcomes [27–29]. Studies demonstrate successful measures that reduces the gap from TB diagnosis to treatment completion in HIV infected and uninfected populations. These include: electronic monitoring of treatment adherence and retention in care [30,31], adherence motivation and behavioural counselling of patients [32], and patient cash incentive to support treatment adherence and completion [33]. Implementation research evaluating the applicability, scalability and sustainability of these interventions in settings that vary in HIV and TB disease burden remains outstanding.

2.4. Poor scale up of TB preventive treatment services

Provision of TB preventive treatment is an opportunity to prevent progression of latent TB to active TB disease [34–36]. The WHO recommends treatment of latent TB infection (LTBI) for high risk

populations that have higher rates of progression from LTBI to active TB disease [37], especially HIV infected patients who are at 19–21 [38] times higher risk of contracting TB [38,39]. The evidence that TPT is effective in preventing TB and reducing mortality among PLWH is compelling [40–42] with the recent TEMPRANO study demonstrating a 37% reduction in mortality at 6 years among PLWH receiving 6 months of TPT [43].

Notwithstanding widespread guideline uptake, globally in 2017, 67 countries reported initiating TB preventive Therapy (TPT), while the number completing TPT is not known [2]. Reviews assessing the quality of LTBI care are limited, however a recent systematic review and meta-analysis identified gaps in screening for LTBI, correct referral, appropriate recommendation for treatment post medical evaluation, and poor completion of treatment once started [44].

A review of TPT uptake demonstrated that cohorts from low-and-middle income countries had lower TB preventive therapy completion rates compared to cohorts from high income countries. From a population intended for TB screening (100%), losses along the care cascade is evident in the remaining proportion completing each step: 71.9% [95% CI:71.8–72.0] of those screened completed TB testing, among these 43.7% [95% CI: 42.5–44.9] completed a medical evaluation, with 35.0% (95% CI: [33.8–36.4] initiating TPT, and 18.8% [95% CI: 16.3–19.7] achieving TPT completion (Table 1) [45].

Advances in TB preventive treatment include recommendations of shorter and safer regimens for treatment of LTBI [2]. Rifapentine and isoniazid (HP) given either over one month or three months are recommended alternatives to INH given over nine-twelve months to prevent TB. Importantly, this regimen is suitable for use in HIV infected patients, and may offer a useful tool to prevent development of active TB disease [46]. Shorter regimen will help address gaps in patient adherence and regimen completion. It is important to note however, that gaps in screening and in supply chain management of TB screening diagnostics and TPT will continue to undermine the benefit of these recommendations to affected populations.

Notwithstanding the remarkable progress made by South Africa in ensuring that 56% of all new HIV care enrolees initiate TPT [2], initiation and completion of TPT remain undermined by interrupted drug supply and global stock out of Isoniazid and Tuberculin Skin Tests [47,48].

2.5. Approaches to analysing gaps along the TB cascade of care

Notwithstanding the importance of quantifying treatment success rates as a metric of TB control program performance, the call for improved quality of TB care and treatment services has warranted unpacking the TB care cascade with attention to outcomes for all cases of TB, including among PLWH (Table 1). This offers a simple way to identify and address gaps in TB diagnosis, linkage to care, TB treatment initiation, and in TB treatment outcomes. One approach is use of cohort analysis, initially popularized by Styblo to evaluate treatment outcomes [49] in Tanzania, has become a requirement for global reporting. Using the cohort analysis approach, every patient initiated on TB treatment is accounted for and assigned a treatment outcome, including those that do not complete treatment. The limitation of this approach is that it only captures those that are reported to the National Tuberculosis Program (NTP) and does not capture information for every TB patient initiating TB treatment, or those diagnosed but not initiated on TB treatment. Two other approaches are (1) patient care cascade analysis and the (2) patient pathway analysis (Table 1) [50].

Two types of care cascades are used in evaluating TB care: patient pathway analysis (PPA) and cascade analysis [52]. The care cascade enumerates losses at each step across the care continuum, providing indirect estimates of disease burden based on expert opinion and epidemiologic data [44,55]. The care cascade analysis facilitates targeted interventions aimed at points of attrition along the care continuum. PPA seeks to assess alignment in entry of patients into the care continuum with availability of diagnostic and treatment services at a national level, with the goal of identifying bottlenecks [56]. Data that informs PPA include qualitative surveillance and survey data obtained at a patient and household level coupled with care seeking behaviour, care access and location, coverage of diagnostic and treatment services and treatment success (Table 1). A limitation to this approach is the overreliance on coverage of diagnostics and treatment services without accounting for quality of diagnostics and ability of healthcare workers to implement guidelines that relate to TB diagnosis and treatment [57]. Analysis of the TB care cascade in India showed that only 45% of notified tuberculosis cases completed treatment in 2013 [10]. In parallel, TB care cascade data from South Africa, using data from laboratory services, TB registries and published studies, showed that only 53% of all tuberculosis cases were successfully treated. Patient attrition occurred along various points of the TB patient care cascade as follows: 5% of individuals did not access TB testing and 13% were lost between TB testing and diagnosis, due largely to failure of health care workers to follow the TB diagnostic algorithm. Among known diagnosed TB cases, initial loss to follow-up (i.e. TB diagnosed but TB treatment not initiated) was 12% (25% in Rifampicin resistant TB, and 11% in drug susceptible TB), while 17% did not successfully complete treatment [52].

Patient pathway analyses from 13 countries that carry 76% of all estimated incident TB cases and 92% of all “missing” TB cases globally have been published with authors proposing several recommendations [57,58]. First, since fewer than 30% of public sector facilities have access to microbiologic services, they highlight the critical need to close this diagnostic access gap to find missing TB cases. Second, improving quality of TB care in the private sector is essential since 60% of TB patients initiate care in the private sector, where TB treatment services are often unavailable, leading to delayed diagnosis and long pathways to TB treatment initiation in the public sector. Third, functional primary health care networks with proper TB testing, treatment, and referral services coupled will improve access to TB services and help limit high costs of TB diagnostic and therapeutic services [50,52].

Data from TB care cascade analysis or PPA can be used to implement program aimed at finding missing TB cases and reducing initial loss to follow-up among laboratory confirmed TB patients, including among PLWH. Furthermore, implementation science research investigating the optimal use of information systems including automated laboratory notification, linked HIV/TB records, and electronic patient management could help to improve linkage to care, adherence, and monitoring [59].

3. Health systems and quality of care

The definition of quality TB care proposed by Cazabon et. al. (2017) defines quality TB care as *being patient-centred, uniform with international standards, provided in way that is efficient, effective, equitable, timely, safe, and accessible* [51]. The framework of universal health coverage emphasizes components of quality care: patients’ right to care, equitable service delivery and needs based healthcare [60,61]. Quality TB and HIV services include: (i) Screening for HIV and TB with appropriate tests, access to prevention for TB and HIV in those that screen negative, and linkage to appropriate treatment for TB and HIV (ii) Effectiveness of care includes timely identification of both HIV and TB, linkage to appropriate treatment and continued clinical and laboratory monitoring until favourable outcomes are achieved [62].

Health systems weaknesses and underperformance in healthcare delivery contribute to poor quality TB care [1,15,18,63]. Health systems failures exist on multiple levels of the health care system, i.e. at healthcare worker level, management and policy level. In this section we focus on health systems gaps and weaknesses at each stage of the TB care cascade at the frontline where healthcare is delivered. Fig. 1 below is a summary of TB care-related health systems failures extracted from studies or review papers emanating from South Africa.

TB Screening
Non-compliance with TB guidelines[18, 67] • Failure to: - Assess for symptoms of TB - Act on symptomatic patients - Offer sputum microscopy - Screen contacts of index TB patients **Poorly skilled healthcare workers** [17, 18] • Poor understanding and interpretation of TB symptoms
TB Diagnosis
Non-compliance with TB guidelines [17, 18] • Poor Microbiologic coverage of patients with suspected TB • Failure to request repeat samples from patients that test negative • Request for additional samples from laboratories for additional testing and repeat testing not acceded to **Poorly skilled healthcare workers**[68] • Poor specimen quality: insufficient volume, saliva vs sputum • Inadequate staff training on sputum collection and new diagnostic algorithms • Lack of TB treatment knowledge among healthcare workers • Poor implementation of new diagnostic algorithms • Poor healthcare worker attitude in following up on laboratory tests **Weak clinic systems (e.g. patient flow)** [17] • Inefficient patient flow systems through clinics **Inadequate physical infrastructure** [47, 69, 70] • Inadequate infrastructure for safe sputum collection • Lack of patient privacy **Poor/no quality assurance of data collected** [63] • Poorly completed laboratory request forms
Linkage to TB care
Lack of patient engagement [27] • Failure to provide patient education and to engage patients in care • Lack of provision of follow up appointments for patients to access laboratory results • Lack of provision of follow up appointments for patients to commence therapy **Poor/no quality assurance of data collected**[63] • Incomplete or failure to collect patient locator information to facilitate tracing attempts • Lack of unique identifier linking laboratory results to patients **Weak communication systems and infrastructure**[27] • Poor mechanisms of communication of laboratory results to facilities and to patients • Lack of systems for tracing and linking patients to treatment • Difficulty locating and accessing patients' homes particularly in rural areas • Inadequate resources for patient tracing (e.g. lack of telephone, vehicles)

Fig. 1. Health systems challenges impacting quality of TB care. Refs. [17,18,27,47,63,67–70] are used in this Figure.

Fig. 1 illustrates that non-compliance with TB guidelines and under-skilled healthcare workers are the most common health systems weaknesses in the TB program [17,18,63]. TB screening is perhaps the most important step in the care cascade as it marks the entry point into care and failure to screen and act upon signs and symptoms are missed opportunities to diagnose TB [52]. Despite comprehensive TB guidelines informed by years of rigorous research on best practices to reduce TB mortality and morbidity, there remains an implementation gap in executing guidelines [64]. On the 05 May 2017, the South African Department of Health implemented a wide scale roll-out of a quality improvement approach to improve TB healthcare delivery in 9 sub-districts in South Africa [65]. Proponents of the QI approach value its easily implementable, low cost approach to addressing systems failures using inputs from frontline healthcare workers [66]. Understanding the gaps in delivering quality TB care is an important step to enhance the success of the current and future QI initiatives.

3.1. *Infrastructure to provide efficient TB case finding and TB care*

The current SA healthcare system inherited a legacy of poor clinic infrastructure and resources especially the clinics serving poor and underserved communities [71]. Several studies document healthcare workers' (HCW) perspectives on barriers to delivery of good quality TB care [72–77]. HCWs cite lack of private clinic spaces. This is relevant to facilities offering both HIV and TB services as sub-optimal levels of privacy and confidentiality is not conducive to delivering vital counselling, screening and testing services, such as HIV testing in TB patients or sputum induction for TB testing (Fig. 1) [63,69,75,76,78]. Dedicated cough booths for sputum induction are seldom available in clinics resulting in open spaces being used compromising patients' rights to privacy and dignity. Crowded waiting areas, poor ventilation and lack of personal protection equipment (PPE) increases the risk of nosocomial transmission of TB in both patients and HCWs especially given the pervasive presence of HIV in under-resourced countries [72,74].

3.2. Health work force training needs for provision of quality care

Inadequate numbers of trained health care personnel create a challenge for TB programs. In South Africa, provision of TB services has historically been delivered by lower level staff such as enrolled nurses, and community health workers. Professional nurses, and doctors do not routinely offer TB testing, and treatment services. This creates a challenge especially in disease endemic settings, where skilled staff lack adequate confidence, training and experience in screening, diagnosing and managing TB (Fig. 1) [63].

3.3. Patient-level barriers

Stigma and discrimination associated with TB and HIV was reported as a key patient-level barrier to accessing timely TB and HIV services [69,76,77]. Long waiting times at the clinic [76], limited clinic operating times, shortage of clinic staff on weekends and holidays, were factors that discouraged patients from attending clinic visits [74,76]. Provider attitudes present a barrier to health care seeking and is associated with non-enrolment into care, or poor treatment completion [79]. Lack of empathy, improved patient rapport and fostering a caring environment have been shown to improve TB and HIV treatment outcomes [79,80].

3.4. Measuring and improving quality in TB and HIV services

Systems for quality management and quality improvement are critical to address the gaps along the care cascade. In South Africa, a national QI program for TB services aims to reduce TB mortality by 50% and TB incidence by 30% by 2022 [81]. The pilot phase currently underway will deliver a change package of the most impactful interventions across the TB care cascade, for national scale-up [82]. This project aims to enable front line staff, supported by management, to develop their own contextually appropriate implementation approaches to addressing bottlenecks and gaps in the TB care cascade. While this project has been scaled up across multiple districts, no findings are available for reporting.

There is an urgent need to systematically and regularly analyse gaps within TB care cascades and implement measures to address gaps identified in real time. Quality improvement methodologies offer an effective way to improve quality and coverage of TB and HIV care (Table 1) [83,84]. Prior studies conducted in low-and-middle income settings offer various metrics to measure quality of TB care (Table 1) [85]. These ranged from quality metrics derived from the International Standards of TB Care, estimations of TB patient losses, standardized patients or case vignettes to assess healthcare worker knowledge and practice, patient feedback on care provision, and assessment of microbiological coverage, TB case detection and linkage (Table 1).

A recently published systematic review assessing quality within HIV programs found improvements of 14.0% in ART uptake, 22.0% in ART adherence and 26.0% in viral load suppression following quality improvement initiatives concluded that QI interventions can be effective in improving clinical outcomes [86]. Authors highlight critical gaps that warrant further attention including the lack of standardized systems to assess and report QI initiatives and a scarcity of robust research into quality improvement initiatives. Quality improvement methods within TB programs have also proven effective in various settings (Table 2) offering a systematic approach for optimization of processes and interventions.

Within TB programs, there is a paucity of projects that specifically aim to establish and test QI interventions in HIV – TB care (Table 2) [93]. However, there are many examples of interventions that have improved quality of TB care in both public and private sectors [51]. A prospective evaluation of TB diagnostic services at five primary healthcare facilities in Uganda that measured quality using indicators derived from the ISTC found that clinicians only referred 21% of patients with prolonged cough of > 2 weeks for sputum smear microscopy and 71% of microbiologically confirmed TB patients for treatment. Following implementation of a performance monitoring system on key indicators, these proportions increased to 53% referred for smear microscopy and 84% referred for TB treatment. Overall, the cumulative probability of appropriate evaluation and referral for treatment of a coughing patient increased from 11% to 34% ($p = 0.005$), with a four-fold increase in the number of tuberculosis cases identified and treated [45].

3.5. Human rights perspective on quality care

The measurements of success in the TB world are often framed in terms of coverage of diagnosis and treatment. Yet coverage, or in the language of the International Covenant on Economic, Social, and Cultural Rights (ICESCR), availability, is only one aspect (and the bare minimum) in the broader interrelated and essential components of the availability, accessibility, acceptability, and quality (AAAQ) framework of the right to health [94]. Core obligations in the ICESCR are considered to be fundamental, minimal conditions

Moving beyond availability, to accessibility, TB services may be inaccessible due to discrimination, physical distance or a lack of affordability among other reasons [62]. For example, a lack of integration of TB, HIV and other services requires affected patients to travel to multiple treatment sites. This may be considered inaccessible if time and financial costs required create a burden for them. Furthermore, the poor and most vulnerable are least able to pay direct and indirect costs, and may therefore not benefit from improvements in diagnostic and treatment services, resulting in poor acceptability of care. Probably the most neglected aspect of TB diagnosis and care, as well as the least discussed part of the AAAQ framework is quality. Research focusing on quality of patient experience can highlight gaps in care delivery leading to poor outcomes, despite presence of new technologies. For example, recent research in the Republic of Moldova found that patients overwhelmingly preferred ambulatory treatment, even though nearly 75% were hospitalized [95].Despite hospitalization, almost 40% experienced treatment interruptions, mainly due to adverse reactions or feeling too ill to take treatment

Hospitalization for TB treatment puts a heavy burden on people who cannot afford the associated costs of care. While the WHO aims to eliminate catastrophic economic costs for people with TB [96], these costs are the norm in many places, particularly the poor, rural, and among those who migrate for labour. TB services must be accessible to all people, especially those lacking financial and social support to adhere to TB services. A person centred approach that respects human rights and values quality will enable a person to fit treatment into their life, rather than expecting people struggling with TB to reorder their lives around treatment approaches that do not fit their needs.

Gaps in the care cascade, even in places such as South Africa which have ambitiously rolled out universal treatment for all forms of TB and HIV, point to problems of both accessibility and quality. These are problems that cannot be solved through interventions such as patient education and treatment literacy alone. They are symptoms of a global approach to TB that purports to be person-centred, yet fails to provide diagnosis, treatment, and care that meet what is required under international law. It will not be easy to provide TB services that are available, accessible, acceptable, and of quality, yet this is the only way that TB elimination will be possible. Furthermore, because the poor and vulnerable suffer disproportionately from these gaps, human rights, as well as the WHO's ethical guidance require us to act. As Pai and Temesgem argue, quality is the “missing ingredient in TB care and control” [97]. It cannot wait and must be a serious part of every TB program.

4. Conclusion

The persistently high TB-associated mortality rates and TB

Table 2
Case studies of quality improvement programs in TB-HIV.

Author and Year	Country	Problem	Quality improvement aim	Main change ideas	Outcome of the QI initiative
Quality Improvement Programs for TB					
Karamagi (20180 [87]	Uganda	Late presentation of symptomatic patients for TB services	To improve TB case notification rates in populations most vulnerable to TB	QI techniques combined with facility-led active case finding in the community - Targeted key vulnerable populations such as prisoners, PLWH, contacts of TB index patients, communities living in congested settlements - engaged district and facility teams in TB systems strengthening, - Trained health workers on national x-ray diagnosis guidelines for smear-negative patients	- Overall, TB case notification increased from 171 to 223 per 100,000 population between December 2016 and June 2017
Heldal (2019) [88]	Zimbabwe	Poor quality of TB data and poor-quality patient care	To improve the quality of TB patient data and care	- Staff validated, tabulated and analysed data quarterly to identify challenges and agree on action points at 'data-driven' supervision and performance review meetings	- Significant increase in identification of presumptive TB (63% vs. 30%; $P < 0.00001$) and new TB smear-positive cases $P < 0.0001$), decline in rates of pulmonary TB cases without diagnostic smear results (77% vs. 20%; $p = 0.037$)
Quality Improvement Programs for ART					
Webster (2011) [89]	South Africa (Johannesburg)	Low levels of ART initiation in resource limited settings in South Africa	To accelerate ART initiation for those requiring treatment.	- series of activities promoting early identification of ART eligible patients (incl. community awareness campaigns, fast tracking low CD4 count patients to ART initiation rooms, HIV testing campaigns outside of the clinic) - Formed collaboratives between different sub-districts and shared best practices, successes and challenges	- Increased HIV testing from 891/month (SD: 94.2) to 3580/month (SD: 327.7) ($p < 0.0001$). Monthly ART initiations increased from 179/month (SD: 17.22) to 511/month (SD: 44.93) ($p < 0.0001$)
Golden (2018) [90]	South Africa (North West province)	HIV retesting in women during pregnancy was low	Quality Improvement Project (QIP) to raise the performance of antenatal HIV re-testing	- Conducted root cause analyses to identify weaknesses in HIV re-testing systems - Implemented clinic-level customized change processes to address systems gaps - Healthcare worker -in-service training on importance of re-testing	- Re-testing for HIV increased from 36% in three months pre-intervention phase to full coverage at month nine. Re-testing in QI clinics was 20% higher than control clinics. - Overall increase in re-testing within the sub-district
Sunpath (2018) [91]	South Africa (KZN, eThekwini)	Laboratory viral load monitoring is underutilized, jeopardizing the chances of meeting the 3rd goal of the 90–90–90 strategy	Implemented a viral load champion (VLC) program aimed at enhancing VL monitoring and recognition of treatment failure.	- A Viral Load standard operating procedures (SOP) was developed and implemented in study clinics - A VLC at each clinic was assigned to optimize VL monitoring through oversight of the VL SOP in each study clinic. - Baseline pre-intervention catch-up phase of facilities VL data, clean-up and laboratory results were entered into clinical charts and the clinic's ART programme database - Routine VL monitoring, accurate reporting, and expedient follow-up on test results by the VLC	- Pre-implementation VL testing completion rates among patients was 68% (140/205), 54% (84/155) 64% (323/504 respectively), compared to the 6-month post-implementation completion rates of 83% (995/1194), 90% (793/878 and 99% (3101/3124) (P 0.0001 for each site)
- **Quality Improvement Programs for integrated TB-HIV care**					
Ogarkov (2016) [92]	Siberia	Low ART coverage in TB patients	Pre and post intervention assessments following introduction of a bundle of initiatives aimed at improving ART initiation rates in TB patients	Adapting educational messages Reducing delays in ART approval Facilitating CD4 cell count and viral load assessments testing weekly cohort reviews to improve administrative support and expedite ART access for TB patients	ART initiation rates in HIV-TB co-infected patients increased significantly from 17% pre-intervention to 54% post-intervention $p < 0.001$

incidence rates among people living with HIV in TB endemic settings warrants deeper investigation into gaps and weaknesses in delivering quality TB care that is ultimately effective in reducing TB incidence, preventing TB deaths and in improving quality of life among patients with TB. There is critical need to improve efforts relating to the fundamental pillars of TB control; finding, treating, and preventing TB and to doing the basics better [98]. Furthermore, there needs to be a paradigm shift beyond access and coverage of TB services toward improving quality of TB services if we are to accelerate current progress and transition from a strategy focused on TB control to one of elimination [99]. Regular analysis of routinely collected program data aimed at identifying gaps in retention of patients from screening to treatment completion offers a simple readily implementable approach to incorporate quality metrics into assessing the TB care pathway. Additional approaches to assess quality of care provision such as use of standardized patients, chart and prescription audits, and provider knowledge assessments offer opportunities for direct intervention. Instilling an improvement culture through structured context specific quality improvement initiatives within the health system including in TB programs, offers an opportunity to raise quality standards of health care delivery, in improving patients' experience of the health service and in improving health outcomes. Lastly, empowering communities to demand high quality respectful care, will drive health systems accountability for delivering quality care.

Declaration of Competing Interest

All authors declare that there are no conflicts of interest.

Ethical considerations

There are no ethical considerations.

Acknowledgments

We wish to acknowledge Sanisha Rampersad for her assistance with literature searches, data collation, editing and proof-reading the manuscript.

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J Clin Tuberc Other Mycobact Dis 19 (2020) 100144

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Closing gaps in the tuberculosis care cascade: an action-oriented research agenda

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ARTICLE INFO

Keywords:
Tuberculosis
Cascade of care
Continuum of care
Research agenda
Pretreatment loss to follow-up
Medication adherence

ABSTRACT

The care cascade—which evaluates outcomes across stages of patient engagement in a health system—is an important framework for assessing quality of tuberculosis (TB) care. In recent years, there has been progress in measuring care cascades in high TB burden countries; however, there are still shortcomings in our knowledge of how to reduce poor patient outcomes. In this paper, we outline a research agenda for understanding why patients fall through the cracks in the care cascade. The pathway for evidence generation will require new systematic reviews, observational cohort studies, intervention development and testing, and continuous quality improvement initiatives embedded within national TB programs. Certain gaps, such as pretreatment loss to follow-up and post-treatment disease recurrence, should be a priority given a relative paucity of high-quality research to understand and address poor outcomes. Research on interventions to reduce death and loss to follow-up during treatment should move beyond a focus on monitoring (or observation) strategies, to address patient needs including psychosocial and nutritional support. While key research questions vary for each gap, some patient populations may experience disparities across multiple stages of care and should be a priority for research, including men, individuals with a prior treatment history, and individuals with drug-resistant TB. Closing gaps in the care cascade will require investments in a bold and innovative action-oriented research agenda.

1. Introduction

The care cascade evaluates patient outcomes for a disease across stages of care. National-level care cascade analyses have identified that large numbers of individuals with active tuberculosis (TB) experience poor outcomes at critical points in health system engagement, highlighting foundational problems in quality of TB care [1,2]. We recently outlined guidelines for estimating the number of individuals with active TB in a population who successfully reach (or drop out at) different care cascade stages [3]. While such analyses help quantify gaps in care delivery, they do not illuminate why patients fall through the cracks—information that is critical for developing interventions to improve outcomes in TB programs.

Reasons for poor outcomes—and interventions to address these problems—may vary at each care cascade stage. Closing gaps in the care cascade may require interventions at the level of the population or health system (including the private sector), at the level of TB diagnostic and treatment centers, and at the level of the TB patient-health provider interaction. Rectifying gaps at different scales will require diverse interventions—potentially including large-scale public education, increased access to health facilities, initiatives in the private sector, integration of new diagnostic and monitoring technologies, and interventions to address patients' psychosocial needs. In addition, some patients may be at higher risk for poor outcomes, thereby meriting greater attention and specialized interventions. In light of these complexities, in this manuscript, we outline an agenda to start answering key questions regarding poor patient outcomes in the TB care cascade.

2. Frameworks and research questions

2.1. Framework for the TB care cascade

We previously described a care cascade model for individuals with active TB, in which each stage contains a step (number of individuals who reach that point in care) and a gap (those with poor outcomes, quantified as the difference between steps) (Fig. 1) [3]. Key gaps

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https://doi.org/10.1016/j.jctube.2020.100144

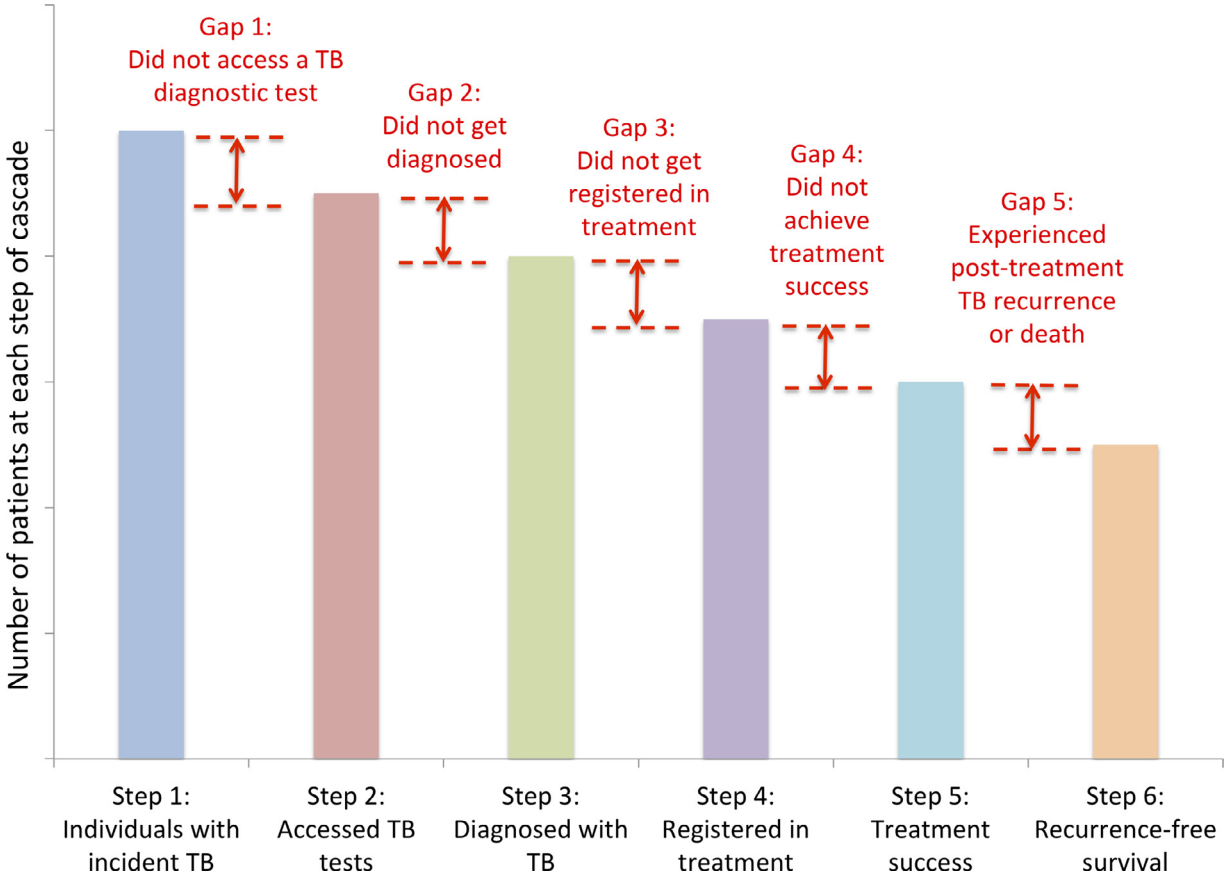

Fig. 1. Generic care cascade model for individuals with active TB in a population [3].

include: individuals with active TB in the population who do not reach health facilities and access a TB diagnostic test (Gap 1), those who access locations where diagnostic tests are available but do not get successfully diagnosed (Gap 2), those successfully diagnosed who do not get registered in treatment (Gap 3), those who start therapy but do not achieve treatment success (Gap 4), and those who finish therapy but experience death or TB recurrence within a year (Gap 5). We describe a research agenda to address each of these gaps below.

2.2. Research questions

The research agenda below is guided by three broad questions. First, *who is disproportionately falling out of the TB care cascade?* Understanding the types of individuals who are at higher risk for poor outcomes at each stage may help to develop and refine interventions that focus on these specific populations, although we acknowledge that quality of care can and should be improved for all people with TB. Risk of dropping out of care may vary by demographics (e.g., age, gender), type of tuberculosis (e.g., pulmonary, extrapulmonary, prior treatment history), microbiological susceptibility (e.g., drug-resistant forms of TB), comorbidities (e.g., HIV, diabetes), or other social factors (e.g., living in migrant, urban slum, or indigenous communities).

Second, *why are patients falling out of the cascade?* Understanding barriers to engaging in TB care that contribute to poor outcomes are important to inform intervention development. Such barriers may occur at the level of the health system (e.g., poor quality of care or user experience), the patient (e.g., substance use, depression), the patient's family and community (e.g., TB-related stigma), or society (e.g., structural barriers).

Third, *what interventions are needed to reduce gaps in the care cascade?* Beneficial interventions might involve using novel technologies to address health system or patient barriers, social and behavioral interventions to address psychosocial barriers, social protection schemes for patients, or incentives to change healthcare provider (HCP) behavior, including in the private health sector. Intervention development would ideally be informed by research on the first two questions described above.

2.3. Pathway for generating evidence

Diverse research approaches will be required to understand which patients are being lost, identify reasons for these losses, develop interventions, and implement these interventions in routine clinical practice (Fig. 2). Systematic reviews help to aggregate evidence about reasons for patient dropout across care cascade stages and the effectiveness of interventions to reduce these gaps. For example, systematic reviews have synthesized evidence on barriers to TB medication adherence from qualitative studies [4] and assessed the effectiveness (or lack thereof) of directly observed therapy (DOT) [5–9] and other interventions for improving adherence, including digital adherence technologies (DATs) [8,10]. Systematic reviews have not evaluated reasons or interventions for other care cascade gaps, such as pretreatment loss to follow-up (PTLFU) (Gap 3) and post-treatment relapse or death (Gap 5). Studies of HIV care delivery provide helpful examples to guide similar systematic reviews for TB [11–15].

By identifying research gaps, systematic reviews may guide further qualitative and quantitative observational research to identify novel risk factors for patient dropout. Findings of observational studies may in turn guide theory-informed intervention development to address risk factors, using iterative implementation and refinement. Implementation research frameworks—including the Unified Theory of Acceptance and Use of Technology (for technology-based interventions) [16], the RE-AIM framework, and the Consolidated Framework for Implementation Research—may guide approaches to designing, evaluating, and

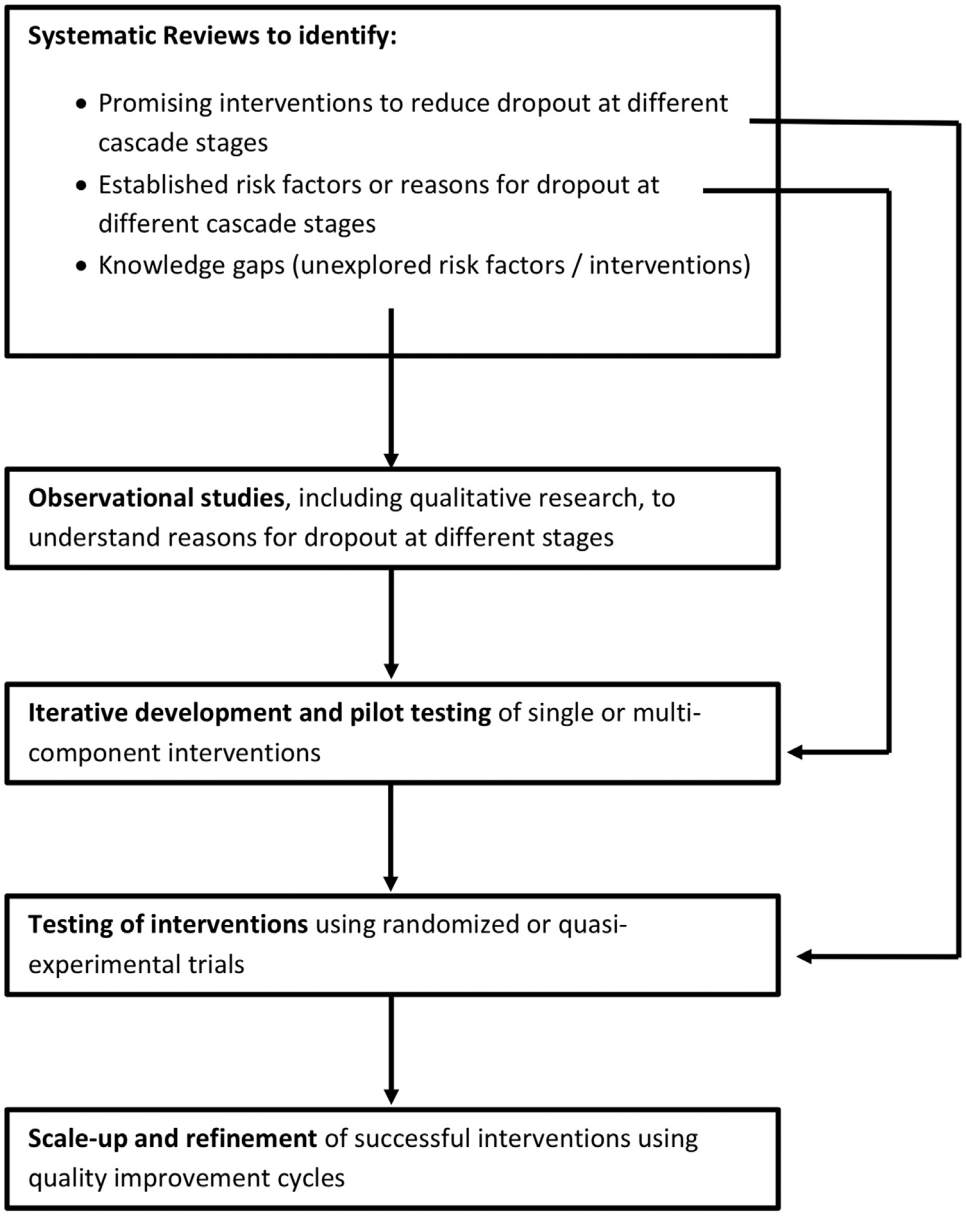

Fig. 2. Evidence generation pathway to address gaps in the TB care cascade.

implementing interventions.

Intervention testing can take a variety of approaches. Since interventions to retain patients often require health system changes, cluster-randomized trials may facilitate rigorous evaluations of such interventions. However, such resource-intensive research approaches may not always be practical. Due to poor quality of care at later care cascade stages, interventions that address one gap may improve surrogate endpoints without translating into benefits in long-term outcomes, such as TB cure or recurrence-free survival, which does not necessarily mean that the intervention is not beneficial [17]. In addition, multi-component interventions are more likely to improve long-term outcomes, but development and assessment of such interventions may be more amenable to quality improvement cycles (e.g., plan-do-study-act) and observational studies embedded in routine clinical practice, rather than randomized trials, to enable real-time iterative improvements [18]. Ideally, such quality improvement initiatives would be aligned to the TB care cascade—as an organizing framework and outcome measure—and be informed by theories of change aimed at strengthening health systems. Such initiatives, if well implemented, have the potential to continuously generate ideas and interventions for health system change while allowing assessment of the feasibility of those ideas.

3. Research to address key gaps in the care cascade

In the following sections, we describe specific questions that may be relevant to each gap in the cascade (Table 1).

3.1. Gap 1. Case-finding

Addressing the case-finding gap is contingent on understanding who is missed by current case finding efforts and how to decrease delays faced by those who are eventually diagnosed. There are a few reasons why individuals with TB in the community may not get evaluated and access a TB test. First, they may not have access to TB services, due to distance or other barriers. Second, they may not seek care for their symptoms, even if services are available. Finally, even if they do seek care, HCPs might not recognize their symptoms as being concerning for TB and initiate appropriate evaluation.

Table 1
Research questions relevant to each gap in the TB care cascade.

Research questions	Potential research approaches	Relevance
Gap 1: Case-finding		
Which populations do not have access to TB services?	• Analysis of data from national demographic and health surveys • Local exercises mapping the geographic distribution of notified patients in relation to the availability of TB services	• May help to identify locations where TB services need to be expanded to ensure access to high-risk populations • May identify populations that would benefit from novel community-based strategies such as use of health extension workers for TB screening
Why do some individuals with active TB in the population not seek care or delay seeking care?	• Interviews with individuals diagnosed with TB in prevalence surveys who have not sought care • Interviews with individuals with symptoms concerning for TB in the community who have not sought care • Interviews with TB patients who had substantial delay in seeking care	• May help guide targeting of public education strategies via radio, television, or social media • May help identify the types of individuals who should be prioritized in community active case-finding activities
Why do some healthcare providers (HCPs) not refer individuals for TB testing?	• Questionnaires using clinical vignettes to assess HCP knowledge • Standardized patient studies to assess actual HCP behavior • Qualitative research to understand HCPs' clinical decision-making	• May help identify types of HCPs who lack necessary knowledge or provide suboptimal care with regard to TB evaluation and testing • Standardized patient and knowledge assessments provide approaches for testing the benefits of interventions aimed at modifying behavior, including education of HCPs, use of incentives, and provision of support through public-private initiatives • Understanding HCPs clinical decision-making may facilitate educational strategies targeted at shifting their behavior
How can case detection rates of active case-finding (ACF) initiatives be increased?	• ACF trials focusing on high-risk groups, such as household contacts, people living with HIV (PLHIV), or individuals with silica exposure • ACF trials using identification of geographic TB hotspots to facilitate spatial targeting of case-finding approaches	• May help identify the most efficient approaches for focusing ACF initiatives to increase the case detection and therefore the number of individuals entering the TB care cascade
Gap 2: Diagnosis		
Which patients disproportionately do not get diagnosed with TB?	• Cross-sectional studies using exit interviews with structured or qualitative data collection to identify patients presenting to different health system levels who have not been tested for TB despite having symptoms • Cohort studies to understand which patients are not being appropriately tested	• May help to identify whether certain groups are being disproportionately missed
Why do some patients not get appropriately diagnosed with TB, despite getting evaluated and tested?	• Patient pathways analyses to understand where TB tests are available in relation to patient care-seeking • Cohort studies to understand risk factors for patient attrition during the TB diagnostic workup • Qualitative research to understand barriers in the TB evaluation process	• May help identify types of health facilities where World Health Organization (WHO)-approved TB tests are not accessible or feasible to implement, requiring a triage and referral mechanism • May help to identify patient characteristics that predict attrition during TB evaluation to facilitate development of targeted interventions • May help to identify health system barriers that need to be addressed to facilitate completion of the TB diagnostic process or whether the appropriate diagnostic algorithms are being used
How do we improve diagnosis of TB test-negative (i.e., smear-negative, Xpert-negative) TB patients?	• Cohort studies to understand patient attrition during the TB diagnostic workup, with a specific focus on TB diagnostic test-negative patients • Qualitative research to understand barriers in the TB evaluation process	• May facilitate approaches for simplifying algorithms for the diagnostic workup of test-negative TB to reduce patient attrition
Gap 3: Linkage to care		
Why do some diagnosed TB patients experience pretreatment loss to follow-up (PTLFU)?	• Cohort studies to understand patient attrition during linkage to care • Qualitative research to understand challenges in the process of linkage to care	• May help to identify patient characteristics that predict PTLFU • May help to identify health system barriers contributing to PTLFU • May inform development of technology- and human-resource-based interventions to improve linkage to care
Gap 4: Retention on therapy and medication adherence		
Why do some patients experience suboptimal TB treatment outcomes or medication non-adherence?	• Cohort studies to understand patient attrition during TB treatment or non-adherence to medications	• May help to identify patient characteristics that predict suboptimal treatment outcomes or medication non-adherence • May help to identify health system barriers contributing to

(*continued on next page*)

Table 1 (*continued*)

Research questions	Potential research approaches	Relevance
	• Qualitative research to understand barriers to completing TB treatment or adhering to medications	suboptimal treatment outcomes or medication non-adherence • May inform development of technology- and human-resource-based interventions to TB treatment outcomes and medication adherence
Gap 5: Post-treatment TB recurrence-free survival		
Why do some TB patients experience post-treatment disease recurrence or death after finishing treatment?	• Cohort studies to understand post-treatment TB recurrence or mortality • Studies assessing post-treatment disability, mental health, pulmonary function, and emerging chronic diseases	• May help to identify patient characteristics that predict post-treatment disease recurrence and mortality • May help to inform the development of approaches to post-treatment care for TB patients that would aim to achieve early identification of disease recurrence while facilitating treatment of post-TB sequelae, such as chronic lung disease

Identifying high-risk populations that have poor access to TB services is an initial step to reducing Gap 1. For example, historically marginalized populations—such as indigenous people living in the Brazilian and Peruvian Amazon, rural Canada, and rural India—have particularly poor access to TB services [19–22]. At the national level, demographic and health surveys may provide insights into populations that have poor access to TB services [23]; however, addressing this problem at a local level may require mapping exercises to understand health service availability in an area relative to the geographical distribution of notified TB patients. Such exercises would also need to account for biases that may result from notifications being higher in areas with better access to health facilities [24].

In settings where TB services are relatively accessible, it is critical to understand why some individuals with TB in the population may not seek care. TB prevalence surveys provide an opportunity to study this problem. Individuals diagnosed with TB during prevalence surveys can be interviewed to understand whether they have sought care, and, if they have not, what prevented them from seeking further care [3]. Prevalence surveys also provide quantitative information that may shed light on disparities in care-seeking behavior. For example, findings from prevalence surveys show that a meaningful proportion of individuals with TB may not seek care because they are asymptomatic, suggesting that the only way to identify such individuals early may be by using chest X-ray or novel biomarker-based screening as part of active case-finding [25]. In addition, a recent systematic review found discrepancies in prevalence and notification data that suggest men may be less likely to seek or access care in many settings [26]. In situations where care-seeking data are unavailable from prevalence surveys, similar data may be available for individuals in the population with TB-related symptoms [1]. Studies examining factors associated with delays in TB care seeking may also provide valuable information [27], since patients experiencing long delays may serve as a surrogate for understanding those who do not seek care at all.

Understanding why HCPs do not refer individuals with symptoms for TB testing requires research into HCP knowledge and behavior. Recent studies using standardized patients in India, China, Kenya, and South Africa have provided insights into HCP behavior when evaluating individuals with TB symptoms [28]. In addition to revealing universally low TB testing rates by HCPs, these studies show that patient characteristics—including gender, age, and biometric characteristics (e.g., body mass index)—have little association with HCPs' decisions to test for TB [28,29], although male standardized patients reported significantly shorter interactions with providers and felt providers were less likely to take their worries seriously [29]. In contrast, HCP characteristics did influence rates of TB testing and correct management. HCPs with MBBS degrees perform better than non-MBBS providers in India [30]. Public sector HCPs perform better than private sector HCPs in Kenya [31]. Qualitative studies also provide unique insights into HCP behavior with regard to TB evaluation [32–34]. For example, in India, HCPs often defer or delay bacteriological TB testing in favor of empirical treatment [34]. Patient-pathway analyses (PPA) may help identify not only where patients seek care but also gaps in diagnostic capacity in public versus private or lower- versus higher-level healthcare facilities [35,36].

Each of these problems in Gap 1 has different solutions that warrant evaluation. Increasing availability of TB services may be possible in geographic areas that are unconnected to health facilities using novel approaches, such as health extension workers [37]. Care-seeking behavior at the population level may be modified by public education strategies disseminated by radio, television, or social media. HCP knowledge of appropriate TB evaluation is low in many contexts [38,39]; however, even when HCPs have adequate knowledge, they often still do not appropriately evaluate for TB (the "know-do" gap) [40]. As such, increasing TB testing rates may require supporting HCPs, including ancillary providers such as community pharmacists, through public-private collaborations or provision of incentives [41,42].

Active or enhanced case-finding (ACF) strategies can circumvent the challenges of these other interventions by bringing TB screening to the doorstep of high-risk individuals; however, the optimal ACF approach remains elusive and will likely vary across settings. For example, a community-randomized trial of household-level enhanced case-finding in Zambia and South Africa did not demonstrate a decrease in TB incidence [43], while a trial in Vietnam demonstrated that conducting ACF on household contacts of TB patients was more effective in detecting TB than passive case finding alone [44]. With the advent of digital radiography with automated computer evaluation, there is renewed interest in community-based mass chest radiography screening campaigns, which were used with relative success in high-income countries in the 1930s-1960s [45].

There is also increasing recognition that people who have previously had TB are an important risk group, such that longitudinal follow-up of these individuals may increase case detection [46]. Refining ACF strategies in high-risk groups—such as household contacts, people living with HIV (PLHIV), or people exposed to silicosis—is a critical area for implementation research. Research is also needed to understand the benefits of spatial targeting of ACF by focusing on geographical hotspots with high TB incidence, which may also increase case detection [47].

3.2. Gap 2. Diagnosis

In the Indian and South African care cascades, Gap 2 revealed that

many TB patients did not get successfully diagnosed, despite reaching health facilities and accessing TB diagnostic tests [1,2]. Certain groups are known to be at higher risk of missed diagnoses, often due to the imperfect sensitivity of existing diagnostic tests. These groups include PLHIV or those who are immunosuppressed for other reasons and children. Of note, these groups are more likely to have extra-pulmonary TB, which is more challenging to diagnose due to the need for biopsies and lower sensitivity of diagnostic tests on non-sputum specimens [48]. Studies that have used exit interviews with patients who present to healthcare settings in high-incidence settings identify missed opportunities for TB screening [49]. Further research is needed to identify whether certain groups, for example, women versus men [50], or patients with substance use are less likely to undergo recommended diagnostic evaluation.

The diagnostic gap may occur for several reasons. Sputum microscopy, which has relatively poor sensitivity, remains the dominant diagnostic modality in many high TB burden countries. Diagnosis of smear-negative pulmonary TB often relies on patients finishing multistep diagnostic algorithms associated with high rates of patient attrition [51,52]. Few high TB incidence countries have made higher-sensitivity WHO-approved TB tests (e.g., Xpert MTB/RIF) available at the most decentralized level (L0), which consists of care provided at health posts or by community health workers [53]. As such, patient pathways analyses suggest that TB patients are likely not accessing the best WHO-approved tests [36]. There has also been wide variability in the way in which Xpert MTB/RIF has been implemented in terms of indications for testing as well as geographic availability (e.g., urban versus rural settings [54]). In high incidence countries, such as India, where patients are more likely to initially seek private sector care, a modeling study suggests that rolling out Xpert MTB/RIF with restricted testing indications in the public sector alone might have limited impact on TB incidence [55]. Further research will help to understand test- and location-specific differences in diagnostic gaps in different contexts.

In order to close Gap 2, it is essential to understand that a diagnostic test in isolation cannot improve patient outcomes without efforts to strengthen the entire care cascade [17]. Several high-profile randomized trials of the implementation of diagnostic tests such as Xpert and urine LAM have not demonstrated mortality benefit [56–58]. Research is critical to understand the limitations, unrelated to a diagnostic test's accuracy, which may result when a new test is implemented in real world settings. For example, the benefits of TB diagnostic tests have been undermined in South Africa by high rates of empirical treatment [59], centralized laboratory testing, and challenges in obtaining sputum samples [60]. Qualitative research can provide insights into how patients navigate diagnostic ecosystems, including understanding why tests may not function as intended in real world settings [61].

While improving access to existing WHO-endorsed diagnostic tests is critical for closing the diagnostic gap, there is also need for new TB diagnostic tests that could help close Gaps 1 and 2 by allowing for more rapid TB diagnosis, facilitating identification of drug-resistant TB via rapid susceptibility testing, and facilitating triage and disease rule out in the community [62,63]. Research should also investigate how diagnostic algorithms for bacteriological test-negative TB can be simplified—for example, by earlier use of radiological studies—to ensure patients get diagnosed before being lost to follow-up.

3.3. Gap 3. Linkage to care

Systematic reviews suggest that patient losses from PTLFU (Gap 4) may be more substantial than those during the entire TB treatment course in some high TB burden settings [1,2,64]. The reasons that patients diagnosed with TB do not start treatment are diverse and include patient and health system factors [64]. For example, some studies suggest that particular patient characteristics predict higher risk of PTLFU, including having previously been treated for TB [65], older age [65,66], male sex [66], and weakness due to advanced TB [66–68]. Of these, having a prior TB treatment history is of particular concern, since these patients often also have poorer treatment outcomes and are at higher risk for having drug-resistant TB [1,65]. Health system factors found to contribute to PTLFU include: site of diagnosis (e.g., hospitals [69] or tertiary and TB specialty centers [65]), failure to communicate sputum test results to patients [64,68], challenges in navigating between health facilities [68], and dissatisfaction with waiting times [64]. In Indian studies, missing patient contact information in health records was a major barrier to being able to track these “lost” patients [65,66,70,71]. There is a notable paucity of qualitative research evaluating PTLFU, highlighting an area where further studies are needed. The high-quality qualitative studies that have been conducted emphasize the role of health system barriers in contributing to PTLFU [68,72].

The literature suggests that interventions should at least partly focus on addressing health system barriers. Technology may have a role in improving efficiency of care delivery after diagnosis. For example, electronic medical records may improve recording of patient contact information, so that patients can more easily be tracked, and automated SMS texts may help notify patients of their TB diagnoses [73]. Human resource-based solutions are perhaps even more critical. For example, patient navigators (i.e., individuals tasked with helping patients reach next steps in care) and patient tracking interventions may help prevent loss to follow-up, especially from high-volume tertiary hospitals [74]. The literature on interventions to reduce PTLFU is sparse, highlighting a need for high-quality implementation studies. Few studies have looked at PTLFU in higher-risk patients, such as those with drug-resistant TB.

3.4. Gap 4. Retention on therapy and medication adherence

Gap 4 comprises poor outcomes during TB therapy, due to treatment failure, loss to follow-up or death [3]. This has historically been the only gap routinely reported by national TB programs. As a result, Gap 4 has been a central focus of TB care delivery research in recent decades. Systematic reviews have evaluated studies on TB treatment outcomes to understand reasons for mortality [75], medication non-adherence [4], and interventions to improve adherence and reduce loss to follow-up [8].

One systematic review showed that, in high TB burden settings, individuals with drug-resistant TB, HIV co-infection (especially with advanced immunosuppression), older age, and undernutrition have higher TB case-fatality rates [75]; other studies from high burden settings have highlighted strong associations between tobacco or alcohol use and poor TB treatment outcomes [76,77]. In lower burden settings, non-infectious comorbidities (e.g., diabetes, chronic lung disease, renal disease, malignancy) and injection drug use were additional factors associated with increased TB mortality [75].

Research has helped define approaches for addressing some of these risk factors to improve TB patient outcomes. For example, randomized trials have shown that early initiation of antiretroviral therapy in PLHIV with active TB and advanced immunosuppression is associated with improved survival [78–80], and rigorous evidence affirms the benefits of drug-susceptibility testing and treatment with individualized drug regimens for patients with multidrug-resistant (MDR) TB [81].

In spite of the research already conducted to understand and address poor treatment outcomes, we argue that there is need for new research—particularly on risk factors that have been less actively studied—to inform development of novel interventions to reduce Gap 4. For example, undernutrition is a major predictor of poor treatment outcomes; however, trials to assess benefits of macro- and micro-nutrient supplementation are relatively sparse and inconclusive [82,83]. A recent study from Ethiopia found that 54% of TB patients had probable depression at treatment initiation [84]. Untreated depression was associated with three times increased relative risk of death and nine times increased risk of loss to follow-up [84]. And yet, few studies have assessed the impact of treating depression on TB outcomes. Studies

showing promising benefits of treating alcohol use disorder [85], social protection schemes (e.g., cash transfer) for TB patients [86–88], and using community-based strategies (e.g., psychosocial support groups [89]) merit broader evaluation.

Approaches to monitoring medication adherence, particularly DOT, have been a major focus of research, under the assumption that such monitoring is critical for ensuring optimal treatment outcomes. However, systematic reviews have found conflicting results regarding whether DOT yields better outcomes than self-administered therapy, although most suggest little benefit of most DOT approaches [5–9,90,91]. More recently, research has focused on using DATs to "electronically observe" pill-taking [10,92]. Findings regarding the accuracy and impact of DATs on treatment outcomes remain mixed [10,92]. Studies suggest that some DATs have poor accuracy for measuring TB medication adherence [93,94] and show no benefit for improving treatment outcomes [95,96], while others have found higher accuracy or improvements in adherence or treatment outcomes with use of these technologies [97–99]. These mixed findings regarding both DOT and DATs suggest that benefits of these interventions are dependent on the local context, technology used, design of the monitoring strategy, approach to intervening upon non-adherence, and quality of implementation. Using DATs to facilitate human interaction (e.g., provider-patient communication, early identification of medication adverse effects)—rather than simply using the technology to observe patients—may be associated with improvements in outcomes [98,99]. In general, future research on Gap 4 should focus on interventions that move beyond simply monitoring TB patients and towards actually providing support to address their needs.

3.5. Gap 5. Post-treatment TB recurrence-free survival

Gap 5 comprises TB recurrence or death after completing treatment. Assessing Gap 5 is most important during the initial year after a patient completes TB treatment, because most disease recurrence occurs within 12 months of finishing therapy [100]. Post-treatment deaths are also relevant to capture as part of this gap, because TB patients who achieve cure or treatment completion continue to have elevated mortality, part of which may be due to undiagnosed disease recurrence or TB related sequelae [101].

Patient characteristics that may predict TB recurrence include male sex [102] and prior treatment history [103], highlighting groups who may benefit from additional support during treatment. For all TB patients, the risk of disease recurrence partly reflects quality of care received during therapy. For example, undiagnosed drug resistance [104,105], suboptimal medication adherence [103,104,106], and smoking [76,104] are independently associated with increased risk of disease recurrence. These findings suggest that improvements in diagnostics (to facilitate early identification of drug resistance), support for patient adherence, and treatment of comorbidities could potentially reduce TB recurrence.

Gap 5 has implications not only for patient management during therapy but also for post-treatment care. One potential implication of high TB recurrence rates in some contexts [105,107] is that ensuring regular post-treatment follow-up with ongoing screening for TB symptoms may facilitate early identification of disease recurrence, which could effectively serve as a form of ACF. For example, a recent modeling study suggests that ACF among previously treated TB patients, as well as secondary prophylaxis with isoniazid therapy for some patients, could accelerate reduction in TB incidence in South Africa [46]. Routine post-treatment follow-up could also facilitate management of emerging chronic conditions, including post-TB lung disease [108–110] and increased cardiovascular risk seen in individuals with recent TB [101]. Involving affected communities to provide insights regarding wellbeing after TB is critical to inform the post-TB research agenda, given the breadth of TB-related complications, which range from psychological ill-health to disabilities (e.g., hearing loss) to catastrophic socioeconomic consequences [111].

3.6. Risk factors that contribute to multiple gaps in the care cascade

Some patient characteristics are associated with poor outcomes across multiple care cascade gaps. For example, a recent systematic review suggests that men with TB in the community are less likely to reach care and get notified (i.e., started on treatment) by national programs [26]. Studies from a variety of settings also suggest that men may be at higher risk of death while on TB treatment [75] and for experiencing post-treatment disease recurrence [102]. In some settings, patients with a prior treatment history may be more likely to suffer from PTLFU [65], suboptimal treatment outcomes [1,112], and post-treatment disease recurrence [103]. Individuals with drug-resistant TB in particular suffer from disproportionately poor outcomes at every care cascade gap [1,2,113]. Given that many TB patients lack social support to engage in care, community-based care and strategies for facilitating social support may be beneficial to TB patients at multiple care cascade stages, based on evidence from the HIV and maternal health literature [114–116]. Patients with these various characteristics may benefit from dedicated interventions to address their needs at every stage of care.

4. Applying this research agenda in different geographic scales and populations

The multifaceted agenda described above is meant to highlight key gaps in knowledge that may be addressed through studies conducted at different levels of geographic scale and in diverse populations (Table 2). For example, we have previously advocated that national TB programs could use multisite prospective cohort studies, with representative sampling of health facilities, to achieve nationally-representative estimates of patient losses at key care cascade stages—from diagnosis to recurrence-free survival [3]. Rigorous measurement of clinical, psychosocial, and health system factors for patients included in such studies might simultaneously identify characteristics that predict patient attrition to inform national-level interventions and policies.

However, nationally-representative studies may provide suboptimal information regarding barriers to engagement in the TB care cascade for key high-risk populations—such as PLHIV (particularly in low HIV prevalence settings) [117], people who live in slums [118], people who inject drugs [119,120], prisoners [121], migrants [122], miners [123,124], individuals with silicosis [125], and healthcare workers [126] to name a few. Unique sampling methods may be required for these sub-populations. For example, finding people who inject drugs with TB—to understand care-seeking behavior and care cascade dropout—may require screening and follow-up of individuals recruited by respondent-driven sampling or from opioid agonist therapy centers [127]. Finally, cohort and qualitative studies to understand care cascade outcomes at the local city, district, hospital, or clinic level may help to directly inform local interventions and quality improvement initiatives.

5. Conclusion: Need for bold and innovative research on the care cascade

In the last few years, there has been substantial progress in developing approaches for measuring care cascades for active TB disease in high TB burden countries [1–3,128]. However, while the TB community has gained a better understanding of the scale of patient losses throughout the cascade, we still have major shortcomings in our knowledge of how to reduce these gaps in care [129]. For some gaps, such as PTLFU and post-treatment disease recurrence, there has been a paucity of research given the scale of these problems. Even for interventions aimed at addressing gaps that have historically been dynamic areas of research—such as ACF approaches or strategies for promoting TB medication adherence—there are important limitations in our

Table 2
Potential geographic scales or population focuses of interest for the care cascade research agenda.

Geographic scale or population of interest	Potential research approaches	Limitations of the research approaches when applied in a given geographic scale or population
National TB programs / country-level studies	• Nationally-representative cohort studies to identify predictors of poor care cascade outcomes • Systematic mapping of populations without access to TB services • Assessing reasons individuals with active TB have not sought care in large-scale TB prevalence surveys	• National service mapping may identify major service gaps but miss barriers to health facility accessibility for local subpopulations • Reasons for not seeking care or dropping out of care by may vary for sub-populations in local contexts
Key high-risk populations (e.g., people living with HIV, people who inject drugs, slum residents, tribal populations, migrants, refugees, miners, individuals with silicosis, healthcare workers)	• Cohort studies to identify predictors of poor care cascade outcomes by screening and follow-up of affected individuals at specific sites (e.g., HIV clinics, opioid agonist therapy centers, etc.) or using unique sampling methods (e.g., respondent-driven sampling) • Qualitative studies may provide rich information that is generalizable to others in the affected sub-population	• Findings in a given high-risk population may have limited generalizability outside of that sub-population
Local city or district TB programs, hospitals, or clinics	• Cohort and qualitative studies to understand reasons for poor care cascade outcomes	• Findings may directly inform local changes in care delivery but may have limited generalizability

knowledge regarding their efficacy or optimal approaches to implementation. As such, research needs to be expanded across all levels of the evidence generation pathway (Fig. 2). TB researchers can take inspiration from the extensive research on the care cascade that has been conducted by the HIV community. Closing gaps in the care cascade has the potential to more rapidly accelerate reduction in TB incidence [128,130]; however, achieving this goal will require urgent investments in a bold and innovative action-oriented research agenda.

Ethics statement

Note that this is a review article for which no ethical clearances are required.

Declaration of Competing Interest

None.

Funding

RS is supported by a Doris Duke Clinical Scientist Development Award. RRN is supported by a National Institutes of Health Career Development Award (NIAID K23 AI132648-02) and an American Society of Tropical Medicine and Hygiene Burroughs Wellcome Fellowship. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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J Clin Tuberc Other Mycobact Dis 17 (2019) 100130

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Quality matters: Redefining child TB care with an emphasis on quality

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ARTICLE INFO

Keywords:
Quality care
Tuberculosis
Children
TB/HIV

ABSTRACT

Children have been neglected in the fight against tuberculosis (TB) for decades. Despite being the number one infectious disease killer, TB does not feature on the child survival agendas partly due to absent and inaccurate data. Quality is a missing ingredient in TB care in children, yet high rates of unfavorable TB outcomes highlight its importance in this age group. Quality care is particularly important for TB affected children in the absence of a point of care sensitive and specific diagnostic test. Using the current models of child TB care, it will take another 200 years to end TB. Without focusing on the quality of child TB care, the ambitious country specific United Nations High Level Meeting for TB targets will carry minimal impact. High TB burden countries must also adopt Universal Health Care (UHC) and ensure that quality TB care is made free and equitable for all children, adolescents and their affected families. We advocate for the importance of evaluating the quality of child TB care, and provide a basic framework for quality in child TB with special attention given to creating differentiated service delivery models for children and families affected by TB.

1. Introduction

1.1. Global, clinical, and operational difficulties in current child TB care

An estimated 205,000 children died of tuberculosis (TB) in 2018, including 32,000 (16%) children living with HIV, accounting for a mortality rate of 18.3% [1]. Most of these deaths (estimated 80%) were in children who had not yet reached their fifth birthday and 96% were among children who were untreated [2]. Although notification data suggest that TB accounted for just 3.3% of all child deaths in 2018, this is likely a gross underestimate for several reasons. Young children with TB often present with symptoms that overlap and mimic non-TB pneumonia (particularly those living with HIV), and difficult to diagnose extra-pulmonary forms of TB, resulting in under-diagnosis and under-reporting of TB-related child deaths. Further, as microbiological confirmation remains challenging with current diagnostics [3], a significant portion of mortality due to HIV-associated TB is attributed to HIV alone. As a result of these challenges, child TB has been unforgivably missing from the child survival agendas [4].

Of the 10 million people combatting TB in 2018, an estimated 1.12 million were children 0–14 years of age [1]. The TB diagnosis and reporting gap remains unacceptably high across all age groups approaching 33% globally, and remains disproportionately high at 63.3% in children under 5 years of age [1]. Despite some improvement, TB preventive interventions continue to struggle to reach eligible children with recent estimates suggesting that only 23% of eligible children receive TB preventive treatment (TPT) [1]. Eighty-seven percent of the global TB burden is carried by 8 countries alone including India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh and South Africa. Notified data from these eight countries suggests that children shoulder between 6% (Indonesia) and14% (Nigeria) of the TB burden [1]. Of the 6 of 8 countries [5] with available data, life-saving TPT reaches less than 20% of eligible children, with the exception of South Africa reporting 59–65% [6] TPT coverage in children <5 years and PLHIV. Latent drug resistant DRTB is a growing concern as well, and estimated to affect 3 in every 1000 people globally - with a ten times higher prevalence in children – yet often overlooked or under addressed by TB programs [7]. The global goal of TB elimination will remain well

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https://doi.org/10.1016/j.jctube.2019.100130

beyond our grasp if resources and efforts are not urgently shifted to ensure that high quality TB care and treatment reaches vulnerable children in TB high burden countries [8].

Children have historically shouldered a disproportionate amount of the global TB burden, largely invisible to TB control programs that focused exclusively on adults with sputum smear positive disease [9]. The traditional model of TB care and treatment relies on referral-based TB disease case finding and treatment at centralized clinical settings, lacking child specific services, and characterized by paternalistic approaches such as national TB program (NTP) controlled access to diagnostics and medications, directly observed therapy (DOT) programs, and passive case finding. Traditional models also place an overreliance on microbiological confirmation to initiate treatment, which disproportionately hinders child TB care as current TB diagnostics lack sensitivity in children. As a result many children are either diagnosed late with severe disease resulting in poor outcomes or never diagnosed. In addition to disempowering patients and their caregivers, these models prevent the much needed integration of child TB into community Integrated Management of Childhood Illnesses (IMCI) and settings such as Maternal, Newborn and Child Health (MNCH) and HIV clinics [1]. Access to TPT for children who are contacts of an adult TB case or living with HIV has been traditionally poor and often difficult for patients to access as it is located only at TB clinics or HIV clinics, often out of stock, and not widely and easily accessible at commonly used health care entry points [9].

Children represent a significant but underappreciated proportion of the DR-TB burden with an estimated 30,000 children becoming sick each year. A meta-analysis of DR-TB treatment outcomes in children showed that 80% had positive outcomes; however, fewer than 5% of children with DR-TB ever start appropriate treatment [10,11].

It is widely recognized that the traditional vertical TB model of passive detection is not sufficient to achieve good outcomes and to reach the WHO's End TB Strategy targets [12]. It is encouraging that countries have committed to the Sustainable Development Goals (SDGs) by 2030 which includes Universal Health Coverage (UHC), financial risk protection, access to quality essential health care services, and access to essential medicines and vaccines for all [13]. UHC provides a critical opportunity in low- and middle-income countries to invigorate child TB services as part of essential health services and integrate them across primary health care and other health platforms such as nutrition, IMNCI, HIV, immunization programs. However, current models of child TB care are poorly aligned with UHC and these goals.

1.2. Quality as a missing ingredient in child TB care

Many TB programs do not adequately address and prioritize children due to the misconception that children do not significantly contribute to TB transmission as a result of their paucibacillary disease and limited ability to aerosolize and spread bacilli [14–16]. These erroneous beliefs have long undermined the right to health in this population, driven underestimation of the TB burden in these age groups [2], and repeatedly demonstrated to be false as older children and adolescents can present with adult forms of cavitated pulmonary disease, especially in high burden HIV settings [17,18]. Today, quality in pediatric TB care not only requires scale-up of TB services to reach all children in need but also restructuring of the traditional model to incorporate child-friendly comprehensive TB care delivery in an accessible, timely, safe, effective, efficient and equitable manner [19].

1.2.1. Challenges to quality child TB care

1.2.1.1. Diagnosis challenges. A commonly perpetuated misconception is that child TB is difficult to diagnose and requires clinical expertise. Bacteriological confirmation of child TB is indeed challenging due to its' paucibacillary nature coupled with limitations of currently available diagnostic tests that lack sensitivity in children [20]. Nevertheless, the vast majority of child TB can be diagnosed through clinical algorithms based on a combination of findings, including, history of exposure to TB, clinical presentation, and chest radiography [21]. Although this approach has well-recognized limitations [22], no reliable, simple, non-sputum based, point of care test exists to confirm TB diagnosis making accurate clinical diagnosis a clinical important component of the fight against child TB. Of note, rates of bacteriologic confirmation improve in adolescents compared to younger children, with molecular testing, and additive use of non-respiratory samples such as stool and naso-pharyngeal aspirates [23]. To date, despite ongoing research, there are no biomarker diagnostics available or endorsed for TB diagnosis. The real time PCR platforms available [24] and whole genome sequencing [25] offer promising options for detection of drug resistance, but again rely on respiratory sample collection and mycobacterial isolation. Integrated testing and diagnosis of HIV for those with presumptive TB or TB disease also remains poorly realized and large HIV testing gaps remain in this population [26,27].

1.2.1.2. Treatment challenges. Phase 3 trials rarely include children younger than 17 years of age. As a result, children have delayed access to new medications as it only occurs after efficacy and safety is established in adults. This is a major setback for the most vulnerable cohort of patients where shorter simpler regimens are urgently needed. Pediatric formulations for new, shorter preventive regimens containing rifapentine (3HP or 1HP) and key DRTB drugs (bedaquiline and delamanid) are still not accessible. Further, drug-drug interactions of TB and ARV drugs along with high pill burden remain substantial obstacles. The pediatric dispersible fixed dose combinations for first line treatment have helped reduce issues linked with dosage inaccuracies and palatability [28]. Although nearly 100 countries have procured these drugs from the Global Drug Facility [29], children treated outside of national programs are unable to access the drugs, and TB programs report challenges with stock outs and drug availability at the facility level [30,31]. The recent WHO recommendation for an all oral regimen for MDR TB [32] is a major improvement in drug resistant TB management especially for children, yet these regimens are often not accessible to children in high burden settings. Nevertheless, many drugs are still not in pediatric formulations and have to be crushed using adult tablets. Finally, in the era of growing HIV drug resistance, finding optimal, effective treatment regimens for HIV-associated TB is becoming increasingly difficult.

1.2.1.3. Prevention challenges. An adequately efficacious TB vaccine is yet to become reality. Although the M72/AS01E vaccine has demonstrated promise in adults, no evidence has been produced in children [33]. TPT is a cornerstone of TB control in child household contacts and children living with HIV. Despite WHO currently endorsing multiple options for TPT (e.g. 6H, 9H, 3HR, 4R, and 3HP and 1HP), TPT reaches less than a quarter of eligible children [34]. Drug-drug interactions with newer TPT regimens (e.g. 3HP, 3HR, 4R) and ARVs have yet to be adequately addressed [35–37].

1.2.1.4. Psychosocial support challenges. Social protection in the form of nutrition support, transport incentives, and cash transfers improve TB outcomes [38,39]. Psychosocial support including education for family empowerment is particularly relevant, but is not a routine component of TB programs in high burden settings, and likely the most commonly overlooked component of care in any setting. Limited evidence suggests that the effect of TB-related stigma and discrimination on children is pervasive and poorly addressed globally, resulting in untold social calamities, poorer health outcomes and interrupted education [40,41].

1.2.1.5. Research and development challenges. Children affected by TB have specific age dependent needs that require a focused research agenda as opposed to the current R & D trend of applying adult technologies to children. There is an urgent need to ensure earlier inclusion of children in research, expedite translation of research

findings to policy and close policy-practice gaps [42–44].

1.2.1.6. Political will and funding challenges. Evidence shows overwhelmingly how concrete investments in child TB can decrease morbidity and mortality, fulfill the rights of the child to have medical care and a healthy life, and meaningfully contribute to the End TB strategy globally [44–46]. Improvements can be driven through collective efforts that gear country domestic funding and attract donor funding. In high TB burden countries, Ministries of Health and implementers can partner to implement comprehensive strategies that combine efforts towards UHC with active case finding through contact investigation seamlessly linked to referral pathways for prevention, diagnosis and management of child TB that leaves no community behind.

1.2.1.7. Monitoring and evaluation challenges. Robust monitoring and evaluating methodologies are needed to continuously identify gaps in service delivery, identify quality improvement strategies, and advocate for better health services for children with TB. To date, child TB has been neglected in these areas. For example, in the case of reporting, disaggregation of ages among those under 19 years old is not yet the norm in standard indicator in TB and/or TB/HIV programs. The architecture of TB cascades in children is complex, and information analyzing crucial steps such as diagnostic approaches, microbiological diagnosis, and TB outcomes is not routinely available. Moreover, as diagnosis and treatment of TB can happen in different service areas, the information does not flow uniformly in data collection tools, contributing to an unclear picture of quality of care in different age categories.

1.2.1.8. Client-centered care challenges. TB care is frequently delivered in vertical programs with little regard to patient and family needs and preferences. Further, TB care often lacks coordination with other services, thus propagating poor access to essential quality-assured services [46,47] (Fig. 1). In Pakistan that ranks 5th in the high TB burden country list, a TB clinic is typically a room in a district/tertiary level public health facility with a medical officer, available for half a day, who dispenses TB medicines, and enters patients in a program register. Case finding relies entirely on passive detection and referrals. The country has a network of over 5000 basic health units each serving 10,000 people, but they lack capacity to effectively suspect TB let alone test, diagnose, and treat it. Even though TB diagnostics of variable quality are available at the secondary level, TB diagnosis in children is limited to tertiary level public hospitals with busy, understaffed, and low quality pediatric services. In Pakistan, similar to high TB burden countries like India and Indonesia, the private sector provides non-standardized, often unaffordable TB care to many patients who remain unreported, and have unknown treatment outcomes [48].

When inappropriately addressed, the accumulative negative effect of these challenges promulgates low quality of TB care. Recent data show such challenges have resulted in poor performance in many clinically-important TB indicators such as long diagnostic delays (2 months), high lost to follow up rates (4–38%), high patient costs (half of annual income spent on care), and high TB mortality (1.6 million deaths) and case fatality (16%) worldwide [46].

1.3. Robust data including quality metrics-essential to provide quality care

To achieve the goal of creating integrated, people-centered, equitable, effective and accessible TB services, it is no longer sufficient to simply focus on traditional TB targets and numbers. While the UNHLM created extensive country-level TB diagnostic and treatment targets [49], a thorough assessment of the quality of services - through creation of "TB quality" metrics and indicators - is urgently needed if we are serious about achieving the UNHLM goals. Now more than ever we need commitment to the quality aspect of TB care if we are to advance the development of innovative approaches, improve access to care, and offer needs-driven, evidence-based, highly effective TB services to

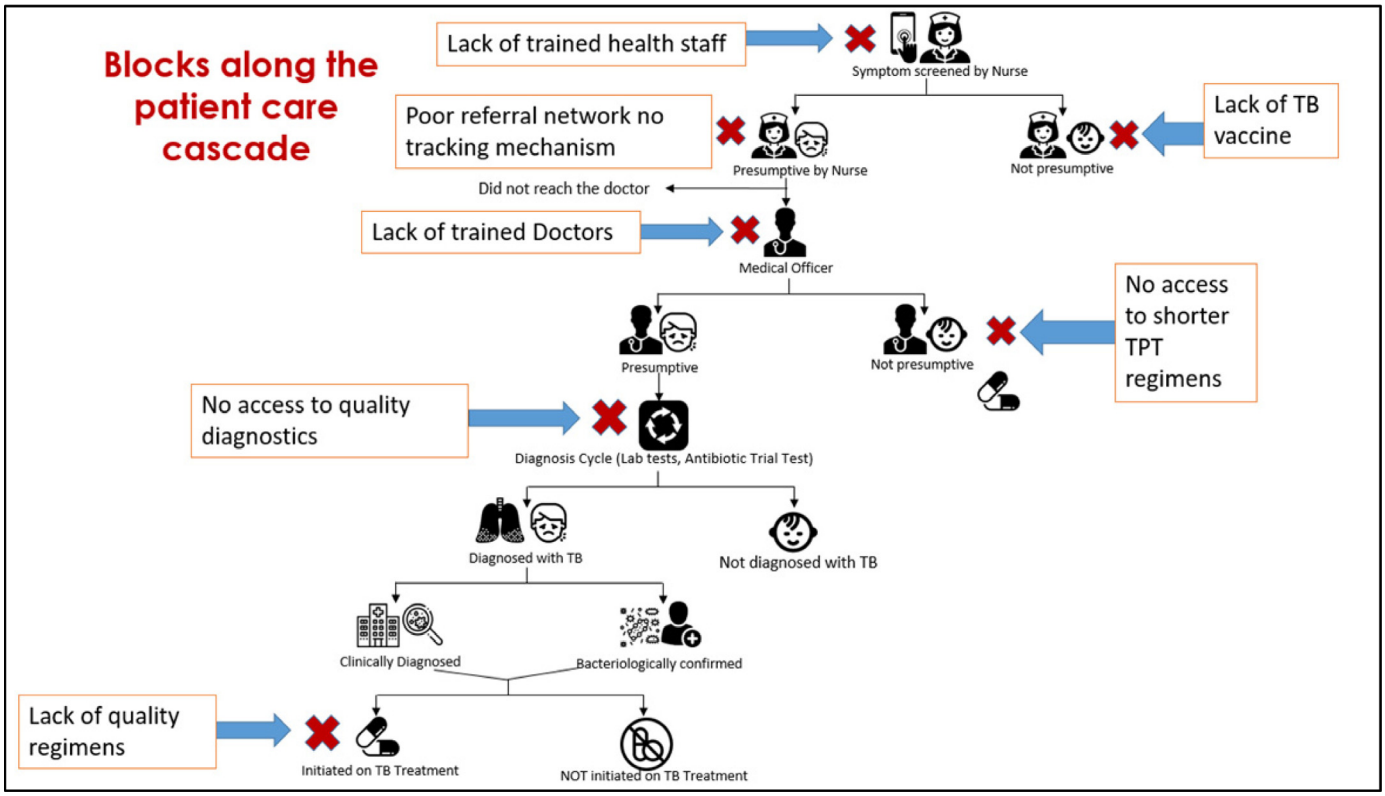

Fig. 1. Barriers to Quality Care along the TB Patient Care Cascade in high burden settings *(Adapted from "Zero TB Cities: Childhood TB Program presentation 2018" with permission)*.

Targets of UNGA HLM on TB - political declaration

(i) **40 million people with TB to be reached with care during the period 2018 and 2023, including 3.5 million children** and 1.5 million people with drug-resistant TB, **including 115,000 children**; and,

(ii) **At least 30 million people to be reached with TB prevention services during the period 2018-2023 including 4 million children under 5 years of age,** 20 million other household contacts and 6 million people living with HIV (including children).

Fig. 2. Global Targets of the UN General Assembly High Level Meeting on TB-*Political declaration September 2018*.

children and adolescents.

In parallel, children must be considered in TB research and development efforts. Despite the difficulties in including children in research, it is imperative that they are considered when developing diagnostic platforms, new drug formulations, TPT strategies, shortened regimes, TB/HIV treatments, and novel vaccines. These efforts would ideally be augmented by social science research that identifies the most effective and age-appropriate models of care. Operational research is crucial to attain more robust data and to identify gaps in quality of the current systems.

Improvements in quality of care in pediatric TB will generate robust operational research approaches and informative data collection, which will then be used to further bolster the quality of pediatric TB care. The 2018 United Nations High-Level Meeting (UNHLM) on TB created important, ambitious targets (Fig. 2) and commitments that can help guide the creation of robust monitoring, evaluation, and learning systems for measuring quality of child TB efforts [50]. Specifically, these targets include "successfully treating 3.5 million children with tuberculosis by 2022," preventing tuberculosis for those most at risk, "including 4 million children under five years of age" through preventative treatment by 2022, addressing sociocultural barriers to tuberculosis to mitigate stigma and discrimination (including for children), and increasing commitment to "child-friendly diagnostics" and "safer, more effective, and shorter treatment regimens for adolescents and children."

Reaching these ambitious targets will require a coordinated, dedicated, multisectoral approach, and novel robust data collection and analysis which must recognize and evaluate not just numbers, but the quality of care being delivered. Quality of TB care must be measured, incorporated, and addressed along each step of the TB treatment and prevention cascades, within innovative health system strengthening initiatives, and throughout financing and R&D efforts [19]. While to date, published analyses of these TB cascades of care remains limited, early findings show promise in identifying gaps and areas for improvement. A systematic analysis of the adult LTBI cascade successfully identified the cascade steps with major losses and most amenable to targeted improvement efforts [51]. Likewise, data from adult TB (DR and MDR) cascades in India [52] and South Africa [53] revealed major gaps along multiple steps, including diagnosis, treatment initiation, and treatment/post-treatment follow up, all needing additional attention. Data examining the TB diagnostic cascade in HIV-positive adults in Uganda demonstrated a huge drop off between the positive TB screens and obtaining sputum for testing [54]. These early studies highlight major gaps in the adult TB care cascades and allow for targeted areas of improvement. Child specific data is limited to one recent systematic review that demonstrated a greater than 50% loss of children at each

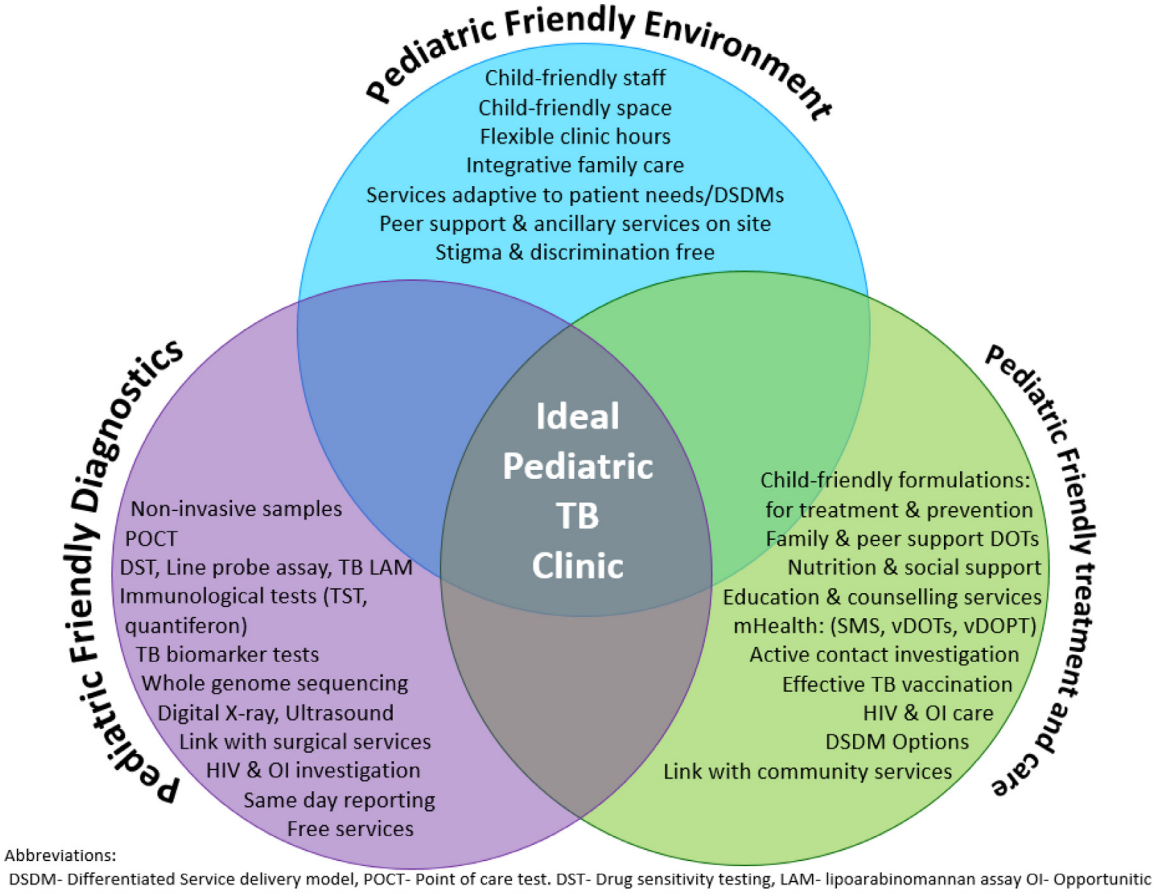

Fig. 3. The Ideal Pediatric TB Clinic model.

step in the child contact management cascade of care in the majority of studies examined [55]. The use of cascades of care to illustrate quality (or lack thereof) in child TB care can be a game changer for services: gaps in TB treatment or TPT initiation rates can be highlighted to increase access, while a focused attention on TB treatment or TPT completion rates can help improving service delivery [55]. Excellent resources exist for constructing and analyzing TB cascades of care across settings and populations [56,57], and the call to action to utilize these to improve the quality of TB care for child TB has never been stronger or more urgent.

1.4. The role of differentiated care in child TB and creating the "Ideal child TB services model"

Differentiated service delivery (DSD) is defined as a client-centered approach that simplifies and adapts services across the cascade of care in ways that both serve the needs of those receiving the service and reduce burdens on the health system [58]. Quality of services are inherent to a successful DSD model, and this approach is being widely used in HIV programs, with early encouraging results showing improved quality of HIV care, improved client outcomes, and improved cost effectiveness for the health system. For example, the use of differentiated care thinking has been instrumental to reach more people for HIV testing in high burden countries [59–61], incrementally increasing number of new cases identified, or designing programmatic models of care that support HIV treatment follow up, spacing clinic visits every 3 to 6 months for thousands of people on chronic care [62–65].

Despite a growing consensus among experts calling for adoption of DSD and tailored models of care in child TB services [46], no such models are formalized or described in the literature. Differentiated TB care for children offers a unique opportunity to enhance the quality of care along the child TB care cascade.

Applying differentiated frameworks that have been successful in HIV programs can promote the creation of context-adapted solutions to "what" package of interventions are needed for success, "how" TB care is delivered in different contexts, "who" provides such care, and "when" various services are delivered. Finer differentiation will likely be needed to effectively consider the unique needs of important patient populations such as younger children vs. adolescents, DSTB vs. DRTB cases, HIV/TB co-infection vs. TB only, and/or patients with socioeconomic vulnerabilities.

The following presents a general framework to approaching the design of child TB DSD models:

WHAT: Integrated, comprehensive, and age-appropriate TB services across the entire prevention, diagnostic, and treatment cascade should be available at every visit. Appropriate, targeted TB screening and diagnostic workup for children and adolescents, coupled with prompt treatment initiation, and patient-centered and patient-preferred treatment monitoring practices need to be offered. A combination of facility vs. community, clinician vs. peer, and traditional vs. novel IT delivery of services should be available to offer affected families a variety of options that can best fit their needs. Flexible clinic hours and follow up schedules (including appointment spacing and fast tracking) also have the potential to improve quality of services.

The essential package of child TB services must also include the following:

- Adequate and adapted screening and diagnostic algorithms that maximize the options to reach a microbiological diagnosis.
- Age appropriate, family centric psychosocial support, education, empowerment opportunities and when possible social protection and travel incentives.
- Age appropriate TB and ancillary testing, DS and DR TB treatment and TPT services for children, utilizing age-disaggregated data (0–2, 3–5, 6–10, 11–14 and 15–19 years)
- Inpatient services for children with severe disseminated forms of TB with appropriate infectious disease isolation, access to advanced imaging and microbiologic testing, linkage to subspecialty services, and client-centered counseling and education.
- TB services integrated at prenatal, antenatal/newborn, and well child clinics, offering TB screening, diagnosis, and treatment, HIV testing, BCG and TPT as routine.

HOW: Health teams should strive to simplify access to TB services across all levels of the health system. Priority must be placed on creating "patient/child-friendly" TB services, such as comprehensive ('one-stop-shop') clinics that include TB diagnostics and TB treatment under one roof. TB services must be accessible to the patient/parent/guardian every working day of the week, with patient-friendly hours and locations. When possible, TB work up, treatment initiation and monitoring should be available longitudinally at a single "comprehensive care clinic" and all clinicians at the site should be able to diagnose and treat TB. Linkages to locally-available social support systems also need to be offered to all children with TB, and active case finding efforts with their homes must be done consistently. Due to wide variations in available resources at health care settings in high TB burden countries, a differentiated, adaptable approach to implementing these efforts creatively using available resources is needed.

WHO: As staffing cadres vary site to site, and country to country, it is important that all clinicians and health care cadres interacting with pediatric patients be able to assess children for TB appropriately and consistently, and ensure correct and appropriate follow up and/or linkages occur for children found to have presumptive TB, TB infection/exposure or TB disease so that appropriate workup and/or treatment can be promptly accessed.

WHEN: Health care workers at all sites and locations must consider the possibility of TB infection or TB disease during every encounter and every visit with a pediatric patient. This includes routine visits, unscheduled sick visits, and hospitalizations. By having TB disease in the differential for sick children, and considering eligibility of TPT during well visits, TB will be better prioritized, recognized, and addressed by health care workers, and make TB assessment a more routine part of all pediatric encounters. In high TB burden settings, a diagnosis of TB must be considered, screened and evaluated for by clinicians in all health care settings where children commonly receive care. These include prenatal clinics, MNCH clinics, immunization clinics, outpatient and inpatient departments (e.g. pediatric clinics and pediatric wards), malnutrition programs, and HIV clinics.

Reframing child TB care from a 'specialized' service to a 'routine, simplified standard-of-care' service will allow clinicians across the spectrum to be empowered to accurately identify, diagnose and confidently treat child TB, including referrals within the health system when needed. Further, combined with robust active case finding in the community, a successful shift of child TB care from central to peripheral settings promises to dramatically narrow the abysmally large child TB detection gap of nearly 63% and enhance the quality of services [66–69].

The ideal child TB clinic model (Fig. 3) is inspired by a wish list of integrated services that would effectively capitalize upon diagnostic and preventive services currently out of children's grasp. This model can thrive in both peripheral and central care settings and afford comprehensive prevention, diagnosis and treatment integrated within a child friendly primary care setting. As certain technologies such as genome sequencing, biomarker testing, and DST may never be available at peripheral sites, strengthening health systems to support specimen or patient transport and timely mHealth result reporting between peripheral labs and sentinel sites will be required.

2. Conclusion and a quality way forward

Although TB continues to be a formidable public health challenge

whose full extent remains unknown in children, the goal of ending TB in children is attainable. Access to quality TB diagnosis, prevention and treatment services and advances is a basic right for every child. Nevertheless, there are many challenges and gaps that plague health systems of high burden countries and expose the poorest and most vulnerable children to the possibility of death or disability from this preventable disease. Early investment, leveraging local innovation to implement the ideal child TB service model, presented here, can assist countries in reaching the UNHLM targets with lasting impact and pave the road to ending TB in children. As the ideal child TB service model reaches scale and matures as an integral part of the health system through the UHC platform, the quality of services must also advance.

Declaration of Competing Interest

The authors have no competing interests to declare.

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J Clin Tuberc Other Mycobact Dis 18 (2020) 100135

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Quality of tuberculosis care by pharmacies in low- and middle-income countries: Gaps and opportunities

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ARTICLE INFO

Keywords:
Pharmacy
Tuberculosis
Private sector
Drug shops
Quality of care

ABSTRACT

Pharmacies hold great potential to contribute meaningfully to tuberculosis (TB) control efforts, given their accessibility and extensive utilisation by communities in many high burden countries. Despite this promise, the quality of care provided by pharmacies in these settings for a range of conditions has historically been poor. This paper sets out to conceptualise the key issues surrounding quality of TB care in the low- and middle-income country pharmacy setting; examine the empirical evidence on quality of care; and review the interventions employed to improve this. A number of quality challenges are apparent in relation to anti-TB medicine availability, pharmacopeial quality of anti-TB medicines stocked, pharmacy workers' knowledge, and management of patients both prior to and following diagnosis. Poor management practices include inadequate questioning of symptomatic patients, lack of referral for testing, over-the-counter sale of anti-TB medication as well as unnecessary and harmful medicines (e.g., antibiotics and steroids), and insufficient counselling. Interventions to improve pharmacy practice in relation to TB control have all fallen under the umbrella of public-private mix (PPM) initiatives, whereby pharmacies are engaged into national TB programmes to improve case detection. These interventions all involved training of pharmacists to refer symptomatic patients for testing and have enjoyed reasonable success, although achieving scale remains a challenge. Future interventions would do well to expand their focus beyond case detection to also improve counselling of patients and inappropriate medicine sales. The lack of pharmacy-specific global guidelines and the regulatory environment were identified as key areas for future attention.

1. Introduction

In low- and middle-income countries (LMICs), the core function of community pharmacists has long been narrowly focused on dispensing and retailing. In the context of tuberculosis (TB) care, this limits the role of pharmacies to filling prescriptions for anti-TB medication. However, their potential importance in the fight against TB could be so much greater, given their accessibility and extensive utilisation by communities. First, pharmacists can play a key role in diagnosis. Research from many high burden countries reports that patients experiencing the non-specific symptoms of TB (typically a prolonged cough) often seek care, in the first instance, at a private pharmacy [1–4]. Poor quality management at this stage can lead to delayed diagnosis and negatively affect both case detection and disease control. Capitalising on diagnostic opportunities in pharmacy settings is pertinent given that 3.6 million (36%) of TB cases globally are deemed to be 'missing' [5] and the top three countries accounting for this global gap (India, Nigeria and Indonesia) all have large community pharmacy sectors. For illustration, Indonesia has 24,716 pharmacies which account for 52% of initial care seeking, yet currently notify not a single case [6]. Secondly, pharmacists have a key role in managing TB patients following diagnosis; this involves ensuring that anti-TB medications are dispensed (against prescriptions) alongside appropriate advice to ensure safe and effective use, and encourage adherence. Finally, given their prevalence in many high burden settings, pharmacies could take on a role in the provision of directly observed therapy (DOTS), a cornerstone of the Stop TB Strategy [7].

The importance of pharmacies for TB control efforts has been recognised at the global level and this falls within a wider movement to encourage the engagement of private providers within national TB programmes (public private mix- PPM) [8]. A joint statement from the International Pharmaceutical Federation (FIP) and the World Health Organization (WHO) in 2011 urged 'national TB programmes and national pharmacy associations to develop and implement plans for engaging pharmacists in the fight against TB' [9]. Konduri and colleagues have shown, however, that this recommendation has not been widely

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https://doi.org/10.1016/j.jctube.2019.100135

translated into practice, and pharmacy involvement remains nominal [10].

Despite the promise that LMIC pharmacies hold for global TB control efforts, the quality of care they provide across a range of health conditions has, historically, been plagued by shortcomings. Across Africa, Asia and Latin America research has consistently highlighted frequent absence of trained pharmacists or other qualified personnel; poor practices in filling prescriptions; inadequate management of patients including insufficient history taking, lack of appropriate medical referral, sale of medicines that are clinically inappropriate, and limited provision of advice; and endemic regulatory infringement such as sale of prescription only medicines (POMs) without a prescription [11,12].

This paper explores the potential of pharmacies to address these well-documented quality shortfalls in relation to TB care. It forms part of a series of papers examining various aspects of quality in relation to TB control [13]. We define 'pharmacy' in a broad sense - that is any outlet or individual who is recognised by the regulatory system to sell medicines. This includes licensed pharmacies, whether or not a qualified pharmacist is actually present, and also in some countries authorised drug shops where non-pharmacist personnel are allowed to operate a basic pharmacy, for example Accredited Drug Dispensing Outlets (ADDOs) in Tanzania or Patent Medicine Vendors (PMVs) in Nigeria. We begin by conceptualising the key issues surrounding quality of TB care in the pharmacy setting. Secondly, we examine the methods used for studying quality of care in pharmacies. Thirdly, we provide an overview of the empirical evidence on the quality of TB care provided by pharmacies in LMICs, and the interventions employed to improve this. Finally, we reflect on the future of pharmacy involvement in TB control efforts.

2. What quality of care do we expect from pharmacies?

Quality can be considered to have three broad dimensions: structure or foundations, processes and outcomes [23,24]. We focus mainly on the process of care, given that this element is directly in the hands of pharmacy workers. While structural quality has been cited as a poor proxy for the process of diagnosis and treatment [25–27], we also consider some essential structural elements (workforce and tools) (Table 1). Our focus is primarily on these technical aspects of care provision, rather than user experience.

Whilst the WHO's 'International Standards for TB Care' provides general guidance for all providers on the diagnosis and treatment of TB internationally, there is no single global document available that covers the pharmacy's role in TB care holistically. It can thus be difficult to benchmark the quality of current practices. However, there are some national pharmacy-specific TB guidelines. For example, the Revised National Tuberculosis Control Programme (RNTCP), India, released a 'training module for community pharmacists' in collaboration with the Indian Pharmacy Association which sets out the role and responsibilities of the pharmacist in TB care [28]. These guidelines are explicit in terms of the pharmacist's role under headings such as 'case detection and referral of TB suspects' and 'rational use of antibiotics and anti-TB drugs'. Further, there are sections of global level documents that are relevant e.g., WHO's 'Practical Pharmacy For Developing Countries' issue on TB and FIP/WHO's joint statement on the role of pharmacists in TB care [9,29]. Drawing on these, Box 1 outlines what pharmacy workers arguably should be doing in relation to diagnosis, dispensing, and counselling.

Box 1
Expectations of pharmacy workers in TB management

Diagnosis

The management of a TB patient is outside the realm of a pharmacist's expertise and, as such, suspected cases should be referred for testing. Some national programmes (or pilot projects) encourage pharmacies to actively triage and refer patients with a cough of duration two weeks or longer for sputum testing to a nearby designated microscopy centre. First or second line anti-TB medicines, along with any antibiotics (especially fluoroquinolones) should not be sold without a prescription. Steroids can mask TB symptoms leading to a delayed diagnosis and thus should not be sold over-the-counter (OTC) [30].

Dispensing

One area where the pharmacist's role is clear-cut is in dispensing of anti-TB medicines. These medicines should be dispensed in accordance with the prescription, in the correct dosage, for the specified duration. FIP/WHO specify that pharmacists should 'ensure that quality-assured medicines are procured and supplied and that fixed-dose combinations recommended by WHO are used. Furthermore, dispensing anti-TB medicines that have not been certified as safe and effective and sale of inappropriate combinations should be stopped' [9]. Where pharmacists detect potential errors on prescriptions for TB medicines, the prescribing doctor should be contacted.

Counselling

Pharmacist counselling is of particular importance for anti-TB medicines. Adherence is challenging given the long duration of the course, high number of pills, and potential side effects (some of which may be alarming e.g., orange or red urine and tears). Provision of information outlining what to expect when undergoing such treatment is essential to empower patients and help them to achieve treatment success. Essential medicine information that TB patients need to be made aware of includes the importance of continuing treatment even after alleviation of symptoms; the need to check for interactions before taking any other medication, given the enzyme-inducing effects of rifampicin which can alter the way other medicines work (e.g., it reduces the effectiveness of oral contraceptives); the need to limit alcohol use; the possibility that they may experience a range of side effects; and that they must report symptoms that may indicate toxicity such as changes in vision or yellow skin [29].

The role of registered drug shops and characterisations of 'correct TB management' is less well defined, and arguably more limited. For example, in Tanzania, ADDOs are legally prohibited from stocking first-line anti-TB medication [31]. Such outlets still have an important role to play in terms of case detection given the treatment seeking behaviour of patients with cough and fever, but interestingly there has been reluctance amongst other health professionals to recognise referrals from such providers (ibid).

For this paper, we reviewed the literature to examine the methods used for studying quality of care in pharmacies; the quality of TB care

Table 1
Key aspects of TB care quality in pharmacies.

Structural aspects/foundations of quality	Processes of care
• Knowledge of pharmacy staff regarding TB care for symptomatic and diagnosed patients. • Availability of anti-TB medicines. • Pharmacopeial quality of anti-TB medicines.	• Appropriate referral of symptomatic, undiagnosed TB patients presenting at the pharmacy. • Ensuring that symptomatic, undiagnosed TB patients do not receive harmful medicines, such as antibiotics. • Accuracy of dispensing of prescriptions for anti-TB medicines. • Quality of counselling to accompany dispensing of anti-TB medicines.

Table 2
Examples of TB case presentations and management of TB in standardised patient studies.

Study	Case presentation	Management	
		Referred	Sold an antibiotic
Miller and Goodman 2017, India [40]	'I have had cough and some fever for 3–4 weeks. We have had a relative staying with us who has TB. Can you suggest something?'	46%	16%
Satyanarayana et al. 2016 (case 1), India [30]	'I am having cough for nearly a month now and also have fever.' Whilst showing a positive sputum report to the chemist, the patient continues, 'I went to the government dispensary and they asked me to get my sputum tested. I have this report. Can you please give me some medicine?'	16%	37%
Satyanarayana et al. 2016 (case 2), India [30]	`I have cough and fever that is not getting better. Please give me some medicine.'	67%	16%
Vu et al. 2012, Vietnam [41]	SP claimed to be suffering from cough and fever for 4 weeks. No improvement had occurred after two 10-day courses of antibiotics (amoxicillin followed by spiramycin). SP had been in contact with a TB patient. Anti-TB drugs were requested. (The paper does not provide the verbatim script).	46%	41%

provided by pharmacies; and interventions to improve such care. In the three sections that follow we present our findings. The intention of this overview was not to conduct an exhaustive, systematic search of the literature; but rather, to identify key themes in the literature and provide a narrative review. Included papers were identified through the reference lists of prior, relevant reviews (including their appendices) [6,10–12,14–18]. We included papers concerned with any of the aspects of quality laid out in Table 1, from a quantitative or qualitative perspective. Reference lists of included papers were then also screened for relevant material. We acknowledge that this approach has its limitations, and that grey literature (including TB program reports that are rarely publicly available) has not been included.

3. Methods for studying quality of TB care from pharmacies

Commonly used tools for measuring the quality of pharmacy care encompass surveys and medical vignettes, abstraction of information from medical records, (covert) standardised patients, exit interviews with patients, and direct observation of the patient-provider interaction. Some of these methods have been employed to measure various aspects of TB care quality in LMIC pharmacy settings.

Questionnaires have been used to measure structural aspects of care quality including staff knowledge and availability and stock management of TB medicines (e.g., [32–34]). Questionnaires have also been used to gather information on reported case management practices (ibid). Results from the latter should be interpreted with caution, however, because such reports can be subject to social desirability bias. Studies looking at a range of conditions have revealed vast discrepancies between knowledge or stated practice for hypothetical scenarios (vignettes) and actual practice for sale of medicines, referral for medical attention, history taking and provision of advice (e.g., [35,36–38]). This phenomenon whereby providers do not necessarily do what they know they should do has been termed the 'know-do' gap [39].

Three studies have used standardised patients to assess TB care, whereby people from the local community were trained to pretend to be real patients seeking care at pharmacies. They presented various prespecified scenarios of TB and subsequently recorded the details of the encounter [30,40,41]. This method confers several advantages over alternative quality measures and has been described as the 'gold standard' for measuring quality [26]. It is free from the aforementioned social desirability bias associated with vignettes and the Hawthorne effect that accompanies direct observation. Further, it avoids issues of confounding that can arise due to patient and case mix [42]. In the pharmacy context, it is unsurprising that there are no studies that report using exit interviews or observation of encounters to measure TB care quality. This is because TB patients are unlikely to make up a large proportion of conditions seen at the pharmacy on a daily basis. It would therefore be logistically difficult and time consuming to collect data on this condition through such means. Pharmacies tend not to keep records of encounters with patients (asides from for the sale of restricted POMs e.g., opioids) which rules out the use of retrospective record abstraction.

Anthropologists have used ethnographic methods to better understand and describe the pharmacist-client interaction [43,44], though no such studies have reported on TB management, again likely due to its relatively uncommon presentation. However, there are examples of ethnographic work based in the community seeking to understand pharmaceutical consumption that have provided insights into care seeking and the role played by community pharmacy in TB management (e.g., [45]).

4. Empirical evidence on quality of TB care from pharmacies in LMICs

4.1. TB medicine availability

Empirical evidence on availability of anti-TB medicines from private pharmacies in LMICs is scant. It shows that availability across settings is variable, with gaps in stocking first-line anti-TB medicines ranging from a third to three quarters. A study in Cochabamba city, Bolivia, reported that 99 out of 100 sampled pharmacies were unable to completely fill a prescription for one week's supply of rifampicin 300 mg, isoniazid 150 mg, ethambutol 400 mg and pyrazinamide 500 mg [46]. Only 25% stocked at least one of the medicines. The most commonly stocked was rifampicin (23%) which was said to be used for indications other than TB. In Hanoi, Vietnam, 49% of 128 pharmacy workers said they stocked at least two first-line anti-TB medicines [41]. Surveys from Latipur, Nepal [47] and Ho Chi Minh City (HCMC), Vietnam [32], have revealed that 74% and 60% of pharmacies reported stocking anti-TB medication respectively. In Cambodia, drug availability data collected from 66 private pharmacies in 14 provinces showed that the most frequently available anti-TB medicines were pyrazinamide (71%), rifampicin (70%), streptomycin (62%), and ethambutol (56%) [34].

4.2. Anti-TB medicine quality

Several studies have reported on the prevalence of substandard and falsified anti-TB drugs in LMICs (e.g., [48,49]). Perhaps the largest one of its kind assessed the quality of isoniazid and rifampicin procured from private pharmacies across 19 cities in Angola, Brazil, China, DRC, Egypt, Ethiopia, Ghana, Rwanda, India, Kenya, Nigeria, Russia, Thailand, Turkey, Uganda, Tanzania, and Zambia. The authors report that of the 713 treatment packs procured, 9.1% failed basic quality testing for required levels of active pharmaceutical ingredient or disintegration [50]. Failure rates were 17%, 10% and 4% in Africa, India, and other middle-income countries respectively. These results are similar to an earlier multi-country study which tested isoniazid, rifampicin, and fixed-dose combinations (FDCs) from selected TB programmes in Colombia, Estonia, India, Latvia, Russia and Vietnam. Overall 10% of samples (4/40) were found to contain $<85\%$ of the stated content [51]. More FDCs were found to be substandard than single drug samples.

Worryingly, a study from India reported that TB FDCs purchased from pharmacies all failed accelerated stability testing at 3 months having passed the initial ingredient content assays (range 90–100%) [52]. This indicates that under common Indian climatic conditions, TB medicines being purchased may be unstable.

4.3. Knowledge of TB amongst pharmacy providers

Across a range of studies knowledge was variable, with some indicators revealing poor results. Several studies have collected data on knowledge pertaining to the activities of the national control programme. For example, a study of 300 randomly selected pharmacies in Tamil Nadu, India, reported that all pharmacists were aware of the availability of free anti-TB medicines from government facilities; but fewer (15%) had heard of the national TB programme and only 5% knew about the DOTS strategy [53]. Figures differed in other settings with two thirds of pharmacies in the Vietnamese capital, Ho Chi Minh City (HCMC), stating they were aware of the national programme; in another large Vietnamese city, Hanoi, 27% of study pharmacies were aware that the national programme provided free treatment; and in Nigeria, a study of PMVs revealed that over half had never heard of DOTS [32,33]. Studies have also sought to measure knowledge of TB management and symptoms; results have tended to be disappointing. In Nepal, 14% of study pharmacy workers believed TB treatment duration was less than four months and only 1/50 knew the correct regimen [54]; in Vietnam, when presented with a case description of a patient with cough for 4 weeks and fever, only 18% of participants in HCMC and 42% in Hanoi mentioned TB as a potential diagnosis [32,41]; in Nigeria around half of PMVs did not know the cause of TB [33].

4.4. Reported management practices for TB patients

We are only aware of a handful studies that have explored self-reported management practices for TB patients among pharmacy providers. A high proportion (88%) of pharmacies in HCMC said that a patient with pulmonary TB required medical attention to ascertain a diagnosis [32]. Over half of these same participants reported selling anti-TB drugs sometimes or often, and of those, 24% reported selling such drugs without a prescription. Of 388 PMV study participants in Nigeria, fewer than 10% reported sending patients with prolonged cough or suspected TB for a laboratory test, and just over half (57%) reported referring TB cases to a higher facility [33].

4.5. Actual management practices for TB patients

Standardised patients have been used to show how TB suspects are managed in practice, in both India [30,40] and Vietnam [41]. These studies have used varying case presentations (Table 1). In Vietnam, we are not aware of any specific guidelines for the management of TB patients by pharmacists. As per Box 1, we would expect patients presenting with TB symptoms to be referred. The study reports that fewer than half of 126 pharmacies [46] referred the SP for diagnosis; only 9% referred to a designated TB facility; 53% sold medicines to the SP; and 41% sold an antibiotic [41].

The SP studies in India benchmarked the management of these patients against the recommendations of the RNTCP and the Indian Pharmaceutical Association [28]. ‘Correct’ management in both studies was defined as referral to a TB clinic/DOTS centre or heath care provider without dispensing any antibiotics or steroids (which were deemed to be harmful). Depending on the case presentation, correct management ranged from 13% to 62% and dispensing of an antibiotic from 16% to 37% [55]. In a pooled analysis of results across the three Indian cities from both studies, the authors reported that behaviour improved markedly as the certainty of the diagnosis was more apparent (ibid). For example, those presenting with cough and fever, for which there are several differential diagnoses, were only managed correctly by 13% of providers. This increased to 45% when the SP mentioned contact with a relative with a TB diagnosis; and to 62% when they presented a confirmed positive sputum test. Miller and Goodman [40] also reported on history taking and advice provision. They found that less than a quarter of providers asked the SP any questions to determine a diagnosis (a necessity given that the symptoms of cough and fever are non-specific); fewer than 2% advised that TB treatment was available free of charge from government facilities. Encouragingly, none of the providers in either India or Vietnam sold first line anti-TB drugs to the SPs.

5. Interventions to improve TB care from pharmacies in LMICs

In its 2006 document ‘Engaging all health care providers in TB control’ the WHO outlined the importance of engaging pharmacists and drug outlets in national TB control efforts and provided guidance on how to implement public-private mix (PPM) approaches [8]. Konduri and colleagues conducted a comprehensive review of ‘engagement of the private pharmaceutical sector for TB control’ and identified 52 interventions involving retail drug outlets [10]. However, the majority of these interventions were identified from conference abstracts, which provide limited detail. 15 provided data on the number or percentage of referrals of presumptive TB cases or resulting positive cases. These interventions (carried out between 2003 and 2014) involved between 60 and 683 retail drug outlets; referrals ranged between 0.25 and 9 per retail outlet; of referrals, the percentage screened ranged from 27% and 91%; and the number of smear positive cases ranged from 3 to 395 (ibid). This review concluded that, to date, efforts to engage pharmacies have been limited. In this section, we focus on seven interventions (for which full research papers are available) that have sought to address at least one aspect of quality of care laid out in Table 1 (see Table 3 for details). All were carried out in conjunction with the national TB programme of the study country and are classified as PPM projects [56–63].

All interventions aimed to improve the management of TB patients by participating pharmacies through training of pharmacy staff to screen patients and appropriately refer TB suspects, with the ultimate aim of improving case detection. Most training focussed on symptoms of TB and identifying patients to refer for testing. A minority of interventions also focussed on rational medicine use and antibiotic stewardship [58,59]. One study mentioned that the training covered counselling for patients prescribed anti-TB medication [59]. In addition to improving case detection efforts, one intervention additionally sought to stop pharmacies from selling anti-TB medicines [60]. Two interventions in India and Vietnam incorporated financial incentives for pharmacy referrals [58,63].

Most programmes had a relatively low engagement with around 30–40% of pharmacies actively participating in the referral process; Daftary and colleagues [58] are the exception, reporting 81% active participation in Patna, India. Workload, patient demand for OTC medicines, doctor fees, programme paperwork, fear of losing patients to other pharmacies (and hence the opportunity to sell medicines such as antibiotics and cough suppressants), and concern that patients would criticise the pharmacist were they to receive a negative TB diagnosis all negatively affected engagement [58,61]. Across the studies, of patients referred by pharmacies, positive TB diagnoses ranged from 7 to 27% of patients tested. In India, an intervention which added several components to a broader PPM programme, reported a TB diagnosis rate that was 25 times higher than the standard programme alone, indicating that a multi-faceted approach including financial incentives, regular SMS reminders, and regular supervision and monitoring could have a key role in maintaining high levels of pharmacy engagement [58]. One study using SPs to assess the effects of the intervention reported reductions in both antibiotic and cold remedy sales, alongside improved detection rates [62]. Finally, a lack of cost data is evident, with only one study considering the cost-effectiveness of its case finding efforts.

Table 3
Interventions to improve management of TB in the pharmacy setting in LMICs.

Author	Country and programme	Details of intervention	Key findings/outcomes
Bell et al. [56]	Phnom Penh, Cambodia National center for Tuberculosis and Leprosy Control public/private mix TB Referral Programme	- 170 private pharmacies. - Clients with TB symptoms are referred by pharmacy to public sector DOTS clinics. - 3-day training for pharmacy staff and visits to DOTS clinics.	During previous 3 months: - One third of the pharmacies reported referring one or more clients. - The 170 pharmacies referred a total of 125 clients. - 96% stated they always referred all clients with TB symptoms to DOTS clinics.
Colvin et al. [57]	Kisarawe district, Tanzania National Tuberculosis and Leprosy Programme, PATH, and USAID.	- 15 pharmacists (and 15 traditional healers) received 2 days training. - Pharmacies given referral slips and registers to track referrals to DOTS, and directory of DOTS facilities.	- Between 2009 and 2011 smear-positive TB case notification increased from 28 to 47/100,000 - Pharmacies referred 434 people to diagnostic facilities. 97% acted on the referral, and of these, 25% were diagnosed with TB. - New TB case notifications (in the study district) referred through the network ranged from 38% to 70%.
Gharhat et al. [59]	Mumbai, India Mumbai District Tuberculosis Control Society, colleges of pharmacy, professional associations of pharmacists and physicians.	- 119 pharmacist - 2 interactive workshops - Advised to refer patients with suspected TB and to counsel patients prescribed anti-TB medicines	- Anecdotally, participation in the workshops was associated with a high degree of professional satisfaction. - No measurement of pharmacist performance post training.
Lonnroth et al. [61]; Quy, et al. [63]	Ho Chi Minh City, Vietnam	- 150 pharmacies trained according to NTP guidelines - New referral and recording system. - Clients with TB symptoms referred for sputum smear microscopy at a District TB Unit. - US $1 for each sputum-positive detected case	- 39% referred at least one client to a TB - 310 TB suspects were referred during first 9-month monitoring (only 28% went for testing). - An additional 63 patients were referred and tested in 2nd follow-up. - 7% of the 149 patients tested were sputum-positive (accounting for 1.6% of cases detected in the intervention (others resulted from GP and physician referrals).
Mitchell et al. [62]	Santo Domingo, Dominican Republic	- Intervention aimed at pharmacies and local grocery stores - Components of intervention involved a 1 h educational workshop and a motivational 'detailing visit' - Participants were invited to sign a pledge and receive a certificate of recognition. - SPs (reporting a set of chronic TB symptoms) were sent 3–6 weeks before the interventions began and again 2–6 weeks afterwards.	- Pharmacies exposed to the intervention improved by 2.12 points (score based on TB behaviours e.g., recognition of symptoms) on average compared with an improvement of 0.9 in the comparison group ($p = =0.06$) - Half of intervention pharmacies referred SPs directly to the national TB program vs. 18.2% of the control group. - After intervention attempts to sell a medicine including antibiotics without a prescription (e.g., amoxicillin, cephalosporin, rifampicin) fell from 38% of pharmacies to none. - At 6 months follow-up, 33% of pharmacies referred 70 TB suspects of which 7 cases (10%) resulted in a smear positive diagnosis. - At 2 year follow-up, detection of new smear positive cases averaged 150 per quarter vs. 67 per quarter in the pre-intervention period.
Daftary et al. [58]	Patna, India Intervention nested into Universal Access to TB Care (a PPM programme between Bihar state government and PPIA World Health Partners).	- Broader PPM programme involved 554 pharmacies in standardised TB management plus incentive of US $0.75 for each completed referral. - Intervention (105 pharmacies) had 5 additional components: interactive training workshops; referral of TB suspects for chest radiograph and doctor consultation; financial incentives for referral completion, chest radiograph and positive TB diagnosis ($0.75, $1.50, and $3 respectively), text message reminders and field support.	- 81% of pharmacy providers actively participated in the pilot vs. 16% in original PPM programme. - Rate of registration of patients with TB symptoms and positive TB diagnoses were 62 and 25 times higher respectively in the intervention group. - Microbiological testing and test confirmation was also significantly higher in the intervention group. - 240 additional cases were attributed to the intervention with a cost per case notified of US $100.
Lambert et al. [60]	Cochabamba, Bolivia NTP and local pharmacists association (ASPROFAR)	- A two stage intervention - Phase 1: 170 pharmacists attended a general meeting and local pharmacists association issued a recommendation to members to stop selling anti-TB medicines and refer clients seeking to public services. - Phase 2: 70 pharmacies referred clients with chronic cough to NTP (via referral slip).	- After phase 1, the proportion of pharmacies selling TB drugs decreased (rifampicin: 23–11.5%; isoniazid: 16–3.1%; $P < 0.001$) and the proportion of pharmacies referring to the NTP clients seeking TB drugs increased (22–58%; $P < 0.0001$). - In phase two, 38% referred a total of 41 clients for screening in the NTP; 11 of 41 (27%) were screened and of these, 3 (27%), were diagnosed with smear-positive TB.

6. Discussion and future directions

In this paper we mapped out what is expected of pharmacies in relation to quality TB care and then examined the evidence to shed light on the degree to which this is occurring. The expectations of pharmacists included matters pertaining to accurate dispensing of medicines but also encompassed wider issues such as case management. This is in line with global thinking regarding the role of community pharmacists which has seen a shift from solely retailing of products to taking on a substantial public health role comprising promotion, prevention, and disease management [19]. Mossialos and colleagues argue that no country can boast the latter (ibid). In LMICs there is an increasing

acknowledgement, and advocacy from both national and global pharmacy bodies that pharmacists in these settings could (and should) provide a comprehensive pharmaceutical service. This is evidenced, for example, by the International Pharmaceutical Federation's 'Good Pharmacy Practice (GPP) in developing countries' guide [20]. Further illustrations of this shift include Indonesia's 'Pharmaceutical Services Guidelines' in 'apoteks' (pharmacies) [21] and the Pharmacy Council of India's 2015 'Pharmacy Practice Regulations'. The latter clearly lays out a code of ethics, and the duties and responsibilities of a pharmacist (which include promoting rational drug use, patient counselling, management of minor ailments, and public health duties) [22].

While the empirical literature on quality of TB care from pharmacies in LMICs is relatively sparse, the quality challenges are clearly evident, relating to anti-TB medicine availability, quality of anti-TB medicines, and pharmacy worker's knowledge. Further, management practices suffer from a lack of questioning of symptomatic patients to ascertain whether they require testing, lack of referral of TB suspects, sale of unnecessary and harmful medicines, sale of anti-TB medication OTC, and lack of counselling. These findings are very much in keeping with the shortfalls in pharmacy practice identified for other diseases [11,12].

Given that it is 13 years since the WHO actively encouraged countries to engage pharmacists and drug shops into national TB programmes [8], the number of published interventions in this area is strikingly few (we acknowledge that there are a number of interventions lacking published findings). Of the interventions scrutinised by this paper (Table 3), participants found the interventions to be acceptable and many reported professional satisfaction from their involvement. Whilst active participation in these programmes appears to have been low, with the right set of incentives and support, high participation levels have been achieved and in one study case-detection through pharmacies was shown to be cost-effective [58].

All these interventions have explicitly focussed on engaging pharmacies in the national TB programme to improve case detection. Whilst appropriate referrals and hence improved case detection represents an important aspect of quality, the narrative of these papers appears to lack discussion of other dimensions of quality of care. It is clear that, thus far, a focus on quality has been a 'missing ingredient' in efforts to harness pharmacies to improve TB control [13]. Future interventions would do well to tackle the seemingly neglected areas of OTC prescribing of unnecessary and harmful medicines, and measures to improve patient counselling to accompany the sale of anti-TB medicines. The implemented interventions have generally shown a reasonable degree of success but achieving scale remains a challenge, a challenge also identified with engagement of other for-profit providers [64]. An analysis of the problems in engaging private providers more broadly highlighted a number of barriers to reaching scale in PPM programmes. These include, amongst others, a bias towards public provision, lack of funding, a lack of understanding of private healthcare markets, high level of fragmentation in these markets, market incentives favouring poor quality care, and competing priorities [6]. Building a strong evidence base, advocating for enhanced political commitment and funding, utilisation of digital technology, setting ambitious PPM targets, and monitoring the progress of PPM initiatives may help to overcome some of these obstacles [64].

It was noticeable that none of the interventions included a regulatory component, although regulatory systems exist with mandates for pharmacy in all countries. Lack of regulatory oversight is a clear problem in the pharmacy retail sector in many LMICs and an area that warrants attention (both generally and in relation to TB care). Regulatory interventions have shown promising improvements in pharmacy service quality in the past [65,66]. Whilst studies reported that sales of anti-TB medicines OTC were commonplace in some countries e.g., Vietnam [32]; in other countries, such as India, this was reported to be rare (despite being very common other antibiotics) (e.g., [30,55]). A detailed examination of regulatory policies surrounding anti-TB medicine may provide useful cross-country learning experiences. For example, other countries could explore the possibility of initiating hierarchies of drug control in the way that India has instigated the H1 drug schedule which includes more restrictions and stricter penalties for selling anti-TB medicines in a bid to halt the emergence of resistant antibiotic strains.

This paper has also highlighted the lack of explicit global-level guidelines aimed at pharmacies, outlining how they should manage TB patients. This has similarly been emphasised as a major gap for the management of other conditions that present at the pharmacy, such as childhood diarrhoea [40]. A concise handbook aimed at LMIC pharmacies outlining the key management 'dos and don'ts' for conditions of high public health importance would be a key contribution from the global health community. Such an endeavour could draw on guidelines previously produced by local pharmacy associations (e.g., the India Pharmaceutical Association's guidance on TB management [28]). A key first step would be the identification of all such existing guidance for a range of conditions (which is often not publicly available or only available in a local language). Organisations such as FIP and the WHO (specifically the Department of Essential Medicines and Health Products), which have a strong presence and legitimacy in the global pharmacy space, would be well-placed to spearhead such an initiative. Appropriate training should also be incorporated into pharmacy pre-service education. Additionally, the role of non-pharmacist run pharmacies and drug shops requires clarification.

Looking forward, technological innovations could further extend the role of pharmacies in TB care. Glaze and Rowe have suggested that pharmacists in the US are well placed to administer a purified protein derivative skin test, read the results, and provide education to the patient [67]. Moulding proposes that private doctors in LMICs could prescribe 'monitored self-administered treatment', whereby pharmacies would fill and dispense medication monitors (as opposed to anti-TB medication either loose or in its original packaging) in order to improve adherence in the private sector [68].

While many approaches are possible, the current reality of pharmacy care for TB patients remains substandard. Given the importance of pharmacies in LMICs as an early point of contact for TB patients, there remains a critical agenda of work to ensure the potential benefits for TB control can be maximised. Addressing quality of care at the pharmacy level, will require the participation and collaboration of a wide range of stakeholders, going well beyond the pharmacies themselves. This complex landscape involves organisations at the global level, such as WHO, FIP, and the STOP TB programme; and at the country level, national TB programmes, regulatory bodies, pharmacy associations, pharmacy colleges and ministries of health. Given that in the TB context, community pharmacy sits at the intersection between policies for TB and policies that focus on pharmacy more generally, these two groups of stakeholders will need to come together to effect change.

Ethical statement

This paper is based solely on literature within the public domain.

Funding

RM acknowledges post-doctoral funding from the Economic and Social Research Council, UK. Grant reference ES/T006854/1.

Declaration of Competing Interest

We declare that we have no conflict of interest.

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J Clin Tuberc Other Mycobact Dis 18 (2020) 100136

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Implementation science to improve the quality of tuberculosis diagnostic services in Uganda

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ARTICLE INFO

Keywords:
Tuberculosis
Quality improvement
Implementation science
Uganda

ABSTRACT

Nucleic acid amplification tests such as Xpert MTB/RIF (Xpert) have the potential to revolutionize tuberculosis (TB) diagnostics and improve case finding in resource-poor settings. However, since its introduction over a decade ago in Uganda, there remain significant gaps along the cascade of care for patients undergoing TB diagnostic evaluation at peripheral health centers. We utilized a systematic, implementation science-based approach to identify key reasons at multiple levels for attrition along the TB diagnostic evaluation cascade of care. Provider- and health system-level barriers fit into four key thematic areas: human resources, material resources, service implementation, and service coordination. Patient-level barriers included the considerable costs and time required to complete health center visits. We developed a theory-informed strategy using the PRECEDE framework to target key barriers by streamlining TB diagnostic evaluation and facilitating continuous quality improvement. The resulting SIMPLE TB strategy involve four key components: 1) Single-sample LED fluorescence microscopy; 2) Daily sputum transport to Xpert testing sites; 3) Text message communication of Xpert results to health centers and patients; and 4) Performance feedback to health centers using a quality improvement framework. This combination of interventions was feasible to implement and significantly improved the provision of high-quality care for patients undergoing TB diagnostic evaluation. We conclude that achieving high coverage of Xpert testing services is not enough. Xpert scale-up should be accompanied by health system co-interventions to facilitate effective implementation and ensure that high quality care is delivered to patients.

1. Introduction

The World Health Organization (WHO) estimates that at least one-third of tuberculosis (TB) patients worldwide are not being diagnosed or treated - the so called “Missing 3 Million” [1]. Better diagnostics are critical to improving case finding and ultimately patient and public health outcomes. Smear microscopy has been the standard of care for over 100 years but has poor sensitivity, missing at least half of all TB cases [2]. Smear microscopy also requires patients to make multiple visits to health centers, resulting in high rates of loss to follow up [3,4]. To improve case detection, there has been considerable donor and country investment in novel diagnostics. However, there has been relatively little attention paid to the quality of care provided alongside new diagnostics to patients undergoing TB diagnostic evaluation.

In 2010, Xpert MTB/RIF (Xpert) became the first nucleic acid amplification test endorsed by the WHO [5], with subsequent guidelines in 2013 endorsing Xpert as the first-line TB test for all patients [6]. Xpert is a semi-automated PCR-based test that is more sensitive than microscopy (85% vs 50–60%) [7] and provides results within two hours, including whether or not rifampin resistance is present. Since its

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https://doi.org/10.1016/j.jctube.2019.100136

endorsement by the WHO, Xpert testing capacity has been scaled-up rapidly in high burden countries [8]. By the end of 2016, a total of 6659 GeneXpert instruments (comprising 29,865 modules) and more than 23 million cartridges had been procured in the public sector in 130 of the 145 countries eligible for concessional pricing [9]. The number of modules and cartridges has continued to increase exponentially in the past few years.

Uganda has been a leader in the scale-up of Xpert on a population basis [8,10,11]. Similar to many other high burden countries, the Uganda National Tuberculosis and Leprosy Program (NTLP) and National Tuberculosis Reference Laboratory (NTRL) established a hub-and-spoke model for nationwide roll-out of Xpert in 2012 [12]. Testing sites (i.e., hubs), now present in most districts of the country, are linked with 3–5 peripheral microscopy units (*i.e.*, spokes). Sputum samples collected at the peripheral microscopy units are transported to the testing hubs and results are returned to the microscopy centers after testing is completed. The NTRL has also installed GxAlert (SystemOne, USA) software at testing hubs to enable central monitoring of test results and device performance.

No formal impact studies of this massive scale-up of Xpert testing have been carried out. Review of national case reporting data indicates a nearly four-fold increase in confirmed MDR TB patients from 2009 to 2017, small increases in TB case notification from 40 to 42,000 cases before 2010 to 57,756 cases in 2017, and an increase in the proportion of bacteriologically-confirmed cases from 60% to 65% to 87% in the same period [13]. However, while some of these increases are potentially attributable to Xpert scale-up, there remain unresolved questions critical to understanding the effectiveness of Xpert scale-up and to identifying opportunities to further improve case finding. These include: How rapidly and efficiently are Xpert referral networks functioning from both the health system and patient perspectives?; What is the variability in quality of TB diagnostic care within Xpert referral networks?; and What policy changes and co-interventions could further enhance Xpert implementation?

Over the past 3–4 years, we have tried to address some of these questions in a collaborative partnership with the Uganda NTLP and NTRL. Our objectives have been to:

1) Quantify gaps in the process of TB diagnostic evaluation at peripheral health centers linked to Xpert testing sites.
2) Identify modifiable barriers to high quality TB diagnostic evaluation; and
3) Develop and test theory-driven interventions to improve the quality of TB diagnostic evaluation.

All summarized studies underwent review by Institutional Review Boards (IRBs) at both the University of California, San Francisco (UCSF) and Makere University, and participants were appropriately consented except when IRBs granted an explicit waiver of informed consent.

2. Defining the quality gap

To define the quality gap, we assessed adherence to national and international guidelines [12,14,15]for evaluation of patients with presumed TB at 24 peripheral health centers (hubs) linked to 16 Xpert MTB/RIF testing sites (spokes; **Fig. 1**) [16]. We included health centers that: (1) used sputum smear microscopy as the primary method of TB diagnosis; (2) participated in NTLP-sponsored external quality assurance for sputum smear microscopy; and (3) referred sputum samples to a district or regional health facility for Xpert testing. We excluded health centers that (1) performed sputum smear microscopy on less than 150 patients per year and (2) diagnosed less than 15 smear-positive TB cases per year using data from 2015. 24 health centers meeting these criteria and located outside of, but within 150 km of the capital region of Kampala were selected in consultation with the Uganda NTLP. We prospectively extracted individual patient data from routine TB registers on all adults evaluated for pulmonary TB at these health centers. We excluded data on patients who (1) had sputum collected for monitoring of response to anti-TB therapy; (2) had sputum collected as part of active, community-based case finding (e.g., contact tracing, community outreach campaign); (3) had a documented prior history of TB treatment (e.g., reason for Xpert testing or TB treatment marked as treatment failure, relapse, or treatment after loss to follow-up); (4) were referred to a study health center for TB treatment after a diagnosis was established elsewhere; (5) were started on treatment for presumptive extra-pulmonary TB only; or (6) were less than 18 years old. Data from TB registers were used to capture their outcomes at each step of the TB diagnostic evaluation cascade of care, including whether they underwent sputum-based TB testing, TB testing dates and results, and treatment initiation dates. We used these data to assess quality indicators derived from national and international guidelines for TB care [12,14,15]: 1) the proportion of patients with presumed TB referred for sputum-based TB testing; 2) the proportion completing TB testing if referred (defined based on national guidelines as a single valid Xpert result or examination of at least two sputum smears (if HIV-negative); and 3) the proportion rapidly (i.e., within 14 days) initiated on TB treatment if smear- or Xpert-positive.

Over a 12-month period from January to December 2017, 6744 adults underwent evaluation for pulmonary TB at the 24 study sites [16]. We found that 79% were referred for sputum-based TB testing, 56% completed TB testing if referred, and 75% were treated within 14 days if smear or Xpert results were positive. The gaps at each step indicate that the cumulative probability of a patient with sputum smear- or Xpert-positive TB being diagnosed and treated upon presenting to these health centers was only a 43%. In addition, with respect to Xpert utilization, only 20% of patients with presumed TB (33% of people living with HIV infection (PLHIV) and 7% of people living without HIV infection) were referred for Xpert testing, and only 53% of patients with positive Xpert results were initiated on treatment within 14 days. The low uptake of Xpert testing for PLHIV is particularly concerning as rates of smear-negative disease are higher and thus continued reliance on smear microscopy can lead to unacceptably high rates of false-negative results [17].

Data from quality indicators at 24 peripheral health centers in Uganda demonstrated that despite rapid scale-up of Xpert testing using a hub-and-spoke model, the overall quality of TB diagnostic evaluation remains poor and that there are considerable opportunities to enhance Xpert implementation. In particular, few patients received Xpert testing (including those recommended to have Xpert as a first-line test) and nearly half with positive Xpert results were not being rapidly linked to treatment. In addition, we also showed that it is possible to use routine data sources to monitor and improve the quality of TB services at the facility-level, a capacity that is an important pre-requisite for establishing any mechanism for continuous quality improvement.

3. Understanding the quality gap

We conducted a series of mixed methods studies using the Theory of Planned Behavior as our conceptual model. This is a well-known behavioral theory proposed by Ajzen in 1985 to understand factors that affect an individual's intention to carry out a certain behavior [18]. According to this theory, clinicians' knowledge and attitudes, perceived social pressure, and perceived behavior control will impact their intention to follow TB diagnostic evaluation guidelines. In addition, we hypothesized that certain patient- and health system-level factors might make it easier or harder to take up or consistently adhere to guidelines (**Fig. 2**). We collected data on these factors using qualitative and quantitative approaches.

From interviews ($N = 22$ staff at 6 health centers) and field observation of health center staff (one 2–3 day field visit at each of 6 health centers), we identified key barriers across four thematic areas: human resources, material resources, service implementation, and

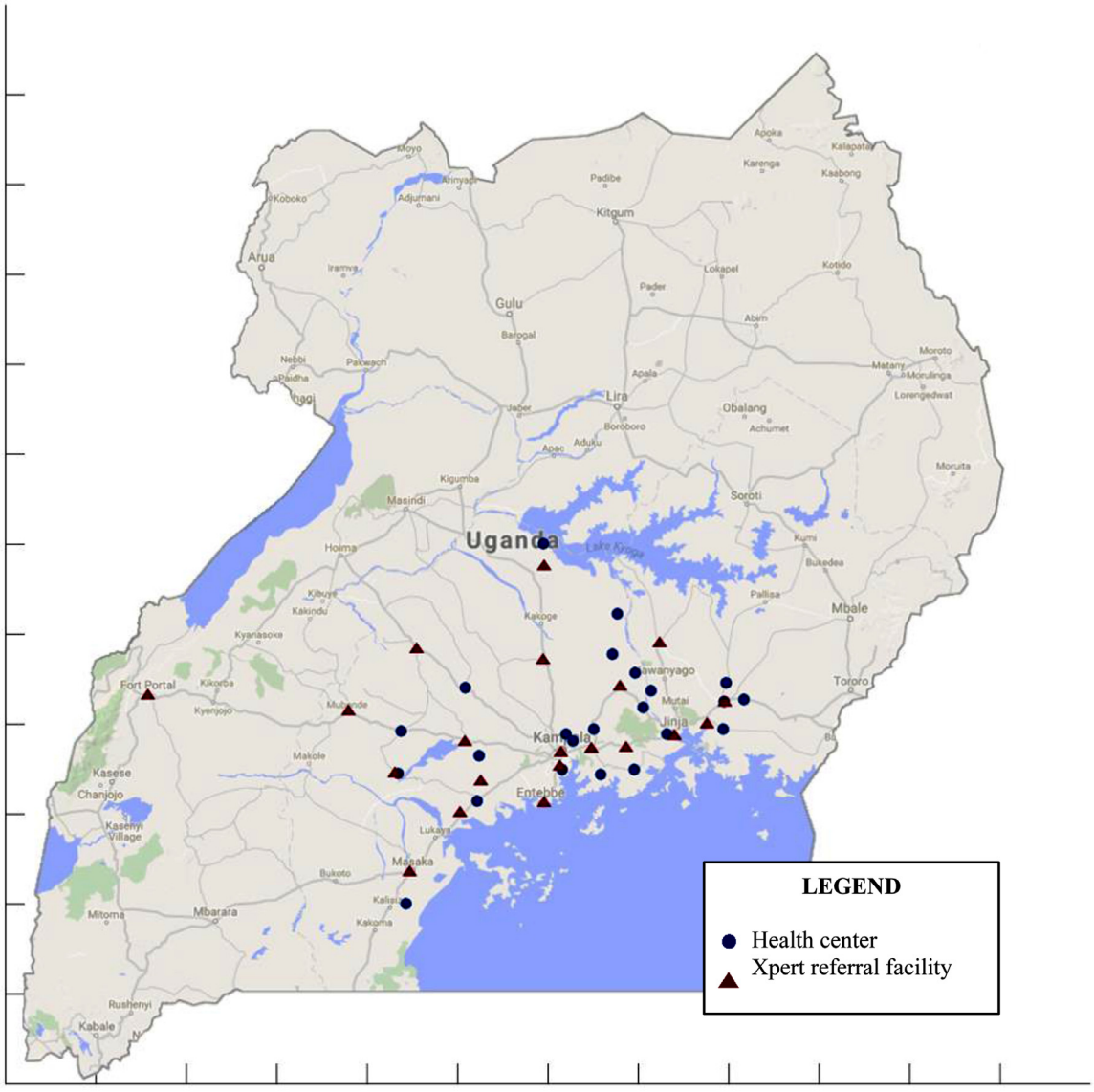

Fig. 1. Location of study sites. The map shows the location of study sites, including 24 peripheral health centers with TB microscopy units (circles) and the17 Xpert testing sites (triangles) to which they refer sputum samples.

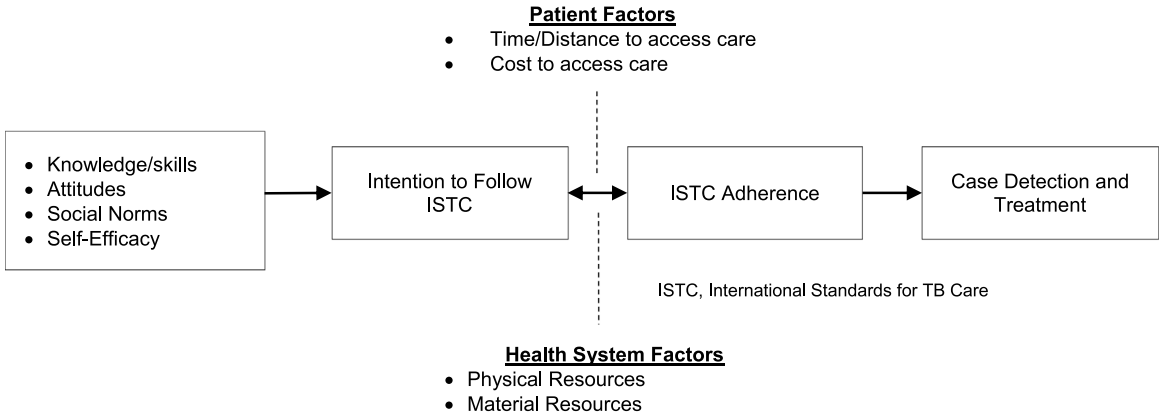

Fig. 2. Conceptual model for understanding reasons for gaps in TB diagnostic evaluation. We used the Theory of Planned Behavior to identify factors associated with provider's intention to follow guidelines for TB diagnostic evaluation. We also collected data on patient and health system factors that might influence sustained guideline adherence.
ISTC International Standards of Tuberculosis Care [29].

service coordination [19]. Human resource barriers to guideline adherence included lack of knowledge about current guidelines; a lack of skills (microscopy); belief that TB evaluation is not urgent; and low self-efficacy due to heavy workloads in the laboratory and low confidence that patients will return regardless of their efforts. Providers at local facilities also cited issues with the material resources required to conduct their work, including stock outs of sputum cups, reagents, and medicines; limited space for assessing and counseling patients; and poorly ventilated laboratory facilities. Barriers to service implementation included high staff turnover, inconsistent and delayed specimen transport to Xpert testing sites, and the inability to track and follow-up with patients with positive TB test results. Finally, health center staff noted several examples of poor service coordination that contributed to their inability to provide high quality care. These included a lack of regular communication among health center staff and insufficient oversight from NTLP supervisors.

Through surveys of patients ($N = 64$) and community members ($N = 114$) [20], we learned that pathways for patients seeking care for chronic cough were complex and costly. Most (>80%) patients made repeated health facility visits (median 3 visits), and most visits (88%) were to health facilities that did not provide TB diagnostic services. The most common health facilities visited were pharmacies, community health posts and private clinics, and many patients made repeated visits to the same facility. The costs of seeking care for TB symptoms were high, accounting for on average 29% of monthly household income. Visiting a Level IV health center where TB microscopy and Xpert referral are possible alone accounted for 11% of monthly household income and took upwards of 9 h to complete. The substantial time and cost inherent in seeking care for TB symptoms impacts patient behavior – 40% of patients surveyed indicated they were unlikely to complete additional visits, even when recommended, to obtain additional testing or receive results.

Last, we conducted additional interviews and observations at 23 peripheral health centers and the 15 sites to which they referred sputum samples for Xpert testing. [21] The results identified barriers at each step of the process for referring samples for Xpert testing. Challenges with sputum collection for Xpert testing included a shortage of sputum containers (8/23 health centers) and lack of refrigerators for sputum storage prior to transport (10/23 health centers). The latter resulted in health centers only collecting specimens for Xpert testing on days when transport was expected to happen. Sputum transportation to Xpert testing facilities (hubs) was irregular and varied in frequency from 1 to 3 times/week. Xpert testing at hubs was limited by non-functioning modules (5/15 testing sites), lack of back-up electricity (2/15 testing sites) and failure to implement daily device maintenance (7/15 testing sites) resulting in unacceptably high (>5%) error/invalid rates (10/15 testing sites). Notification of results to referring health centers was often delayed, typically taking up to 2 weeks.

In consultation with multiple key local stakeholders involved in the provision of TB care, including NTLP officials and clinicians involved in front-line TB care, we prioritized and selected barriers to target for intervention using the PRECEDE framework, a well-validated framework for designing behavior change interventions [22]. The framework classifies barriers as predisposing, enabling, or reinforcing factors (**Table 1**). Interventions that target barriers within all three of these categories are more likely to result in successful behavior change [22]. The barriers selected to target for intervention included: 1) predisposing factors: low self-efficacy due to time and resource constraints, and the belief that TB evaluation is not urgent; 2) enabling factors: failure of patients to return after their initial health center visit (due to time and costs), inconsistent and delayed transport to Xpert testing sites, and inability to track and follow-up patients; and 3) reinforcing factors: a lack of communication and coordination among staff and insufficient oversight from NTLP supervisors (**Table 1**).

4. Improving the quality gap

We sought to design an intervention to improve the quality of TB diagnostic services within the hub-and-spoke model for Xpert testing that targeted the key barriers that we had identified through our formative research. To do so, we reviewed the literature and consulted with stakeholders (health workers, health center directors, district health officers, NTLP officials) regarding the feasibility and acceptability of each of the potential intervention options. The resulting "SIngle-saMPLE (SIMPLE) TB evaluation strategy included four key components:

1) Single-sample LED fluorescence microscopy was selected because of its ability to provide a TB diagnosis and initiate treatment at the initial visit for the majority of patients with TB. The patient barriers targeted included the high-cost of clinic visits. The health-system barriers targeted include the high laboratory workload and the prevailing belief among clinicians that TB evaluation is not urgent. The intervention involved on-demand preparation/examination of two smears from a single sputum sample, an approach we have previously shown is as accurate as examining smears from different samples [23].
2) Daily sputum transport to Xpert testing hubs was selected to facilitate same-day (or next-day) Xpert testing for all smear-negative patients. The barriers targeted included the failure of patients to return after their initial health center visit and inconsistent or delayed specimen transport to Xpert testing sites. This intervention involved identifying a primary and alternate boda boda (motorcycle) rider for each peripheral health center, linking the riders to laboratory staff, and tracking sample pick-up and delivery using a paper logbook.
3) Short Message Service (SMS)-based communication of Xpert results to health centers and patients was selected to reduce delays in reporting results and improve linkage to treatment. The barriers targeted included the failure of patients to return after their initial health center visit and inability of health center staff to track and follow-up such patients. This intervention involved installing GxAlert software (System One, Northampton, USA) and a USB modem at all Xpert testing hubs, establishing an automated SMS platform linked to a central GxAlert server at the Uganda National TB Reference Laboratory and training staff at Xpert testing hubs to use GxAlert software.
4) Performance feedback was selected to facilitate continuous quality improvement. The barriers targeted included lack of communication and coordination between health center staff and insufficient oversight from NTLP supervisors. It involved providing health centers with a monthly report card with quality indicators reflecting adherence to each step of TB diagnostic evaluation and training health center staff to review and discuss report cards amongst themselves at monthly staff meetings using a Plan-Do-Study-Act (PDSA) framework [24,25].

We had previously shown that performance feedback was feasible as an informal quality improvement (QI) strategy and led to a 15% (from 52% to 67%) increase in the proportion of patients receiving guideline-adherent care at 6 peripheral health centers [26]. To assess the feasibility and potential impact of the remaining three components, we conducted a single-arm interventional study at 5 peripheral microscopy units linked to an Xpert testing hub [27]. Using data from all adults ($N = 1212$) undergoing TB evaluation over a 14-month period from February 2015 to April 2016, we showed that 99% were referred for sputum-based TB testing, 99.6% completed testing if referred and 86% of patients with confirmed TB were treated rapidly (within 14 days). The probability of a patient with sputum smear- or Xpert-positive TB being diagnosed and treated was 85%, nearly double what was observed under the routine hub-and-spoke model. With respect to Xpert

Table 1
Barriers targeted for intervention development. We used the PRECEDE framework to prioritize and select barriers to target in order to improve the quality of TB diagnostic services.

PRECEDE framework	Recurring themes
Predisposing factors (Knowledge, attitudes, beliefs, intention)	• Time and resource constraints (i.e., high workload) → low self-efficacy • Beliefs that TB evaluation is not urgent
Enabling factors (Factors that if addressed make it easier to initiate the desired behavior)	• Failure of patients to return after initial visit (due to time and costs) • Inconsistent/delayed specimen transport to Xpert testing sites • Inability to track and follow-up patients *"When they have a cough for more than 2 weeks they are sent to the lab. But the problem is they get the first sample and sometimes, actually most times they don't bring the second sample."*
Reinforcing Factors (Factors that if addressed make it easier to continue the desired behavior)	• Lack of communication and coordination among staff • Insufficient oversight from NTLP supervisors *"…Actually at times we have met but we don't meet [regularly], only when we realize there is a problem that's when we communicate and say why is this happening, then we try to rectify."*

utilization, 83% of smear-negative patients were referred for Xpert testing within one day and 76% of Xpert-positive patients initiated treatment within 14 days, both considerable improvements relative to routine care. In addition, automated notification of Xpert results reached referring health centers 95% of the time and patients 49% of the time [28]. These data demonstrate that the theory-informed SIMPLE TB strategy is feasible and effective at improving the quality of TB diagnostic evaluation. However, there remain further opportunities for improving linkage to care, particularly for patients with smear-negative but Xpert-positive TB.

5. Conclusion

To make progress towards elimination, donor and country funding for scaling-up novel diagnostics is essential. However, there needs to be greater investment focused on improving the quality of TB care that accompanies funding to achieve maximal impact of novel diagnostics such as Xpert. This investment should include specific funds for co-interventions such as training, process re-design, performance feedback and ancillary infrastructure (specimen transport, results notification, etc.) relevant to the local context and barriers to high-quality service delivery. Proper implementation supports are essential for new diagnostics to fully realize their promising potential. Implementation science-based approaches can facilitate a systematic assessment of key barriers and enablers and guide selection of the most appropriate and feasible implementation supports for a given context.

Declaration of Competing Interest

None for all authors.

Acknowledgments

We thank the staff and patients at study health centers for participating in study activities and the staff of the Uganda NTLP and NTRL as well as staff of the Uganda Tuberculosis Implementation Research Consortium (U-TIRC) for facilitating study activities.

Funding

Funding for this work was provided by the U.S. National Institutes of Health (R01HL130192 and R21AI096158) and U.K. Medical Research Council/Wellcome Trust/Department for International Development Pilot Grant.

Ethical statement

All summarized studies underwent review by Institutional Review Boards (IRBs) at both the University of California, San Francisco (UCSF) and Makere University, and participants were appropriately consented except when an explicit waiver of informed consent was granted by the IRBs.

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J Clin Tuberc Other Mycobact Dis 18 (2020) 100142

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Identifying gaps in the quality of latent tuberculosis infection care

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ARTICLE INFO

Keywords:
Latent tuberculosis infection
LTBI
Quality care
Cascade of care
Preventive treatment

ABSTRACT

Latent tuberculosis infection (LTBI) occurs after transmission and acquisition of infection, when the tuberculosis (TB) bacteria lie dormant in a person. Nearly one-quarter of the world's population is estimated to have LTBI, yet few studies have been published assessing the quality of LTBI services globally. This paper reviews issues to providing patient-centered LTBI services and offers an example framework to formally assess the quality of LTBI patient care. By applying the LTBI cascade of care model, TB programmes can evaluate the gaps and barriers to high-quality care and develop locally-driven solutions to improve LTBI services. Quality care for LTBI must address some of the key challenges to services including: (1) low prioritization of LTBI; (2) gaps in healthcare provider knowledge about testing and treatment; and (3) patient concerns about side effects of preventive treatment regimens. TB programmes need to ensure that these issues are addressed in a patient-centered manner, with clear communication and ongoing evaluation of the quality of LTBI services. Quality LTBI care must be a central focus, particularly identifying and engaging more household contacts in preventive treatment, in order to halt the progression to active disease thereby stopping TB transmission globally.

1. Introduction

It is estimated that nearly one-quarter of the world's population has latent tuberculosis infection (LTBI) [1]. Of the nearly 1.7 billion individuals with LTBI, approximately 10%, or almost 170 million people, will progress from LTBI to active TB disease [2]. The World Health Organization's (WHO) End TB Strategy has called for patient-centered care and increased provision of preventive treatment for LTBI to reduce the reservoir of individuals who are latently infected [3]. To meet the target of a 90% reduction in TB incidence (i.e., incidence of less than 10/100,000) expanded LTBI services and preventive treatment will be required globally [2,4].

In 2018, the United Nations convened the first High Level Meeting on TB (UNHLM-TB), after which a declaration was announced with a commitment to end TB by 2035. To achieve this goal, the target of providing 30 million people with preventive treatment for LTBI by 2022 was established including: 4 million children under 5 years of age, 6 million HIV-infected individuals along with 20 million household contacts older than 5 [1,5]. In 2018, it was estimated that 49% of people newly enrolled in HIV care were started on preventive treatment and 27% of the 1.3 million estimated eligible children aged under 5 years were on treatment. Yet in the same year, less than 2% of the eligible contacts over 5 years of age were on preventive treatment globally, representing an important gap in preventive services [1].

Both the WHO and UNHLM declaration affirm the *Lancet Global Health* Commission on High Quality Health Systems (HQSS) focus on providing person-centered, high-quality TB care [1,5,6]. The Lancet's Commission called for a radical change to approaches to healthcare delivery in low- and middle-income countries (LMICs) by quantifying and measuring the quality of services, which was previously primarily a focus in high-income countries (i.e., Canada and USA) [6]. However, there is insufficient local- and national-level data available on the quality of health systems across the continuum of care [6]. The call for improved healthcare delivery and research on current practices is particularly relevant for LTBI program scale-up. There is a dearth of data on quality of LTBI care and human resource needs to achieve the target of reaching 30 million people with preventive treatment worldwide by 2022.

2. Framework to assess gaps

2.1. LTBI cascade of care framework

In order to provide quality care for persons with LTBI, it is necessary

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https://doi.org/10.1016/j.jctube.2020.100142

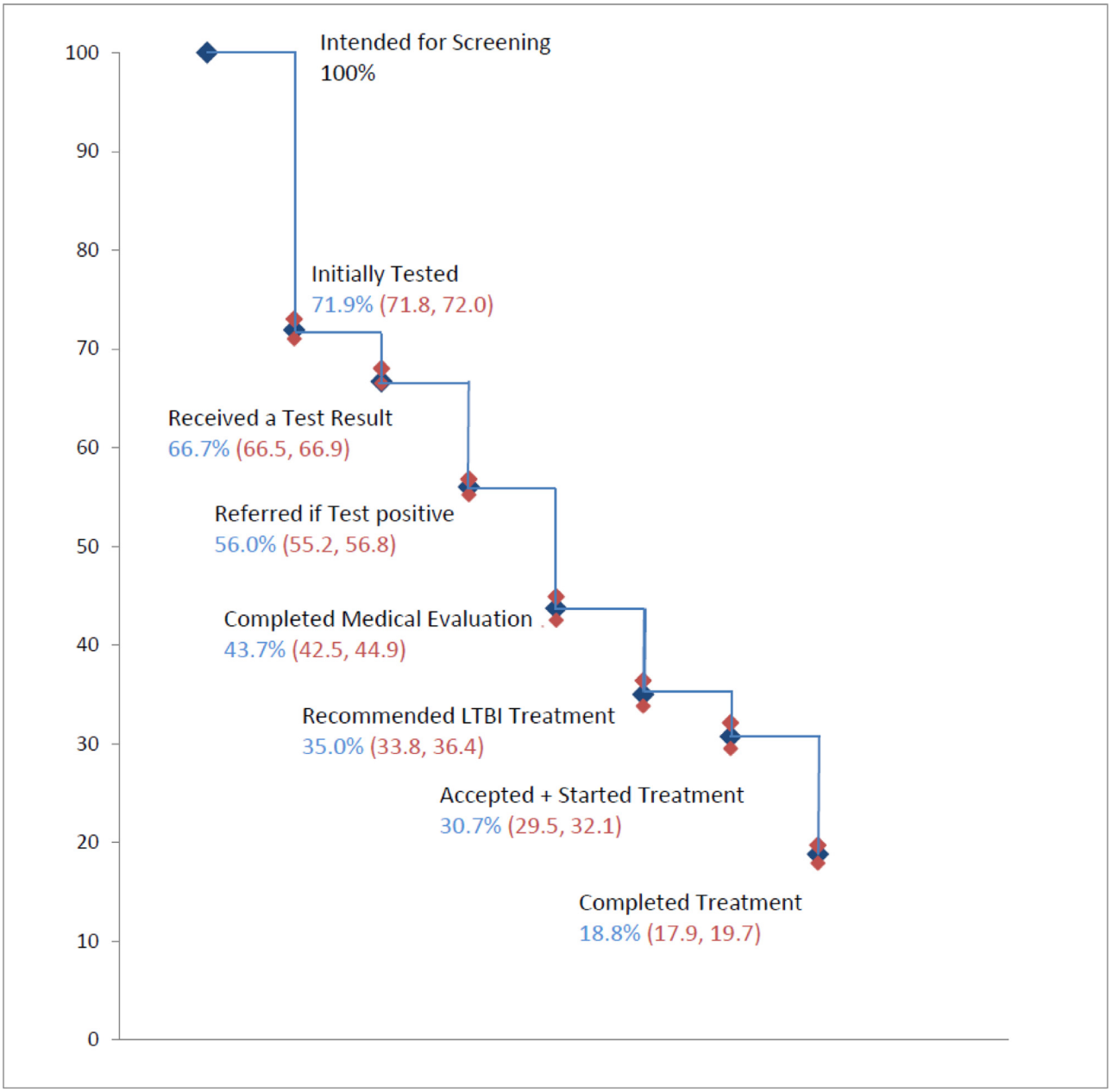
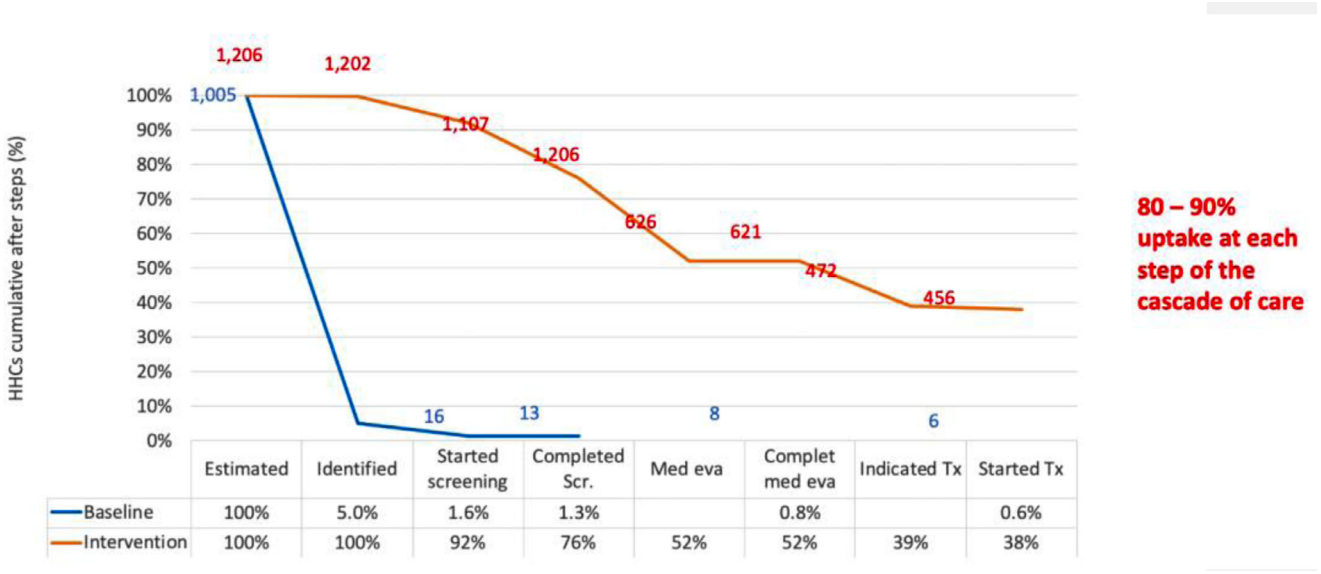


Fig. 1. Losses and drop-outs at each stage of the cascade of care in latent tuberculosis infection (LTBI). Numbers in parentheses are 95% confidence intervals. The value for each level is calculated as the product of the valude from the preceding step, multiplied by the pooled estimate for that step (from fixed-effects analysis). Source: Alsdurf H et al. Lancet Infect Dis 2016 [7] (reproduced with permission).

to understand the complex, multi-staged patient journey known as the LTBI cascade of care. A recent systematic review and meta-analysis identified gaps along the LTBI cascade of care including the following steps: (1) identification of household contacts; (2) initial screening of contacts by placing a tuberculin skin test (TST); (3) reading a TST; (4) conducting a medical evaluation; (5) recommending and initiating LTBI treatment for eligible contacts; and (6) monitoring and completion of LTBI treatment [7]. This systematic review demonstrated that less than 20% of all eligible contacts completed LTBI treatment, however it was also shown that there are losses at all other steps along the cascade (see Fig. 1) [7]. While this review highlighted the importance of addressing the losses of patients along all steps in the cascade, to date the majority of research has focused on the completion of treatment in patient care among those who began treatment, including compliance and adherence research or RCTs of shorter regimens [8].

Although the relative loss is highest at the last step in the LTBI cascade of care (i.e., completing treatment), almost 70% of household contacts do not even start preventive treatment [7]. Public health solutions targeting the steps upstream from treatment initiation, the points in the patient journey where people do not engage with the health facility (i.e., are not identified or screened or do not complete a medical evaluation), are the main drivers of poor treatment outcomes. Gaps in provider knowledge and understanding about the importance of improved contact investigation efforts [9], ease of TST for screening [10], and effectiveness of shortened [11] regimens must be addressed. Only by confronting these misconceptions and enahncing training will TB programmes be able to increase the numbers of contacts who complete initial steps in the LTBI cascade and initiate preventive treatment.

In response to the gaps identified at each stage in the LTBI cascade of care, a pragmatic, cluster-randomized controlled trial entitled “Enhancing the public health impact of latent TB infection diagnosis



	Estimated	Identified	Started screening	Completed Scr.	Med eva	Complet med eva	Indicated Tx	Started Tx
Baseline	100%	5.0%	1.6%	1.3%		0.8%		0.6%
Intervention	100%	100%	92%	76%	52%	52%	39%	38%

Fig. 2. Cumulative proportion completing each step along the LTBI cascade of care (Vietnam) before (blue line) and after (red line) the ACT4 intervention to evaluate and strengthen LTBI services. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

and treatment 'ACT4'" was conducted in five countries: Benin, Canada, Ghana, Indonesia and Vietnam. The aim of the ACT4 trial was to evaluate and strengthen the LTBI cascade of care through locally-developed solutions [12]. The primary objective of the trial was to estimate the increase in the number of household contacts initiating LTBI treatment per newly diagnosed active TB patient (index case) within three months of diagnosis [12]. Initial research findings from this trial are not yet published but a country-specific cascade of care identifying the steps with major losses and local solutions to improve outcomes in Vietnam was presented at the 50th Annual World Lung Conference (see Fig. 2). These study results provide an example of how interventions to address local losses of patients along the cascade could be used by TB programmes in other settings to improve outcomes for LTBI patients.

2.2. Improving quality of LTBI care

As highlighted by the Lancet's Commission, a key to providing quality LTBI patient care is to define, measure and then monitor services [6,13]. The LTBI cascade of care provides a clear, practical framework for evaluation of each step to equip TB programmes with data on where gaps in care occur at the local level. Care cascades offer two key benefits for TB programmes: (1) an approach to measuring TB outcomes and (2) a conceptual framework for assessing quality of healthcare services across the patient journey [14]. The cascade analysis can be presented in various formats, such as a simple graph (see Fig. 2) or as part of dashboards or other tracking systems as a way to engage HCW by presenting results in a timely manner. TB programmes can use cascade analyses for long-term monitoring and evaluation on a local- and national-level, which can then be used to leverage political commitment and financial support for TB care and services [15].

2.3. Applying quality improvement (QI) methods

Quality improvement (QI) in TB programmes was identified by the Lancet Commission as a key approach for improving quality healthcare [6]. QI focuses on improving the quality across all six dimensions of healthcare: safety, effectiveness, patient-centeredness, timeliness, efficiency and equitability [16]. A recent review highlighted that a QI approach will be a necessary strategy to improve outcomes and ensure patient-centered care along the LTBI cascade [17]. In order to provide quality LTBI services, local data should be used in order to maximize the number of household contacts identified, screened and placed on treatment [17]. Applying a QI approach to LTBI program expansion will enable interventions to adapt and target different steps along the LTBI cascade in an iterative manner to measure progress in quality of patient care [17].

3. Key steps to improving LTBI services

3.1. Improved identification of household contacts and screening services

Contact investigations are performed when people who have close contact (i.e., spend over 5 h per week) with active TB patients are systematically investigated for TB infection or active disease [18]. A key challenge to improving LTBI services is identifying all household contacts who are eligible for preventive treatment. In most LMICs, although contact investigations are technically included in national TB control policies, contact tracing is inconsistently performed due to resource limitations, as well as poor standards, lack of clear definitions of index cases or procedures for contact investigation [18]. A proactive approach to contact screening is necessary to ensure everyone that has been in contact with the patient with active TB disease, including high-risk individuals (i.e., HIV positive patients), is properly screened and tested for LTBI.

In low-incidence countries, such as Canada, LTBI screening for recent immigrants at the time of entry based on demographic factors has been shown to be the most effective, albeit resource-intensive approach [19]. Lonnroth et al. outlined priority areas for global TB strategy in low-incidence countries which includes five priorities related to LTBI patient care directly: (1) providing political commitment, funding and planning for high-quality services; (2) screening for active TB and LTBI in TB contacts and providing appropriate treatment; (3) ensuring continued surveillance, program monitoring and evaluation and data management; (4) investing in research and new tools; and (5) supporting global TB prevention, care and control efforts [20]. But key challenges in this setting include inadequate political commitment to TB elimination, reduced awareness of TB in the general public and diminished clinical expertise [21,22].

3.2. Healthcare workforce training for TB testing

One barrier to proper testing of patients for LTBI is the lack of

knowledge by health providers on how to use simple tools to test for latent tuberculosis, such as a tuberculin skin test (TST). Yet testing is key to determining if someone has active or latent TB. Incorrect administration of TST is a problem, particularly in LMICs. Although international guidelines recommend either TST or interferon-gamma release assays (IGRAs) may be used to test for LTBI, the TST remains the most widely used test in LMICs due to its low cost and ease of use [23]. TST is a relatively simple test but it requires careful training and supervision to establish HCW proficiency to administer and read the TST [10]. To address the lack of simple TST training tools available online, a study tested the accuracy and reproducibility of an mhealth approach for mobile TST (mTST) to train HCWs how to measure the size of swelling directly following injection (TST injection bleb) and 48–72 h (TST induration) [10]. Results showed that the mTST approach was reliable for assessments of injections, and for detecting indurations 15 mm or larger [10]. This study highlights how innovative approaches, such as the use of mobile health technologies, can provide simple, affordable solutions to increase screening and testing for LTBI, particularly in LMICs.

3.3. Comprehensive medical evaluations

Alsdurf et al. identified a key loss along the LTBI cascade at the point of patients completing medical evaluation [7]. Chest radiography (CXR) is a highly sensitive test to detect pulmonary TB, and is used in medical evaluations to rule-out active TB disease before providing preventive treatment [18,24]. But the lack of skilled readers, high cost of equipment as well as the need for expertise to interpret chest x-rays in resource limited settings, poses a challenge to ensuring medical evaluations are completed properly [24,25]. Computer-aided detection (CAD) uses software programmes to interpret digital radiographs and detect radiographic abnormalities consistent with possible active TB [24,25]. Findings from a systematic review of five studies on CAD for TB demonstrated that CAD software was capable of achieving similar accuracy as non-expert clinicians [24]. And a recent study in high-burden TB countries, found that CAD had the potential to be used for TB screening [25]. While additional research is needed on CAD technologies, this is an exciting potential solution for the longstanding barrier of diagnostic delays for LTBI patients.

3.4. Shorter and safer LTBI treatment regimens

LTBI preventive therapy has been available for over 60 years to prevent the progression to active TB disease, which is an important public health benefit [11,26]. As with any preventive health service, however, it can be difficult to treat people with LTBI who are asymptomatic and feel otherwise healthy [11]. Like many chronic diseases, it can be emotionally draining and confusing for patients who do not feel sick to take medication for long periods of time [27], and thus many patients fail to complete preventive treatment. Yet the consequence of progressing to active TB disease are serious and thus preventive treatment for LTBI should be prioritized. This will require high-quality, patient-centered care approaches to educate and discuss treatment options with household contacts to ensure they understand and agree to treatment [11].

There are currently four available treatment regimens for LTBI that have evidence to support their use: (1) isoniazid for 6–9 months, (2) rifampin daily for 4 months (4R), (3) isoniazid and rifapentine weekly for 3 months (3HP), or (4) isoniazid and rifampin daily for 3–4 months (3–4HR) [9,28]. Based on results from two recently published randomized controlled trials 4R was non-inferior to 9H among high-risk groups, and treatment completion rates were significantly higher in the 4R group [29,30]. Concerns about safety of preventive treatment has historic significance, particularly given the hepato-toxicity that has been a serious concern for isoniazid preventive therapy (IPT) [31]. Preventive treatment regimens with 4R and 3HP have been shown to be safer than isoniazid in trials and observational studies [29,30,32–35] a notable improvement to the patient treatment experience. Providing patients in LMICs with shortened treatment regimens that are easier to complete and less toxic would enable more people to get on treatment, thereby closing the gap in the last step of the LTBI cascade [11]. Furthermore, a reduction in time on treatment will have an enormous impact on the quality of life for patients [11], by alleviating the psychological stress and fatigue from taking medication daily over such a long time period.

4. Shifting to prioritize quality LTBI care

There is more than sufficient evidence that preventive treatment of LTBI should be part of a comprehensive and epidemiologically sound strategy for TB elimination [11]. The joint push from the WHO and UNHLM-TB has provided clear justification and strong support for expanded LTBI services globally [1,5]. Recent emphasis on the need to improve the quality of healthcare in global health [6,36,37], has increased the attention on providing comprehensive LTBI services.

Patient-centered care should be driven by continuous input from the intended beneficiaries (i.e., LTBI patients) [15]. TB programmes looking to expand LTBI services must work hard to better identify all eligible contacts and seek patient input to determine local solutions to keep patients engaged in their care journey. It is also critical to consider how expanded health services for better LTBI patient-centered care will impact the workload of HCWs, particularly in high-burden TB settings. Initial results from the ACT4 trial showed a statistically significant increase of 11% in the proportion of HCW time spent on LTBI activities following the intervention to evaluate and strengthen LTBI services (data submitted for publication). Importantly, these increases in HCW time resulted in LTBI services that were signficantly improved following the ACT4 intervention. As seen in sites such as Vietnam, less than 5% of eligible contacts completed all steps along the LTBI cascade at baseline (see Fig. 2, blue line) compared to over 80% completing each step following the intervention (see Fig. 2, red line). These results demonstrate that extensive planning and resource allocation will be needed to ensure there is well-trained and sufficient staffing of TB programmes. HCWs must have adequate time throughout their workday devoted to LTBI services in order to be able to provide patient-centered care and expanded LTBI services without negative impacts to care for other patients (i.e., active TB).

However this will require significant financial commitments which are currently not available for LTBI services globally. The 2019 WHO Global TB Report estimates show that US$10.1 billion was required for TB prevention, diagnosis and treatment, yet there was a gap of almost US$3.3 billion. And of the estimated total, US$0.3 billion was for TB prevention services thus accounting for less than 3% of the total TB funding globally [1].To achieve the End TB Strategy goals, it will be particularly important that political and financial commitments to TB services not only continue but also support the expansion of LTBI patient care activities.

5. Conclusion

The Lancet Commission's HQSS framework has emphasized the importance of strengthening the healthcare workforce to improve patient-centered care. The numerous steps along the LTBI cascade of care pose challenges, but also opportunities to engage patients to ensure services meet their needs. TB programmes can improve the quality of latent TB services by implementing regular and standardized evaluations of the LTBI cascade of care with implementation of interventions to resolve gaps in care. This will lead to improvements in identification, diagnosis, treatment and retention in care of persons with latent TB. Ultimately, this will reduce the numbers of persons developing active TB disease thereby bringing an end to TB globally.

CRediT authorship contribution statement

Alsdurf Hannah: Conceptualization, Writing - original draft, Writing - review & editing. **Menzies Dick:** Supervision, Conceptualization, Writing - review & editing.

Declaration of Competing Interest

Neither of the authors of this manuscript have any conflicts of interest to declare.

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J Clin Tuberc Other Mycobact Dis 19 (2020) 100154

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

User experience and patient satisfaction with tuberculosis care in low- and middle-income countries: A systematic review

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ARTICLE INFO

Keywords:
Tuberculosis
User experience
Patient satisfaction
Health system
Public
Private

ABSTRACT

Background: Patient-centered care is at the forefront of the End TB strategy, yet little is known about user (patient's) experience and patient satisfaction with TB services. Our study aims to systematically review quantitative studies evaluating user experience and TB patient satisfaction within the health care system.
Methods: Five medical databases were systematically searched between January 1st, 2009 and December 31st, 2018. English studies assessing user experience and patient satisfaction within the healthcare system from a TB patient's perspective in low and middle-income countries, were included.
Results: Thirty-five studies from 16 low and middle-income countries evaluated three major themes; facilities and patient centeredness (n = 23), patient-provider relationship (n = 22) and overall satisfaction (n = 19). Overall study quality was low as they used varying tools to measure user experience and patient satisfaction.
Conclusion: Our study shows large variability in measurement of user experiences and patient satisfaction. Studies reported that patients were mostly satisfied with TB care services, and those that were dissatisfied were substantially more likely to be lost to follow-up. The high satisfaction rates could have been due to lack of education on good quality patient care or fear of losing access to health care. A standardized patient centered tool could be designed to help assess user experience and patient satisfaction to allow comparisons among health systems and countries.

1. Background

Tuberculosis (TB) is the leading cause of infectious diseases mortality worldwide, affecting 10 million people globally and killing 1.3 million in 2018 [1]. In the same year, there were an estimated 500,000 new cases of rifampicin- resistant TB (RR-TB) of which 78% were multidrug resistant TB (MDR-TB) cases, partly a consequence of the mismanagement of TB [1]. The End TB Strategy has an objective of providing TB patients with high-quality care, in which a patient's human rights are central to the design and delivery of TB services [2].

Although patient-centered care is the focus of the End TB strategy, poor quality care is widespread across many low- and middle-income countries (LMICs) [3–5]. Several studies have assessed the quality of TB care in different settings and the resulting impact on patients. In India and South Africa there have been large losses to follow-up of patients at different points of the cascade of care, where 50% of patients are diagnosed and treated adequately. This was evaluated for latent TB infection (LTBI) globally where 20% of patients were diagnosed and treated adequately [6–8]. Healthcare providers are only correctly managing 21–50% of TB patients, and patients often visit multiple providers before receiving a correct diagnosis [9–12]. Furthermore, once patients in LMICs enter the health system, they are faced with long diagnostic delays and often have trouble accessing adequate treatment [13,14]. For TB patients, this can lead to devastating outcomes. Poor quality care has led to an estimated 469,956 amenable TB deaths in 2016 [15].

The recently published Lancet Global Health Commission on High Quality Health Systems in the SDG Era has acknowledged the need to

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https://doi.org/10.1016/j.jctube.2020.100154

improve quality of care in LMICs and has recommended that health systems be measured according to elements of competent care and user experience [5]. Improving user experience in health care is crucial to improve retention in care, adherence to treatment and public trust in the health system. The Lancet Global Health Commission defined a positive user experience as being treated with dignity and respect, having a health provider who communicates clearly, provides autonomy and confidentiality and avoids discriminatory behaviours [5]. Health services should also be easy to navigate, with short wait times and be attentive to people's values and preferences. This can also be defined as patient centered care. TB being a disease that is stigmatized and primarily effects vulnerable social groups, emphasizes the importance of patient-centered care [16]. Previous studies have highlighted complex pathways to diagnosis [17,18] and high healthcare costs for patients [19], but little is known about the user experience and satisfaction with the health system. To our knowledge, there has been no systematic review of the literature examining TB user experience or satisfaction within the health system. The themes identified in this review can serve as a first step in understanding the reasons for poor quality user experience in TB care.

2. Methods

Our study aims to systematically review the current quantitative literature on user experience and satisfaction within the health system, synthesize current evidence, and identify further areas of research.

The protocol for this exploratory systematic review was registered on PROSPERO (CRD42018091504). The systematic review was classified as exploratory as the studies were expected to have varying exposure and outcome definitions. Hence, a broad definition of user experience and patient satisfaction were used for this review. In this study, user experience was defined as a patient's experience in the health system [20]. Patient could be a presumptive TB patient, asymptomatic patient and/or a confirmed TB patient. Patient satisfaction was defined as a patient's evaluation of the services offered within the health system, relative to their expectations of care [20]. Finally, the health system was defined as services received from both formal and informal healthcare providers.

2.1. Search strategy

Using a broad search strategy, five medical databases were searched; PubMed, Embase, Ovid Global Health, CINAHL, and Web of Science. The initial search strategy for PubMed was approved and verified by a medical librarian at McGill University (see Appendix A). An initial search was conducted on October 24th, 2017 and an updated search was conducted in April 2019. The search included all articles from January 1st, 2009 to December 31st, 2018. No language or geographic restrictions were applied.

2.2. Study selection

Two independent reviewers conducted the title/abstract and full text screening of all articles (Fig. 1). Articles were assessed using predefined inclusion criteria, and any conflicts were resolved by a third independent reviewer. The following studies were eligible for inclusion; (1) quantitative study design (2) studies with full text articles in English, (3) studies assessing user experiences with standard of TB care within the health system, (4) studies assessing user experiences from the patient's perspective (first person), (5) studies involving all types of TB patients and presumptive TB patients (including latent TB infection), and (6) studies conducted amongst adults (>15 years old). Studies were excluded if: (1) qualitative study design, (2) conducted in high-income countries (as defined by the World Bank), (3) assessed user experience outside the health system (including accessibility to health care facilities) (4) evaluated costs of health care, (5) assessed user experience or satisfaction through a third person perspective (i.e. from health care worker perspective), (6) in the grey literature, (7) involved services provided outside of the health system's standard of care (e.g. prisons, interventions), (8) studies assessing user experiences outside the standard of TB care (i.e. quasi-experimental studies, RCTs) and (9) studies where no full text could be found were excluded.

2.3. Data extraction

A data extraction form was created and piloted. It aimed to collect information on study characteristics, themes of user experience and patient satisfaction, frequencies and associations to outcomes (i.e. treatment outcomes, treatment delay and treatment adherence). Data was extracted by two independent reviewers using Excel. All discrepancies were resolved by consensus between the two reviewers.

2.4. Quality assessment

A quality assessment was conducted for all studies, however studies were not prioritized and/or excluded due to their quality. The Cochrane and National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment Tools for Observational Cohort, Cross-Sectional Studies, and Case-control studies [21] were used. The main elements of quality assessed were selection bias, information bias, measurement bias, and confounding. All discrepancies between quality assessments were discussed among the two independent reviewers and resolved.

2.5. Data analysis

Studies used a wide number of measures that reflected components of user experience and satisfaction. Hence an inductive approach, informed by qualitative methodology, was applied to identify key themes relating to the review question. Measures of patient satisfaction from a random sample of 5 (14%) articles were accordingly first coded independently by two reviewers, after which consensus on 3 key themes was reached through full team consultation. Each study was then reviewed for reporting on one or more of these 3 themes (see Table 1).

Studies were categorized based on theme (e.g. patient provider relationship) and were analyzed based on frequency of themes identified, using Excel. Subsequently, descriptive statistics such as mean, median and frequencies were reported for themes of TB patient experience and patient satisfaction. Associations between aspects of user experience and treatment outcomes, delay or adherence (odds ratios, risk ratios and/or hazards ratios) were also reported.

Study variables, and exposure and outcome measures varied largely thus pooling and meta-analyses were not conducted.

3. Results

As shown in Fig. 1, 35 quantitative studies were eligible for inclusion in our systematic review. Studies assessed user experience in TB care by evaluating the patient's perspective on the health care facilities, the providers, or by assessing overall satisfaction. Table 1 shows the main study characteristics and themes identified for each study. Studies were conducted in 16 LMICs namely; Botswana, Brazil, China, Ethiopia, India, Indonesia, Kenya, Morocco, Myanmar, Nigeria, Pakistan, Peru, Serbia, South Africa, Sudan, and Uganda.

3.1. Quality assessment

Figs. 2 and 3 represent the quality assessment for cross sectional, cohort and case-control studies (n = 35). Most studies (22, 63%) did not report sample size and power calculations. Among cross-sectional and cohort studies (n = 25), 18 (72%) either did not report or did not have a participation rate of over 50% which could have led to selection bias. In the cohort study, the exposure was measured only once over

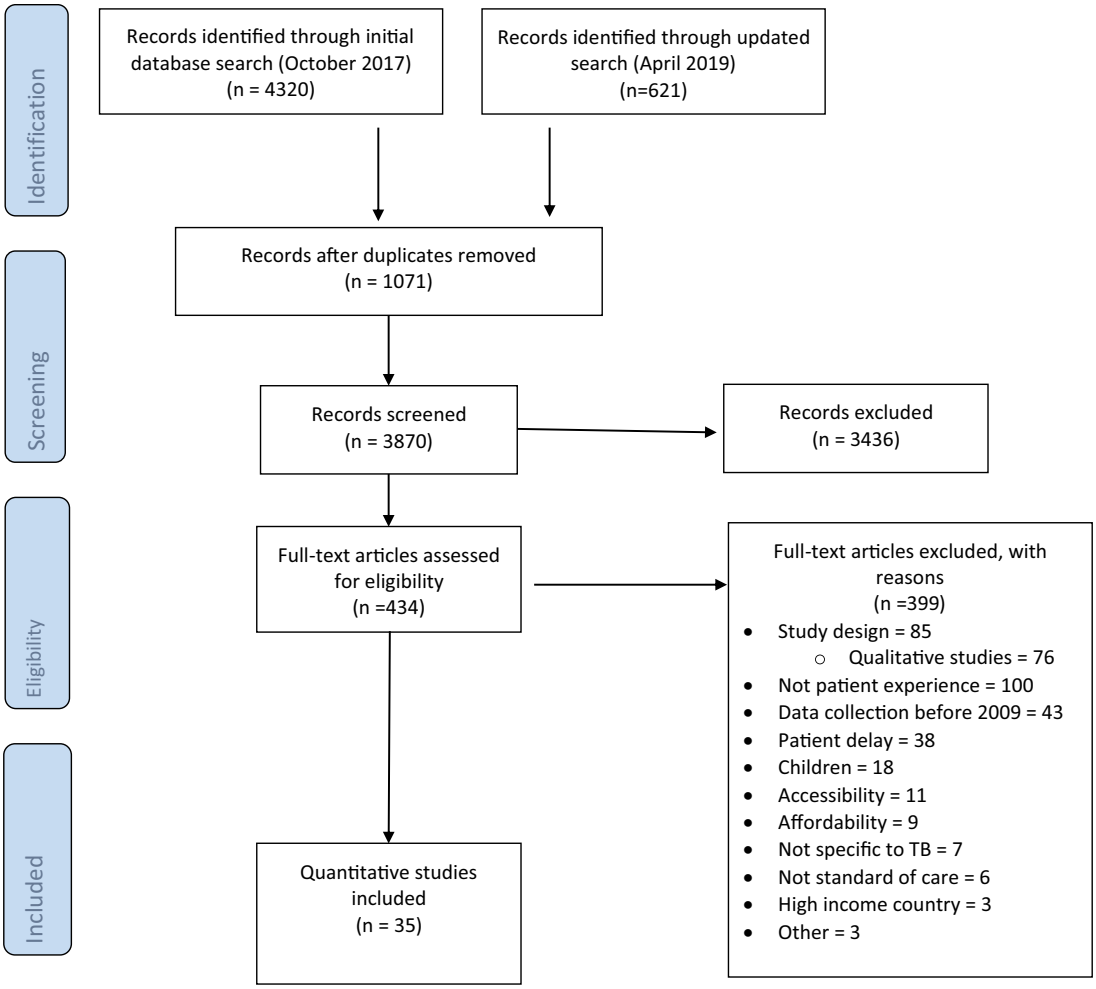

Fig. 1. PRISMA diagram on study selection.

time. All case control studies, and the cohort study did not blind or did not report on whether the assessors of exposure (i.e. patient experience) were blinded to the patient's case or control status (n = 10). Further, there was large variability in tools used for measuring user experience and patient satisfaction (Table 1). Ten (29%) studies adapted pre-existing tools; of which two (20%) were based on each other [22,23]. Five (14%) tools were developed by the authors of the studies but were not validated before use, while six (17%) studies developed and validated their tools. One (3%) study used a pre-validated stigma scale. Eight (23%) did not report the details of their tool.

3.1.1. Facility infrastructure and patient-centeredness

Twenty-three studies (23/35, 66%) identified characteristics and patient-centeredness of the facilities as a theme influencing patient's experience with TB care. The theme of facility patient-centeredness was divided into four subthemes: wait times, ease of use, availability of equipment/supplies, and cleanliness. Six (6/23, 26%) studies evaluated overall satisfaction with facilities. For example, a study in Nigeria used a five-point Likert scale to evaluate patient satisfaction scores with different aspects of patient care. 'Amenities' was given an overall average satisfaction score of 3.27/5.00 [0.49] by patients, which was one of the least satisfying areas of care [24]. A study from Pakistan found that the lack of gender specific facilities in the health centers contributed to patient delay [25]. Five studies (5/23, 22%) reported that the cleanliness of the facility affected patient satisfaction. Cleanliness referred to comfort and proper hygiene.

Fifteen studies (15/23, 65%) examined how a patient's wait time contributed to their experience. Seven studies (7/15, 47%) measured satisfaction with wait times. Responses varied among studies, where studies in Uganda, South Africa and India [26–28] reported that long wait times contributed to low satisfaction with services but studies in Brazil, Ethiopia and India reported that patients were satisfied with wait times [23,29–31]. Five studies (5/15, 33%) reported associations of wait times with loss to follow up (LTFU). For example, one study reported that patients were more likely to be LTFU if wait times exceeded 2 h (OR = 4.2, CI 2.18–8.02) [32]. Certain studies observed that inconvenient clinic hours resulted in LTFU. A study in South Africa described that TB patients enrolled in public health facilities were more likely to be LTFU during treatment when clinic hours were inconvenient (OR: 3.4, CI 2.2–5.2) [33]. In Indonesia, being unable to collect TB medication from a community lung clinic was significantly associated with patient LTFU (HR 22.00, CI 3.88–124.78) [34].

Eight (8/23, 35%) studies highlighted that the medical equipment or supplies in a facility affected patient experience. Two studies, in Thailand and India, reported that availability and quality of drugs influenced their choice of provider and sector [27,35]. Further, two studies observed that the absence of drugs and supplies such as syringes, needles, and microscopes in public facilities led to non-adherence to treatment and dissatisfaction, respectively [30,36]. In contrast, another study in Ethiopia demonstrates that 278 (99%) of patients in public facilities reported that drugs were always available [37].

3.1.2. Patient-provider relationship

Twenty-two (22/35, 63%) studies reported patient-provider relationship as a theme affecting a patient's experience in the health system. The subthemes identified were confidentiality, technical

Table 1
Study characteristics and themes of TB patient experience (n = 35).

Author	Year	Country	Study design	Sample size	Health care sector	Disease type	Data collection methods	Data collection tool used	Gender distribution				Age distribution (mean, SD)		Themes identified		
									Male		Female						
									N	%	*N*	%	Mean	SD	Patient provider relationship	Facility infrastructure and patient-centeredness	Overall satisfaction
Ali and Prins	2016	Sudan	Case control	315	Public	PTB/EPTB	Medical records and interviews	NR	205	65.1	110	34.9	33.7	14.7	Yes	Yes	Yes
Adane et al.	2013	Ethiopia	Cross sectional	280	Public	PTB/EPTB	Self administered questionnaire	Self made, not validated	157	56.1	123	43.9	32.9	14.8	Yes	Yes	No
Babikako et al.	2011	Uganda	Cross sectional	133	Public/ private	PTB	Individual interviews	Adapted the PS-13 and SIMS scales	67	50.4	66	49.6	33.6	10.55	Yes	Yes	Yes
Brunello et al.	2009	Brazil	Cross sectional	100	Public	NR	Individual interviews	Self-made, not validated	69	69.0	31	31.0			Yes	No	Yes
Burapat et al.	2009	Thailand	Cross sectional	756	Public	PTB/EPTB	Individual interviews	Self-made, not validated	528	69.8	228	30.2	34	NR	Yes	Yes	No
Charles et al.	2010	India	Cross sectional	606	Public/ private	Presumptive TB	Individual interviews	Self-made, not validated	NR	NR	NR	NR	NR	NR	Yes	Yes	Yes
Chimbindi et al.	2014	South Africa	Cross sectional	296	Public		Individual interviews	Self-made, validated	140	47.3	156	52.7	38		Yes	Yes	Yes
Culqui et al.	2012	Peru	Case Control	870	Public	Pulmonary TB	Individual interviews	Questionnaire adapted from Lalone Laframboise model[a]	522	60.0	348	40.0	NR		Yes	No	No
Elbireer et al.	2011	Uganda	Case Control	344	Public	NR	Individual interviews	Self-made, not validated	176	51.2	168	48.8	36	8	Yes	Yes	No
Finlay et al.	2012	South Africa	Case Control	1164	Public	PTB/EPTB	Self administered questionnaire	Self-made, adapted from previous study	100	8.6	1064	91.4	NR	NR	Yes	Yes	No
Hla et al. [50]	2009	Myanmar	Case Control	400	Public	NR	Self administered questionnaire	Self-made, validated	NR	NR	NR	NR	NR	NR	Yes	Yes	No
Lafaiete et al.	2011	Brazil	Cross sectional	88	Public	NR	Self administered questionnaire	Validated and adapted from Villa and Ruffino-Netto[b]	NR	NR	NR	NR	NR	NR	Yes	Yes	No
Mehra et al.	2013	India	Cross sectional	555	Public	PTB	NR	NR	379	68.3	176	31.7	NR	NR	Yes	No	Yes
Ndwiga et al. [51]	2016	Kenya	Cross sectional	140	Public	NR	Self administered questionnaire	NR	86	61.4	54	38.6	35	NR	Yes	No	No
Nezenga et al.	2013	Ethiopia	Cross sectional	531	Public	NR	Self administered questionnaire	Adapted from Birhanu et al. 2010 and Grant Marshall and Ron Hays (1994)[c]	291	54.8	240	45.2	NR	NR	Yes	Yes	Yes
Onyeonoro et al.	2015	Nigeria	Cross sectional	258	Public/ private	NR	Individual interviews	Adapted from used by Nwabueze et al. (2010) (PS-38)[d]	139	53.9	119	46.1	34	12.8	Yes	Yes	Yes
Pinto & Udwadia	2010	India	Cross sectional	200	Private	TB	Individual interviews	NR	NR	NR	NR	NR	NR	NR	Yes	Yes	Yes
Portela et al.	2014	Brazil	Cross sectional	4345	Public	NR	Individual interviews	Adapted from Babikako et al. (2011)	2507	57.7	1838	42.3	40.9	NR	Yes	Yes	Yes
Rankosha and Ehlers [52]	2016	Botswana	Cross sectional	101	NR	PTB/EPTB	Individual interviews	NR	56	55.4	45	44.6	NR	NR	Yes	No	Yes

(*continued on next page*)

Table 1 (*continued*)

Author	Year	Country	Study design	Sample size	Health care sector	Disease type	Data collection methods	Data collection tool used	Gender distribution				Age distribution (mean, SD)		Themes identified		
									Male		Female						
									N	%	*N*	%	Mean	SD	Patient provider relationship	Facility infrastructure and patient-centeredness	Overall satisfaction
Rashmi and Vijaykumar	2010	India	Cross sectional	30	Public	NR	Individual interviews	Module 6, Agha Khan foundation	NR	NR	NR	NR	NR	NR	No	Yes	Yes
Rutherford et al.	2013	Indonedia	Cohort	265	Public	PTB/EPTB	Individual interviews	Self-made, validated	119	44.9	146	55.1	NR	NR	Yes	Yes	Yes
Salame et al. [53]	2017	Brazil	Cross sectional	236	Public	LTBI	Individual interviews	Adapted from Rutherford et al. (2013)[e]	NR	NR	NR	NR	40	NR	Yes	Yes	Yes
Satti and Nagaraj	2016	India	Case Control	240	Public	PTB/EPTB	Individual interviews	Self-made, validated	144	60.0	96	40.0	36.5	9	Yes	Yes	No
Shalini and Harsh	2014	India	Cross sectional	220	Public	TB	Individual interviews	NR	160	72.7	60	27.3	NR	NR	Yes	Yes	Yes
Slama et al. [54]	2013	Morocco	Case Control	320	Public	PTB/EPTB	Individual interviews	Self made, validated	258	80.6	62	19.4	33	NR	Yes	No	No
Ssengooba et al.	2016	Uganda	Cross sectional	178	Public	MDR-TB	Self administered questionnaire	NR	76	42.7	102	57.3	NR	NR	Yes	Yes	Yes
Sulaiman et al.	2013	Sudan	Cross sectional	107	Public	PTB	Individual interviews	Self made, adapted from NTP questionnaire	76	71.0	31	29.0	41	NR	Yes	Yes	Yes
Tamhane et al. [55]	2012	India	Cross sectional	126	Public/ private	PTB	Individual interviews	Self made, validated	75	59.5	51	40.5	NR	NR	No	Yes	No
Xu et al.	2017	China	Case Control	1425	NR	MDR-TB	Other*	NR	1025	71.9	400	28.1	44.5	14.8	No	Yes	No
Megene et al. [56]	2016	Ethiopia	Cross sectional	251	Public	NR	Individual interviews	Self made, adapted from Hill et al. (2005)[f]	119	47.4	132	52.6	40	13.7	Yes	Yes	Yes
Ruru et al. [57]	2018	Indonesia	Case Control	264	Public	NR	Individual interviews	NR	155	58.7	109	41.3	NR	NR	No	Yes	No
Saqib et al.	2018	Pakistan	Cross sectional	269	Public/ private	PTB	Individual interviews	NR	139	51.7	130	48.3	NR	NR	Yes	Yes	Yes
Stosic et al. [58]	2018	Serbia	Case Control	124	NR	MDR-TB	Individual interviews	Health survey in Serbia for 2013 and European Health Survey 2nd wave	84	67.7	40	32.3	NR	NR	Yes	No	No
Yin et al. [59]	2018	China	Cross sectional	1342	NR	NR	Self administered questionnaire	TB related stigma scale by Yang (2016) [g]	905	67.4	437	32.6	47.72	17.06	Yes	No	No
Htun et al. [60]	2018	Myanmar	Cross sectional	210	Public	MDR-TB	Individual interviews	Guidelines of management of MDR-TB, Myanmar (2013)	131	62.4	79	37.6	41	15.02	No	Yes	No

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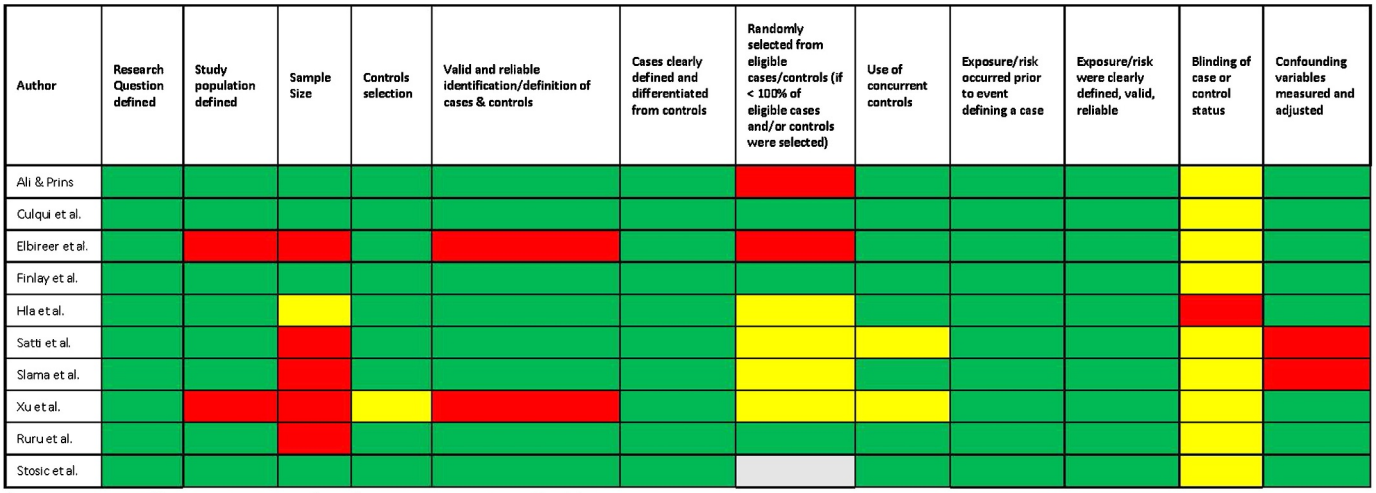

Fig. 2. Quality assessment of included case-control studies (n = 10)
*green = yes, yellow = not reported, red = no, gray = not applicable.

capacity of healthcare workers (i.e. ability to provide diagnosis, treatment and counselling), responsiveness, health education and stigma. Most studies (14/22, 63%) reported overall positive experiences with healthcare providers, and seven (7/22, 32%) reported overall negative experiences. For example, a study conducted in Brazil among patients in the public sector observed that the highest rates of satisfaction (>89%) were due to doctor availability during consultation and privacy during attendance [23]. However, a study conducted in South Africa among patients visiting the public sector observed that 267 (44%) patients were dissatisfied with the provider [38]. Factors

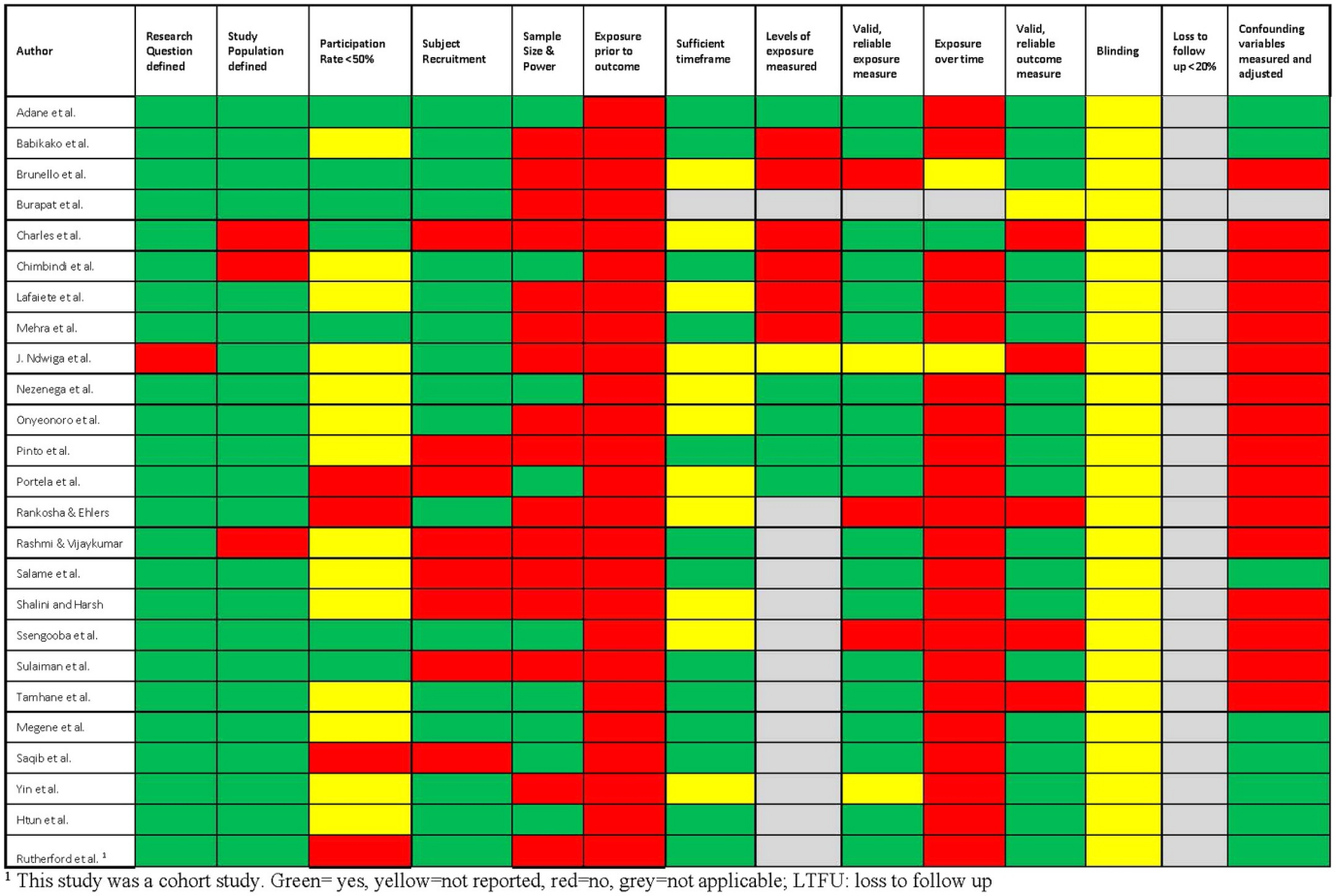

Fig. 3. Quality assessment of included cohort and cross sectional studies (n = 25)
[1]This study was a cohort study. Green = yes, yellow = not reported, red = no, gray = not applicable; LTFU: loss to follow up.

influencing their dissatisfaction were: indifference by healthcare providers, delay and non-availability of healthcare providers. A study in Indonesia observed that patients who were not satisfied with their provider were more likely to be LTFU (Hazard Ratio (HR): 2.58, 95%CI: 0.99–6.75) [34].

Seven studies (7/22, 32%) reported that staff and/or health professional attitudes affected patients' experiences. A study in Sudan reported that 96% of patients found providers to be receptive [39]. However, a study in India reported 20 (9%) of DOTS patients felt that the staff was rude [40]. A Ugandan study reported that bad or fair staff conduct was significantly associated with treatment LTFU (OR 2.7, 95% CI: 1.02–7.25) [32]. Six studies (6/22, 27%) observed provider responsiveness as one of the factors influencing patient-provider relationships. Responsiveness included availability to listen, recording of patients' complaints, referrals from the provider, talking about the disease, and clarification of patients' doubts. A study in Brazil among patients in the public sector found that 56 (64%) of patients felt that reception of providers was good. Further, 53 (60%) of patients felt that providers had good availability and 55 (62.5%) of patients thought there was good guidance from the health team [31]. A study conducted in Uganda found that not being given the chance to express concerns about TB treatment was significantly associated with patient LTFU (OR: 3.5, 95% CI: 1.67–7.21) [32].

Three studies (3/22, 14%) observed that the capacity to keep information confidential and the technical capacity of providers were factors influencing a patient's experience. A study conducted in India identified that confidentiality was the most influential factor in choosing a medical provider for patients (468, 62%) [35]. A study conducted in Peru observed that 175 (67%) of patients felt discomfort during their treatment, due to having a bad relationship with the health worker and doubting their technical capability [41]. Six (6/35, 17%) studies identified information and health education as factors affecting a patient's experience in the health system. A study in Uganda in the public sector identified a significant association between not receiving adequate health education during treatment and the treatment discontinuation (OR 5.3 [95% CI: 1.94–14.57]) [32]. A study conducted in Morocco among TB patients in the public sector found that the perception of a patient having little or no explanation about the disease was significantly associated to LTFU (aOR 2.87, 95%CI 1.53–5.36).

Stigma was observed amongst HIV/TB or multi-drug resistant TB (MDR-TB) patients in eight studies (8/35, 23%). A study in India observed that those working at DOTS centers discriminated against HIV-TB co-infected patients more than other TB patients (aOR: 7.38; 95% CI: 2.32–23.39) [42] . A similar result was found with MDR TB patients, compared to drug sensitive TB patients (OR = 3.32; 95% CI = 1.40–7.86). Five studies (5/8, 63%) evaluated the association between stigma in the health system and TB patient treatment outcomes. A study in South Africa noted that feeling ashamed of having TB was associated with LTFU from treatment (aOR 2.0, CI 1.3–3.0) [33].

3.1.3. Overall patient satisfaction

Nineteen studies (19/35, 54%) measured the level of patient satisfaction with TB services in the health system overall without investigation of the specific aspect of the experience that influenced satisfaction. The tools to measure satisfaction are outlined in Table 1. Thirteen studies (13/19, 68%) measured patient satisfaction in only the public health system, while 4 (4/19, 21%) measured it in both the public and private, and 1(1/19, 5%) the private health system. Overall, studies reported that patients were either fully satisfied or satisfied with the availability and effectiveness of public TB services received [22,24,25,34,38,40,43]. For example, a study in Uganda measured patient satisfaction scores (maximum of 100) of the technical quality of care and management of a public and a private hospital [22]. The technical quality satisfaction score was 49.2 [4.7] for public health care and 96.6 [9.5] for private health care and were significantly different (p-value < 0.001). Management, defined as overall satisfaction with patient care and hospital services in general, was scored at 91.1 [10.9] in the public hospital and 89.7 [13.2] in the private hospital, with no significant difference [22]. Five studies (5/19, 26%) reported that dissatisfaction of TB services was a reason for loss-to-follow-up (LTFU) or delaying treatment. In Indonesia, poor satisfaction of services in a community lung clinic was significantly associated with LTFU during treatment (HR = 3.85, CI 1.17–12.62) [34].

4. Discussion

This exploratory systematic review aimed to synthesize the quantitative published literature on user experience and patient satisfaction with TB care across LMICs. The studies found assessed TB patients' perspectives on the patient-centeredness of facilities (n = 23), the patient-provider relationship (n = 22) and overall patient satisfaction with TB services (n = 19). Studies reported that patients were mostly satisfied with TB care services, and those that were dissatisfied were substantially more likely to be LTFU. Within patient-centeredness of facilities, four subthemes were identified; wait times, ease of use, equipment and supplies, and cleanliness. Patient-provider relationship included six subthemes; staff and/or health professional attitudes, confidentiality, technical capacity of healthcare workers, responsiveness, health education and stigma.

Within each subtheme, negative patient experience was often reported to be associated with LTFU or treatment non-adherence. Healthcare staff and providers have the potential to improve patients' negative experiences, especially regarding increased patient health education, staff attitudes and technical capacity. Improving the technical capacity of healthcare workers and increasing the flow of information to patients can be addressed through healthcare staff trainings and medical workshops. To improve other aspects of care such as staff attitudes and stigma, encouraging the development of skills in patient counselling, cultural sensitivity and other soft skills may be required in medical trainings [16].

Although some studies reported negative patient experiences, the majority of studies reported high overall satisfaction of TB services. This is discrepant with evidence of widespread low quality of TB care (e.g. broken cascades of care and poor medical outcomes) [3]. The measures of satisfaction used in these studies may have been subject to acquiescence response bias, which tends to be more common among questionnaires comprising agree/disagree questions [44]. Further, patients from vulnerable and stigmatized populations are often less likely to express dissatisfaction with healthcare due to low expectations or fear of loss of services. For this reason, they may report a higher satisfaction for low quality care [5, 45]. These lower expectations could be from the lack of exposure to a good quality health system, and little access to information on health care [16]. It is therefore important to assess qualitative data to further understand reasons why patients are expressing high and/or low quality of TB services, as well as increase education on quality care.

Our study also shows large variability in measurement of user experiences and patient satisfaction. All studies used questionnaires to measure different aspects of care. Some studies (n = 10) used previously validated questionnaires, whereas others (n = 5) used self-created questionnaires which were not validated, and some (n = 6) used self-created questionnaires which were validated (i.e. piloted). Further, the questionnaires used had varying types of scales (i.e. 3-point Likert scale, vs yes/no vs 5 point-Likert scale). Since a standard measure of patient satisfaction was not used in these studies, the task of synthesizing the findings was challenging. Standardizing measurements of patient satisfaction can be beneficial, as data can be used for quality monitoring and improvement, within and across health facilities [46]. An example of an assessment tool to measure person-centered care was developed and validated in Kenya in 2017 for maternal health [47]. It contains 30 questions that cover 10 domains, several of which were similar to the themes identified in our study. They include dignity and

respect, privacy and confidentiality, communication, stigma, health facility environment and trust [47]. Of the studies included in our review, data collection was not repeated at a different point in time to document changes in patient experience. A standardized tool would be valuable for monitoring interventions that address user experience or patient satisfaction, in order to assess if quality is improving over time. There is a need for a standardized approach to measure user experience and patient satisfaction within TB care, and to ensure the tool's validity, acceptability, feasibility and reliability [48].

When measuring patient-centered care, patients can be included in the design of these tools, to ensure that their experience is being accurately represented [20]. This can be done through focus group discussions with patients, or through cognitive and pilot testing of questionnaires with patients [20,48]. While a tool can help to document user experience and patient satisfaction, the variability in our results represents the diversity of experiences that a TB patient can have. This can depend on the many factors listed in this review as well as the expectations of each patient [20]. To ensure that TB interventions and a quality improvement programs take into consideration the needs and expectations of patients in differing contexts, it is recommended that TB service and intervention design also directly involve patients. In the United States of America, among eight health organizations known for their successful patient-centered care, a variety of approaches to ensure patient engagement are utilized. This includes patient membership in advisory committees and quality improvement committees [49].

4.1. Limitations

There were several limitations to this study. Firstly, a reference back check was not conducted, which may have resulted in missing studies. Our search strategy was comprehensive, and we purposely searched a wide array of medical databases, but despite this we may have missed certain articles (especially since we limited the study to English language papers). Secondly, studies focusing on qualitative results and using a qualitative data collection method (i.e. focus groups) were excluded. This was due to the large number of articles resulting from our search and feasibility of analysis with a small team. Thirdly, this review may be biased with studies reporting positive results. It is possible that studies with negative patient experiences were not published, or that settings with poor user experience are unlikely to conduct such studies. Lastly, accessibility and cost of TB services were excluded from this review, as there have already been reviews published on these topics. They should continue to be considered when planning quality improvement measurements and programs.

5. Conclusion

Overall, user experience and patient satisfaction with TB care were documented in 35 studies conducted in 16 LMICs, in this systematic review. Areas of care that are important to TB patients were identified including; the patient-centeredness of facilities and patient-provider relationships. There is large variability in patient satisfaction within these areas due to subjective definitions of satisfaction, different methods of capturing user experience, and individual expectations of care. Standardized data collection tools to measure user experience and patient satisfaction with TB care are needed in order to minimize this variability, as well as to monitor and improve on patient-centered quality of TB care. Additionally, patient involvement would be crucial in the creation of these tools in order to reliably and accurately measure their experience and also reduce the frequent loss to follow up associated to user experience. TB programs should focus on improving user experiences and encourage retention to care, in order to help achieve the targets of eliminating TB by 2035.

Ethical statement

This study is a systematic review of published literature. Therefore, no human subjects were involved, and no ethics approvals were needed.

CRediT authorship contribution statement

Danielle Cazabon: Conceptualization, Data curation, Formal analysis, Validation, Visualization, Writing - original draft, Writing - review & editing. **Tripti Pande:** Conceptualization, Data curation, Formal analysis, Validation, Visualization, Writing - original draft, Writing - review & editing. **Paulami Sen:** Data curation, Writing - review & editing. **Amrita Daftary:** Conceptualization, Writing - review & editing. **Catherine Arsenault:** Writing - review & editing. **Himani Bhatnagar:** Data curation, Writing - review & editing. **Kate O'Brien:** Writing - review & editing. **Madhukar Pai:** Conceptualization, Writing - review & editing.

Declaration of Competing of Interest

The authors do not have any conflicts of interest.

Acknowledgements

We acknowledge funding support from the Bill & Melinda Gates Foundation (BMGF OPP1091843). We would like to thank Mrs. Genevieve Gore from the McGill University library for her assistance in developing and piloting the initial search strategy for PubMed. Further, we would like to thank participants of the Quality of TB care course (McGill Summer Institute on Infectious Diseases and Global Health) for their contributions to our discussion.

DC, TP, AD and MP conceptualized and designed the systematic review study. DC and TP wrote the protocol, screened and extracted the papers, performed data analysis and wrote the manuscript. PS and HB assisted in screening, resolved disagreements and helped in data extraction. All co-authors assisted in revising the manuscript.

Appendix A. Search strategy

PUBMED

(tuberculosis[mesh] or tuberculosis[ti] or TB[ti])

AND

((patient satisfaction[mesh] OR patients/psychology[mesh] OR (patients[mesh] AND (qualitative research[mesh] OR “interviews as topic”[mesh] OR “community based participatory research”[mesh] OR narration[mesh])) OR ((patient[tiab] OR patients[tiab]) AND (experience*[tiab] OR perception*[tiab] OR perspective*[tiab] OR attitude*[tiab] OR qualitative[tiab] OR ethnograph*[tiab] OR narrative*[tiab] OR view*[tiab] OR ((action[tiab] OR participatory[tiab]) AND research[tiab]) OR mixed method*[tiab] OR mixed study[tiab] OR mixed studies[tiab] OR barrier*[tiab] OR facilitator*[tiab])) OR patient reported outcomes[mesh] OR patient reported[tw] OR patient acceptance of health care[mesh] OR patient acceptance[tw] OR patients acceptance[tw]) OR (patient satisfaction[tw] or patient rights[mesh]))

AND

((Delivery of health care[mesh:noexp] OR health system*[tw] OR health services[tw] OR health facilities, proprietary[mesh] OR health services[mesh] OR healthcare[tw] OR care[tw] OR patient care[mesh] OR caring[tw] OR health services accessibility[mesh])))

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J Clin Tuberc Other Mycobact Dis 19 (2020) 100155

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Tuberculosis deaths are predictable and preventable: Comprehensive assessment and clinical care is the key

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ARTICLE INFO

Keywords:
Clinical care
Co-morbidity
End-tb strategy
Epidemiology
Tb mortality
tuberculosis

ABSTRACT

The goal of reducing tuberculosis (TB) mortality in the END TB Strategy can be achieved if TB deaths are considered predictable and preventable. This will require programs to examine and address some key gaps in the understanding of the distribution and determinants of TB mortality and the current model of assessment and care in high burden countries.

Most deaths in high-burden countries occur in the first eight weeks of treatment and in those belonging to the age group of 15–49 years, living in poverty, with HIV infection and/or low body mass index (BMI). Deaths result from extensive disease, comorbidities like advanced HIV disease complicated with other infections (bacterial, fungal, bloodstream), and moderate-severe undernutrition. Most early deaths in patients with TB, even with TB-HIV co-infection, are due to TB itself.

Comprehensive assessment and clinical care are a prerequisite of patient-centered care. Simple independent predictors of death like unstable vital signs, BMI, mid-upper arm circumference, or inability to stand or walk unaided can be used by programs for risk assessment. Programs need to define criteria for referral for inpatient care, address the paucity of hospital beds and develop and implement guidelines for the clinical management of seriously ill patients with TB, advanced HIV disease and severe undernutrition as co-morbidities. Programs should also consider notification and audit of all TB deaths, similar to audit of maternal deaths, and address the issues in delays in diagnosis, treatment, and quality of care.

1. Introduction

Tuberculosis (TB) is one of the top ten causes of death globally. Since 2011, it is the leading cause of death due to a single infectious agent, (surpassing HIV) with an estimated 1.2 million estimated deaths in 2018 among the HIV negative people living with TB and another 0.25 million in HIV positive people with TB [1]. The END TB strategy aims to reduce TB incidence and mortality in 2035 (compared to 2015 figures) by 90%, and 95%, respectively [2]. A target of 75% reduction in TB mortality by 2025 is an ambitious milestone, as currently, TB mortality in HIV negative patients is declining by 3% per year [1]. Historically, cure rates in patients with TB of more than 95% were reached in developed countries with effective anti-tuberculosis drugs and assured adherence to therapy [3]. While the case fatality ratio (estimated mortality/estimated incidence) in high-income countries is 5%, it continues to be around 20% in high-burden countries [1]. The eight high TB burden countries that contribute to two thirds of the disease burden are India–27%, China–9%, Indonesia–8%, Philippines–6%, Pakistan–5%, Nigeria–4%, Bangladesh–4% and South Africa–3% [1]. An effort to reduce the disease burden and deaths due to TB in these countries, particularly India, is crucial in achieving these ambitious targets.

Mortality during TB treatment is not merely a function of the infection with M.Tuberculosis, but there are host, disease, and health system related factors that underlie and contribute to mortality. We believe that significant and even dramatic reduction of TB mortality in high burden countries is a goal achievable in the near future if we consider them predictable and preventable and recognize and address three crucial gaps. First, the epidemiological understanding of the distribution and determinants of TB mortality should inform and reflect in programmatic strategies and treatment guidelines. Second, there are significant gaps in the evaluation and management of patients with TB

Ethical Statement: Not applicable

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https://doi.org/10.1016/j.jctube.2020.100155

that are not addressed in the current operational model of patient-centered care. TB programs need to implement appropriate and comprehensive clinical care, as an essential pre-requisite of patient-centered care. Third, there are gaps in the health system preparedness leading to delays in diagnosis, difficulties in access, and lack of comprehensive clinical care to patients with severe disease. We use the WHO definition of TB mortality as mortality due to any cause in a patient who is on treatment for TB according to the international classification of diseases. We recognize there are methodological problems in estimating the mortality in high TB burden countries that lack universal health coverage, have poor vital registration system (VRS) and disease reporting system with poor information on burden of undiagnosed TB [4]. National TB programs may underestimate TB deaths as these do not account for deaths in undiagmosed patients, in those who default during treatment, in patients with recurrent disease or those due to sequel [5]. Several based studies have shown that diagnosis is often missed in patients with smear negative tuberculosis, disseminated and extrapulmonary TB [4–8]. On the other hand, some deaths that are recorded during treatment may not be due to TB [4,5,7,8]. This review outlines the gaps within the framework of epidemiology, clinical care, and health system readiness in reducing TB mortality

2. Addressing the programmatic gaps in the understanding of the distribution and determinants of TB mortality

2.1. The person distribution of deaths due to tuberculosis or who dies of tuberculosis?

There is a socio-demographic gradient to TB mortality. Globally, 95% of TB deaths occur in low and middle-income countries (LMIC) [1]. TB mortality disproportionately affects those living in poverty: as the indigenous populations, marginalized groups, homeless, [9,10] and those engaged in manual work [11]. In a hospital serving a predominantly poor population in Manila, the mortality rate among HIV negative adult patients with all forms of TB was 20.1–37.5% [12,13]. Living in an area of inequality was associated with a 5-fold higher risk of TB mortality [10]. Higher mortality in these groups could be related to delays in the diagnosis of tuberculosis and a lack of access to quality care.

The risk of death due to TB is affected by age, gender, type of tuberculosis and drug susceptibility profile. Age as a predictor of mortality varies according to the countries. In developed countries like those in the European Union, Democratic Republic of Korea, Israel, advancing age is a predictor of mortality [14–16]. On the other hand, there is a higher burden of TB and TB mortality in younger age groups in the LMICs. In patients in the age group of 15–44 years in rural South India, the number of deaths due to TB was found to be 12 times higher than those expected in the general population [17]. In Brazil, age < 5 years and age > 60 years was associated with two-fold and ten-fold higher odds of mortality, respectively [18]. The number of cases in the younger age group is also more than older adults in LMIC. In a population-based survey from Bangladesh, TB was the second major cause of death in the age group of 15–49 years [19]. In the Global Burden of Disease (GBD) study, the largest proportion of TB deaths worldwide (37.4%) occurred in age group under 49 years, of which 84% was contributed by the 15–49 age group [20].

According to the results of the GBD study, the age-standardized mortality and incidence of TB in males is twice that in females [21]. The reason for this is not clear but may result from differential exposure to risk factors, effects of sex-specific factors on immunity and genetic factors. However in rural cohorts from India, the age at death in women was much lower (mean age at death of 32 years) [22] and the standardized mortality ratio in women was higher than in men [17]. Deaths occur predominantly in pulmonary TB (PTB); however, some forms of extra-pulmonary TB (EPTB) such as meningeal TB have a very high rate of mortality (27–60%) documented in reports from Africa [23], India [24,25], and Denmark [26]. While multi-drug resistance (MDR) is a risk factor, the majority of deaths in patients with TB occur in those with drug-susceptible tuberculosis (DSTB). According to the GBD study 2017 results, of the estimated 1.18 million TB deaths, 1.04 million (88%) occurred in patients with DSTB [27]. Thus deaths in patients with DSTB outnumber the estimated number of incident cases of MDR-TB. In India, in the year 2015, while the estimated number of TB deaths was 422,000 the total estimated incidence of MDR-TB was around 100,000 [28]; another indication that a large number of deaths occur in those with DSTB [29].

2.2. The place distribution of TB mortality or where are patients dying of tuberculosis?

In most of the high burden countries, there is no robust VRS, and/or the completeness and accuracy of the data is questionable [4]. In 2005, less than 10% of deaths in the world attributable to TB occurred in countries with a VRS; and in South-East Asia and Western Pacific, the figures were 0.1% and 2.6% respectively [5]. In India, 85% of TB deaths are not medically certified and possibly occur at home [30]. Some of this may have been patients with undiagnosed TB, while others might have been on medication for TB and were at risk of death, but were either not identified as such by the caregivers and treatment supporters; or experienced barriers in access to appropriate care. While the notification of TB cases has now been made mandatory in many high burden countries like India, there is a need to mandate notification of TB deaths. Standard 21 of the Standards of Care for Tuberculosis in India mentions that any TB death should be subjected to Death Audit by a competent authority, and this needs to be initiated as a process [31].

2.3. The time distribution of TB mortality or when do patients die due to tuberculosis?

There is a paucity of programmatic and community-based information regarding the timing of deaths due to TB and the available information is mostly from hospital-based studies, retrospective analysis or postmortem studies. Studies from both higher and lower burden TB and HIV settings suggest that a significant part of the mortality may occur in the first eight weeks of the intensive phase of treatment; and this period has been used to classify ‘early deaths due to tuberculosis’ [29,32]. In an autopsy based studyof TB among gold miners from Africa, deaths from TB occurred within the first two months of treatment in 90% and 85% of HIV negative and positive men respectively [33]. In India in a retrospective review of programmatic data, 65% of deaths occurred in the first two months of treatment [34]. Early deaths have been reported from Ethiopia, Sub-Saharan Africa and Brazil

Fig. 1. Delays leading to disability and death in patients with tuberculosis [85] Reproduced with permission for this figure.

[31,35,36]. Early deaths during TB treatment have also been reported in a series from England [37], Israel [16] and recently from Korea [15, 38]. In a region with a high prevalence of HIV, the risk was higher in the first week of treatment [39] and the first month of treatment [35]. It is clear from these limited studies that patients diagnosed with TB require close monitoring and effective clinical care in the first weeks of treatment in the clinic and programmatic settings if the risk of mortality is to be addressed@@. (Fig. 1)

2.4. The determinants of TB related death or why do patients die of tuberculosis?

The determinants of TB related death may vary according to the epidemiological setting with respect to the burden of TB, HIV, undernutrition, and resources within the health systems. The risk factors which have been identified in a review of 33 studies of TB mortality broadly differ according to the epidemiologic setting. [40]. It was found that in high-TB incidence and high HIV prevalence settings, age > 35 years, smear-negative disease, HIV infection and malnutrition are the major risk factors. In low TB incidence and HIV prevalence settings, the risk factors were age > 50 years, smear positive disease, non-infective comorbidities, alcoholism, homelessness and injection abuse [40]. The above conditions lead to a higher risk of mortality by either contributing to extensive TB disease and/or contributing to a serious co-morbidity. HIV co-infection increases the risk of mortality 3–8 fold [40], therefore assessment of HIV status has become a routine in all newly diagnosed patients with TB and early initiation of antiretroviral therapy is now recommended by the WHO. However, the most prevalent comorbidity in high TB burden but lower HIV prevalence countries like India is undernutrition [22,41]. Studies in India have shown that undernutrition is nearly universal in Indian patients, severe, potentially fatal (with BMI of as low as 10 kg/m^2 recorded), increasing the risk of TB by 2–4 folds [22]. It is consistent risk factor for TB mortality in all regions of the world, irrespective of HIV and drug susceptibility status [40]. Studies across regions have also shown that under-nutrition poses a significant risk for early death [15,36,42–44]. In a cohort study of patients with HIV infection, the incidence of mortality was nearly two fold higher in underweight patients (BMI < 18.5 kg/m^2) compared to those with normal BMI, after adjusting for antiretroviral therapy and CD4 count [45]. Body weight < 35 kg was a major risk factor for death in patients treated under DOTS in India and in Africa [34,35,46].

The WHO has recommended that nutritional assessment should be an integral aspect of TB care and moderate to severe undernutrition in patients with TB should be addressed [47]. Anemia as a result of micronutrient undernutrition (e.g. iron deficiency) or inflammation (anemia of inflammation) or both, is common in patients with TB [48], and is often severe. In the rural cohort from India, anemia was present in 75% of patients with PTB and was severe in a quarter [22]. Anemia could contribute to morbidity due to TB and also to TB mortality [49]. Hemoglobin measurement is not a part of the routine diagnostic workup in most national TB programs of LMICs and should be made a part of routine evaluation.

Apart from the risk factors which predict death, it is also important to understand the direct cause of death in patients with tuberculosis. There have been few autopsy studies of the direct causes of death in patients with TB, and these have been predominantly in HIV infected individuals [50,51]. The proximal causes of death have been examined in a few studies based on autopsies [33,35,52]. It emerges from these studies that the causes of early deaths may differ from those occurring later. Most of the early deaths in patients with TB with/without HIV infection are attributable to TB. Opportunistic infections like cryptococcosis, pneumocystis pneumonia contribute to death in those with HIV coinfection but occurred after two months in the majority of cases (in 89% in one such study [33]. These studies have reported the causes of death as the effects of extensive TB including acute respiratory failure and disseminated TB, bacterial co-infections, and other opportunistic infections (e.g. cytomegalovirus). Bacterial pneumonia and severe bacterial infections can coexist with active TB [51] and can contribute to mortality in both the early and later phases, and in both without/with HIV infection [33,35,52]. In a recent autopsy based study, nearly half of patients with TB had coexisting bacterial disease [51]. In a study from Malawi, the frequency of bacterial infections leading to acute deterioration in patients with PTB was equal in both HIV positive and negative individuals [29]. In a study on HIV negative patients with PTB from the Philippines, bacterial co-infections were associated with a 1.7 fold higher risk of early mortality [53]. The non-TB respiratory pathogens identified in this study where a significant number of patients had coexisting lung disease were H.Influenzae, S.Pneumoniae, and M.Catarrhalis. It is also relevant to note that a sepsis syndrome may occur in patients with active TB, which may result from co-existing bacterial infection or due to TB itself which has been described as M. Tuberculosis septic shock [54]. This sepsis syndrome is associated with increased lactate levels, features of bacterial translocation and features of multi-organ dysfunction [55]. Taken together, the clinical implication of these findings is that seriously ill hospitalized patients with PTB may benefit from the addition of broad-spectrum antimicrobial therapy to reduce mortality [40,51,53].

3. Integrated patient-centered care in tuberculosis: the blind spots in the current framework of clinical care of patients with TB

Tuberculosis is caused by an infection (often drug-resistant) which causes a disease that may be life-threatening and associated with serious infective and non-infective comorbidities, in persons who may face significant barriers in access to diagnosis, treatment and prevention. TB care in the past has been largely focused on treatment of the infection, gradually evolved over time, and now the recent guidelines emphasize

Table 1
Evolution of models of care in tuberculosis: Elements and challenges.

	Infection centered model	Disease centered care	Patient centered or person centered
Elements	Anti TB treatment by effective chemotherapy	Anti TB treatment with management of TB related morbidity (severe disease, complications) and management of TB related comorbidities (HIV, diabetes, undernutrition and substance misuse)	Anti TB treatment with management of TB morbidity, co-morbidities along with responsiveness to the needs and preferences of patient
Challenges	Drug sensitivity testing and availability of drugs for drug resistant TB	Inadequate clinical evaluation, inadequate clinical care. Treatment guidelines still do not address all comorbidities	Lack of support services, Community groups of persons with TB are still in infancy

TB—tuberculosis; HIV—Human immunodeficiency virus.

a patient centered approach. Table 1 discusses the evolution of TB care to illustrate the elements and challenges in each of these models that evolved, some of which persist even in the 'patient or patient-centered care'.

3.1. Infection centered model of care

An infection-centered model of care existed till the 1980s where patients were regarded as "cases" and treatment was self-administered "chemotherapy"[3]. There were gaps in this infection-centered model, as DRTB was either not recognized promptly, or not adequately addressed.

3.2. Disease centered model of care

Since the 1990s with the onset of the HIV epidemic, the coinfection was recognized as a risk factor for TB morbidity and mortality, and later diabetes and under-nutrition were added to this list. The clinical care model thus expanded to incorporate the treatment of selected co-morbidities. In this disease-centered model, the provision of HIV treatment took many years to become a reality but there are gaps in the management of coexisting diabetes, undernutrition and tobacco-related comorbidities which is a work in progress for most programs [56–58].

3.2 Patient-centered model of care

Finally in the END TB strategy, patient-centered care entered the lexicon of TB care [59]. It has been defined as "providing care that is respectful of, and responsive to, individual patient preferences, needs and values, and ensuring that patient values guide all clinical decisions" and in the context of the END TB strategy as "tuberculosis care and support that is sensitive and responsive to patients' educational, emotional, and material needs" [59]. A recent Lancet Commission report recommended high-quality services that are "person-centered" which was defined as "holistic, individualized, empowering and respectful, encouraging informed decision making and self-determination" [60]. However, these terms are more aspirational than operational in most national programs of high TB burden settings. In operational terms, patient-centered care has been defined as care that incorporates one or more treatment adherence interventions (patient education, communication, material support including food support, and psychological support) in conjunction with treatment administration options suitable for the patient [61].

In a disease that claims millions of young lives every year, one would expect a more comprehensive model of care to emerge, addressing the care of patients who are predominantly poor, undernourished and in distress. However, the current model of care is a fragmented one with the foundation of chemotherapy at its base to which has been added the management of selected co-morbidities (chiefly HIV and diabetes) and some treatment adherence interventions. Others like undernutrition and substance misuse remain largely inadequately addressed. The result is that this current model of TB care does not offer comprehensive clinical care which addresses the infection, the disease, all comorbidities and the personal needs of the patient that would be essential to reduce TB morbidity and mortality.

4. Components of comprehensive clinical care

This requires effective chemotherapy, management of TB morbidities (including management of severe disease and complications), and management of co-morbidities (infective, nutritional and non-infective).

4.1. Effective chemotherapy

Effective chemotherapy is the one that is appropriate to the drug susceptibility profile of the infecting organism. This has been a huge challenge for TB programs in past, as they have struggled to establish drug susceptibility testing facilities. Surveillance data on drug resistance is now available with 37 of the 40 high TB burden countries [1]. Drug susceptibility testing for rifampicin has expanded, but while 80% of the diagnosed patients had access to second-line drugs, only 25% of the estimated 558,000 patients with MDR-TB globally, had access to treatment which indicates a large global gap [1].

4.2. Appropriate management of TB morbidity

This primarily includes assessment of the severity of disease and complications and its management in patients with PTB and EPTB. In any potentially fatal disease, one of the primary decisions to be made by the care providers is whether the patient is seriously ill and requires referral to an appropriate level of care. This assessment of the severity of the illness and appropriate triage is essential to prevent mortality and may include tools based on clinical evaluation of vital signs, assessment of specific organ dysfunction with laboratory (or radiological) evaluation. Some of the examples of such tools are the quick Serial Organ Failure Assessment (qSOFA) score for triage of sepsis, the CURB-65 score triage of community-acquired pneumonia. However, the current international treatment guidelines for tuberculosis or the international standards of tuberculosis care lack any recommendation on the assessment of the severity of the illness and predictors of TB mortality [62,63]. As a result, in many high TB burden countries, a patient with pneumonia may receive a clinical evaluation and an X-ray, while the evaluation of a patient with TB may be limited to sputum based tests, without a mandated clinical evaluation or an X-ray which would reveal the extent of disease.

There have been attempts to develop and validate clinical prediction rules to predict mortality risk in TB in both high and low-income countries. In countries with better access to health care and lower TB incidence, the Tuberculosis Risk Assessment Tool (TReAT) [64], a TB prognosis score for in-patients [65], and a predictive fatality score [66] have been developed with reasonable predictive ability. However, these tools are not appropriate for LMICs with limited resources as they require estimation of arterial oxygen, albumin, and X-Rays. Moreover, they have been developed in admitted patients and intensive care unit (ICU) settings, which may not be generalizable to other situations.

In the LMICs, there has been a paucity of attempts to develop clinical prediction rules and severity assessment tools for patients with active TB. These have included variables like symptoms, vital signs, nutritional indicators like the BMI, mid-upper arm circumference (MUAC), anemia and the ability to perform activities of daily living. A TB-score based on five symptoms and six clinical signs was validated and was found to be useful in predicting unsuccessful treatment outcomes [67]. It included variables such as cough, chest pain, respiratory distress, night sweats, hemoptysis, anemia, BMI, MUAC, positive chest auscultation findings, pulse-rate, and temperature. Some of these may be difficult for a frontline healthcare worker to perform. A recent improvisation on this was TBscore II which included only the cough, dyspnea, chest pain, anemia and poor BMI or MUAC[68]. Serial values of the TB score II assessed in 2 LMICs, predicted treatment failure but did not predict death consistently[68]. A simple prognosis score has been proposed recently for validation, which includes 'Clinical form of TB, Age, BMI and HIV infection' (CABI) [69]. A triage tool proposed by the national TB program in India includes one or more of the following: (BMI $\leq$ 14 kg/m^2 or BMI $\leq$ 16 kg/m^2 with pedal edema, or MUAC $\leq$ 19 cm, signs of respiratory insufficiency (assessed clinically by

breathlessness or respiratory rate > 24/min or an oxygen saturation on pulse oximetry < 94%), and an inability to stand as features which indicate high risk and a need for admission [70]. This has not been validated independently although the inability to walk unaided, and a low BMI were independent predictors of mortality in a cohort of seriously ill HIV infected patients with suspected TB [71]. Tachycardia, tachypnea and inability to walk unaided are also danger signs suggested by WHO to identify seriously ill patients with HIV disease [72].

The rationale for the inclusion of the above parameters is that they can be assessed by the community-based health worker using simple skills and equipment. The BMI indicates the severity of under-nutrition, which is an independent risk factor for death. When the BMI falls below 13 kg/m^2 in males and below 11 kg/m^2 in females, it can be incompatible with life [73]. The degree of wasting revealed by the BMI is also a surrogate for the extent of the disease, as it correlates well with the severity of TB disease [74,75]. MUAC < 20 cm was associated with a mortality rate ratio of 3.61 (95%CI: 2.38, 5,47) in a study from Africa [76]. MUAC measurements that were sex-specific (females: 18.5 cm; males: 20.5 cm) predicted mortality in patients with TB in Philippines [12]. The physical activity performance status assessed by a modified Eastern Cooperative Oncology Group scale (0–4) has the potential to be a simple and reliable predictor of early death in patients with TB in the community as well as inpatient settings [65,76]. Scores of 3 (capability for limited self-care, spends >50% of time in chair/bed) and 4 (totally confined to chair/bed) on the performance scale were associated with a mortality of 33% and 51% and hazard ratios of 4.1 (95%CI: 1.4, 12.1) and 9.1 (95%CI: 3.7, 22.3) in a cohort from Africa [77]. Even a single point increase in physical activity performance status score was associated with a 2.3 fold (95%CI: 1.8, 3.0) increase in the hazard ratio of death [78].

Patients who show signs of severe disease need to be hospitalized and programmatic guidelines to outline indications for admission for patients with severe disease will be an important step in reducing TB mortality. At present, the number of beds available for patients with TB is low even in high TB burden countries like India, often citing the lack of facilities with appropriate infection control measures. According to estimates, India has approximately 50,000 beds for tuberculosis patients, i.e. 4 beds /100,000 population while annually there are about 187 new cases/100,000 and about 39 deaths/100,000 population [79].

4.3. Appropriate management of severe disease and complications

The complications of TB include respiratory failure, pneumothorax, massive hemoptysis, pleural effusion and empyema, sepsis syndrome and multi-organ dysfunction, and rarely adrenal insufficiency. In the presence of HIV co-infection, there could be other opportunistic infections including bloodstream infections. All these complications require admission into an inpatient facility with the ability to provide skilled care for severe disease and complications.

An additional factor of relevance in the treatment of the critically ill patient with TB is the altered pharmacokinetics of anti-TB drugs given as fixed-dose combination drugs (FDCs) through the enteral route. Subtherapeutic levels of rifampicin were found in more than half of 10 patients in ICU in a study from South Africa [80]. Moreover, there are alterations in pathophysiology during ICU admission with regard to the volume of drug distribution, increased metabolism due to higher hepatic and renal blood flow and low serum proteins. This leads to subtherapeutic drug levels when injectable drugs may be preferable [81].

Reports have indicated high levels of mortality in admitted patients with severe forms of TB, with figures ranging from 28% − 53% [82,83]. Many forms of EPTB are associated with life-threatening manifestations and/or complications. Abdominal tuberculosis (perforation, obstruction, bleeding), meningeal tuberculosis (hydrocephalus, stroke, seizures, altered mental state), pleural tuberculosis (pleural effusion, empyema, pneumothorax), tuberculosis of joints (joint effusion, cold abscess, ankylosis), tubercular pericarditis (pericardial constriction) require advanced investigations and skilled surgical care. If the number of hospital beds available for TB patients is sparse, ICU facilities and specialized surgical expertise is at a premium, the care available to such patients is likely to be compromised leading to increase mortality.

4.4. Appropriate management of comorbidities

HIV co-infection and diabetes are important co-morbidities and patients with TB undergo screening for both these co-morbidities. The collaborative framework between TB and HIV is in place in most high burden countries. TB in any clinical form is a WHO clinical stage 3 or 4 event which places the patient in the category of advanced HIV disease. Therefore, all such patients with HIV-TB co-infection should receive the care package as per the recent WHO guidelines [72]. This package includes screening and preventive interventions, rapid initiation of antiretroviral therapy and adherence support. However as mentioned earlier, the most prevalent, easy to assess and reversible co-morbidity is that of undernutrition and needs to be listed among comorbidities in the International Standards of Tuberculosis Care, which should be assessed and addressed [62]. Severe undernutrition in the patient with TB needs to be managed with a standardized protocol in a similar line of severe acute malnutrition (SAM) in children, with attention to cautious feeding, hydration, supplementation of electrolytes, and vitamins.

Although food support is mentioned in the current treatment guidelines of the WHO, it is not mentioned in the context of a co-morbidity that needs nutritional therapy but as an intervention which might improve adherence [47]. This is not appropriate in countries like India, where the median weights of adult males and females with TB are as low as 42 kg and 38 kg respectively, and median BMIs are as 16 kg/m^2 and 15 kg/m^2 respectively [22]. Patients with these levels of undernutrition are all eligible for nutritional support which should be considered an essential rather than optional part of treatment. The Government of India has announced a direct benefit transfer of INR 500 ($7.50) per month to enable purchase of nutritious food but the allocation is insufficient and is beset with operational challenges [84].

5. Addressing gaps in the health system to reduce TB mortality

Each death due to TB is a preventable tragedy. The health-seeking behavior of patients, compounded by deficiencies of the health systems and low-quality care are involved in the chain of causation leading to death of poor and young patients with TB in LMIC. This is illustrated in the following figure:

It has been suggested that a TB death should be accompanied by a mortality audit comprising of community-based death review (CBDR) as well as a facility-based medical audit (FBMA) in case the patient was admitted or discharged from a hospital [85]. While CBDR gives the perspectives of the family and identifies factors along the tuberculosis care cascade which may have contributed to the death, the FBMA probes the clinical care that the patient received in the hospital. Such a mortality audit helped health facilities in Malawi reduce their death rate from about 16% to about 3% [85]. TB deaths should be accorded the same importance as maternal deaths and should be accompanied by a mortality audit, which should address the delays in health care seeking, diagnosis, treatment and quality of care.

The health system in high TB burden settings needs to be configured to achieve reductions of TB mortality. A large proportion of TB mortality occurs in those who have not been diagnosed, and universal health coverage and the availability of point-of-care diagnostics in high burden settings are important interventions that can reduce TB mortality [1]. National TB programs should provide a comprehensive risk assessment at diagnosis, identify patients for intensified follow-up and provide clear criteria for admission and referral services to enable such care. Health facilities will require tools, guidelines and skills in the management of comorbidities like severe undernutrition, and availability of intensive medical and surgical care for a limited number of patients who require such interventions.

Box 1 describes the essential and desirable diagnostic tools and therapeutic modalities, which should be available at health facilities to deal with patients with tuberculosis who require admission for management.

Box 1
Essential and desirable diagnostic and therapeutic requirements for tuberculosis

Essential Diagnostics
- Chest radiography
- Anthropometric equipment: Weighing machine, stadiometer/ staturemeter, Mid-upper arm
- Pulse oximetry
- Complete blood count
- HIV testing and Blood sugar
- Renal function tests, Liver function tests
- Blood grouping

Essential Therapeutics
- Oxygen
- Broad spectrum antibiotics, including intravenous drugs
- Non-invasive ventilation for co-existing acute type 1 respiratory failure, chronic obstructive pulmonary disease exacerbations
- Hydrocortisone, vasopressor drugs
- Multivitamins and iron supplements
- Surgical expertise: Chest tube insertion for pneumothorax and empyema
- Blood transfusion facility
- Management of severe acute malnutrition:
- Oral potassium, oral rehydration solution including rehydration solution for malnutrition, enteral feeding with F-75 and F-100 formula feeds (can be made with milk or milk powder, sugar,vegetable oil)

Desirable Diagnostics
- Blood culture
- CB-NAAT
- Serum Cortisol
- Computed Tomography

Desirable therapeutics
- Facilities for invasive ventilation
- Surgical expertise: laparotomy, ventriculo-peritoneal shunt, spinal decompression, decortications surgery
- Bronchial artery embolism for control of massive hemoptysis

6. Conclusion

TB deaths are predictable and preventable. In the era of END TB strategy, comprehensive assessment and clinical care for patients should be implemented as a key component of patient-centered care and an important intervention for the reduction of TB mortality. In countries with a high burden of TB, the poor, the young, those with extensive pulmonary disease or serious forms of the disease, and with comorbidities like HIV and undernutrition are at higher risks of deaths due to TB. It should be closely supervised in the initial eight weeks of treatment when the majority of deaths due to TB occur. Assessment for predictors of death like BMI, MUAC, performance status and vital signs should become part of the routine evaluation of patients with TB and those with critical values should be admitted for inpatient care. Referrals for patients requiring inpatient care should be strengthened and paucity of hospital beds for TB patients should be addressed. Health facilities and the staff will need to be equipped with tools and skills to deliver comprehensive clinical care for patients with severe and complicated disease, and manage comorbidities with the recommended package of care for advanced HIV, diabetes, and severe undernutrition. There is also a need for research to develop and validate simple prognostic scores that can be used by field staff, and on developing comprehensive care packages for patients with TB and comorbidities.

Author statement

AB conceptualized the manuscript structure. Both AB and MB did the review of literature and generated the first draft, worked on the revising and editing the manuscript to give it a final shape.

Declaration of Competing Interest

None.

Acknowledgment

The comments of Dr Carl Britto on the manuscript are gratefully acknowledged as are the detailed and insightful comments of the anonymous reviewers which have enhanced the quality of this article.

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J Clin Tuberc Other Mycobact Dis 19 (2020) 100156

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Improving quality is necessary to building a TB-free world: Lancet Commission on Tuberculosis

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A B S T R A C T

The Lancet Commission on Tuberculosis (TB) set out to establish a roadmap for how high burden countries could get on track to meet the goals established by the UN High Level Meeting (UNHLM) in September 2018. The report sought to answer the question *"How should TB high-burden countries and their development partners target their future investments to ensure that ending TB is achieved?"* It provides a comprehensive analysis and specific recommendations to address this question and, ultimately, remove the barriers to building a TB-free World. Notably, the report highlights the importance of improving the quality of care as an essential component of ending the epidemic. Strategies for improving quality must be hard-wired into how National TB Programs are organized, to ensure greater equity in TB service provision and implementation of evidence-based practices and clinical guidelines. Investing in TB research and development, especially implementation, policy and programmatic research to determine how to deliver high quality care must also be high priority. In addition, improving the quality of TB programs is contingent on strategies that enhance accountability at all levels, from the level of Head of State to the local TB clinics. To this ends it is essential that TB survivors and their advocates have a voice to raise inconvenient truths and demand improvements in quality. The Commission concludes that the prospect of a TB-free world is a realistic objective that can be achieved with the right commitment of leadership and resources but will only be realized as and when quality of care is prioritized as a central tenet of all TB programs.

1. Introductions

In March 2019, the Lancet Commission on Tuberculosis [1] was published to provide a roadmap for how high burden countries and their donor partners could steer a path towards a TB-free world. Building on the momentum of the UN High Level Meeting (HLM) on Tuberculosis six months earlier, the Commission highlights the critical importance of *improving the quality* of TB care as essential to achieving the targets outlined at the HLM.

While most high TB burden countries have focused on expanding coverage of directly observed therapy, short course (DOTS) over the last quarter century, few have sought to evaluate or address the quality of TB care offered [2]. Nonetheless, increasing evidence highlights the importance of improving the *quality of* TB care at healthcare facilities [2–6]. High quality TB care is defined as care that is patient-centric, consistent with international standards and delivered in an accessible, timely, safe, effective and equitable manner [2]. To achieve the UN HLM targets, delivering high quality care must be a central focus across the health system, but especially at the facility level.

2. Reasons for poor quality care

There is substantial evidence that there are big gaps in TB care continua in many high burden countries, in both public and private sector [2,3], and in the management of both adults [7] and children [4] with TB (Fig. 1). Numerous studies have highlighted substantial gaps in the TB care continuum for all forms of TB cases: active disease, DR-TB, latent infection, and childhood TB [2–4,8,9]. Furthermore, simulated patient studies in three countries show that most primary care providers are unable to diagnose TB and referral linkages to the National TB Programme (NTP) are weak. In India, China and Kenya, only 28% to 45% of simulation patients were correctly managed by primary care providers [10–12].

In addition, research on the *process* of care demonstrate that TB patients often endure long diagnostic delays, with significant losses to follow-up in many high burden settings [13,14]. The care quality is especially poor for drug-resistant TB; less than one in five MDR-TB patients complete the cascade of care, globally [15]. Children are also at risk from low quality care; a recent study in Uganda and Kenya demonstrated that up to 80% of children fell out of the care continuum [4]. The consequences of low quality care are obvious: high care costs, treatment delays, increased drug resistance, morbidity, mortality and

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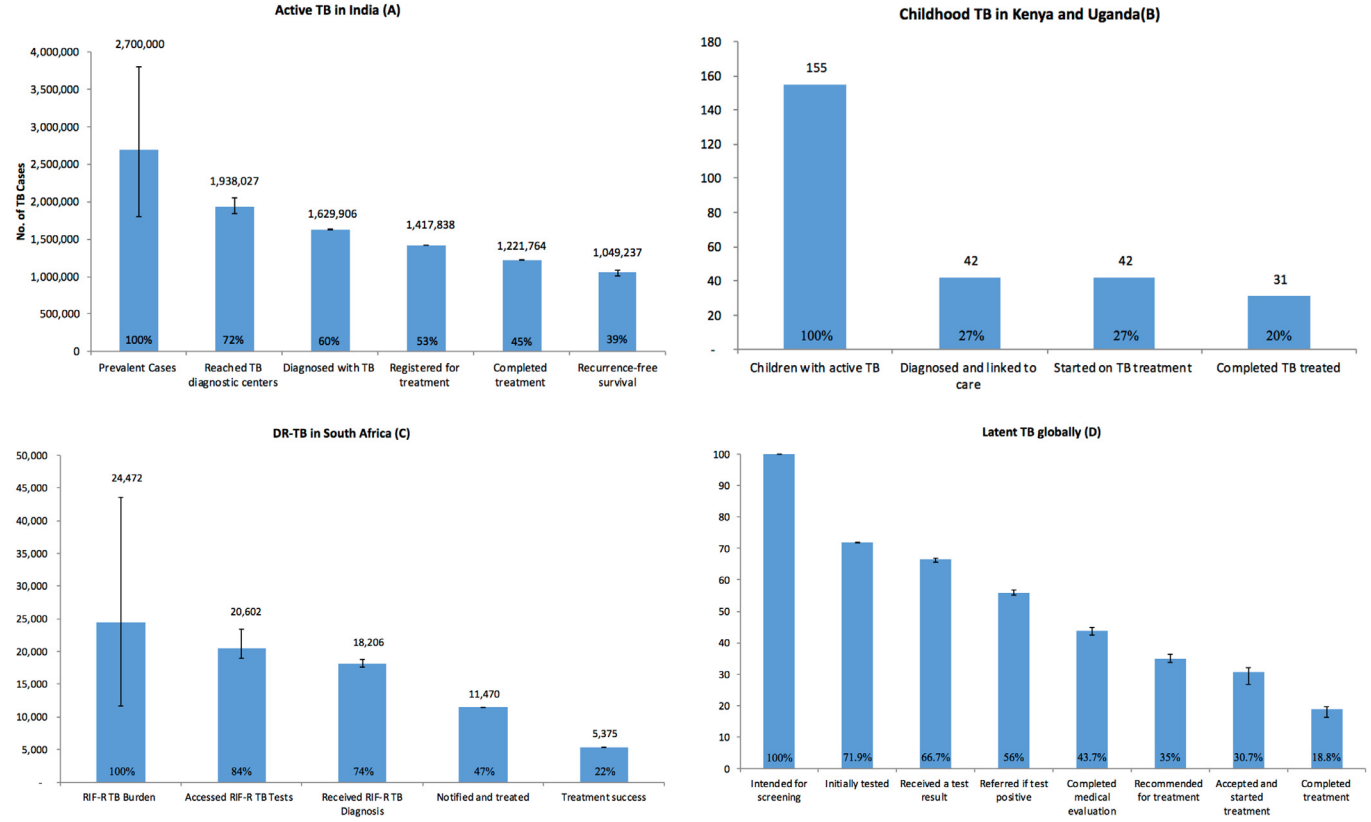
https://doi.org/10.1016/j.jctube.2020.100156



Source: (A) Subbaraman et al (2016) (B) Mwangwa (2017) (C) Naidoo et al (2017) (D) Alsdurf H et al, 2016 [this cascade includes data from 57 research studies evaluating TB

Fig. 1. TB cascades of care.
Source: (A) Subbaraman et al (2016) (B) Mwangwa (2017) (C) Naidoo et al (2017) (D) Alsdurf H et al, 2016 [this cascade includes data from 57 research studies evaluating TB

ongoing TB transmission [6].

Reasons for poor quality are numerous, and as Fig. 2 illustrates. More emphasis is needed to improve links between clinical and laboratory service delivery points and to strengthen the capacity of TB care providers throughout the health system. Enhanced integration at every level of the health system is necessary to ensure TB patients are promptly diagnosed and initiated on effective treatment. Furthermore, huge opportunities exist to improve quality when first-contact care for TB patients occurs outside of the TB system, in general clinics, dispensaries and in the informal setting. Systematic reviews of care costs [16], surveys on implementation of TB policies [17], and market analyses of access to new TB tools [18,19], WHO TB financing infrastructure and outcomes [20] also confirm that a primary driver of inferior quality is under-funding of national TB programs, and inadequate implementation of system-wide evidence-based policies. The public health implications, as well as the poor clinical and financial implications [21] for patients, are self-evident. Substantially reducing TB mortality and incidence will require significantly increasing both the coverage and the quality of TB services across the entire care continuum.

3. Improving quality: Integrating quality management into TB programs

In addition to greater investment in all aspects of TB programming is necessary, the Lancet Commission on TB argued that TB programs must start to systematically analyze gaps in their care cascades, especially at facility and district level, and work towards measuring and incorporating quality of care indicators into all aspects of TB care provision [2]. This can be achieved using a quality improvement (QI) framework which provides a proven, effective way to improve care for patients and improve practice of health care providers [22]. Applied to closing gaps in the care continuum, quality improvements principles can support greater equity, enhance TB-related health and socio-economic outcomes and ensure programs adhere to evidence-based practices and clinical guidelines. The use of QI tools and approaches can be applied not only to clinical care systems but also public health programs and be useful in reducing waste due to inefficiencies in poor service delivery, lack of coordination among health services, improper diagnosis of patients or delayed diagnosis. As has been demonstrated across HIV programs in sub Saharan Africa and Asia, QI also has the potential to optimize the use of limited resources available from governments and donor agencies, reducing poverty and actualizing social justice [23,24]. QI methodologies must be embedded, not just in NTPs but across the wider health system, and deployed as a catalyst to drive progress towards UHC in other health sector dimensions.

For TB programs to be strengthened by QI, it must ultimately be built into existing policies and infrastructure; it must become part of the fabric of care itself, not separated as a standalone initiative. WHO and international partners can play a vital role in advocating for use of QI and/or linking funding to quality performance measures. Demonstrable improvements in TB outcomes may also encourage greater investments in health systems by increasing donor, population and government confidence that resources are being well used [23].

Building the capacity of NTPs to improve the quality of TB services is essential to combating the TB epidemic. It has been an integral component of the HIV response in sub Saharan Africa [25] and has been recognized as a crucial component of strategic planning in President's Emergency Plan for AIDS Relief-supported countries [26,27]. Recent research in Uganda demonstrates the utility of this strategy to close

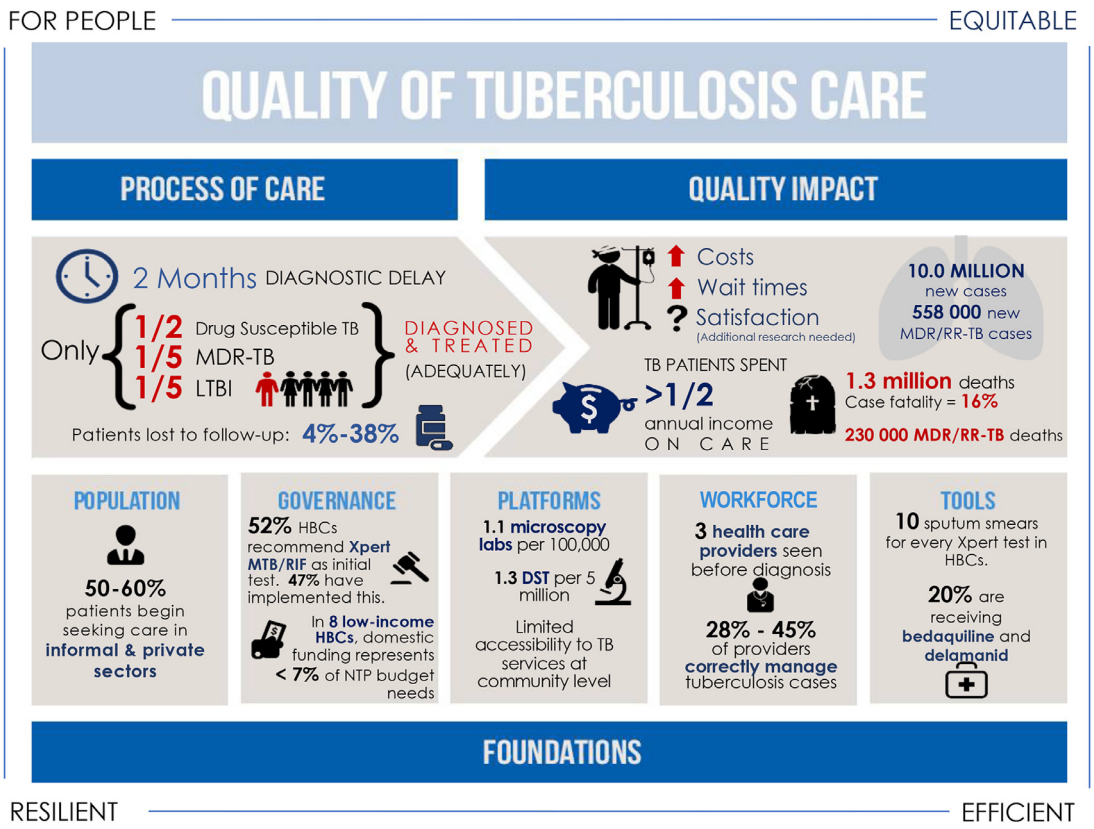


Fig. 2. Dimensions of quality of TB care, and barriers that undermine optimal service quality.
Notes: Data cited above listed by category: Populations: Chin, D et al, (2017). Governance: Out of Step, Stop TB Partnership (2017), Stop TB Partnership (2014). Platforms: WHO (2014); Huddart, S et al (2016). Providers: Sreeramareddy, C. T., (2014); Das, J (2015); Daniels, B (2017); Sylvia, S (2017). Tools: Cazabon, D (2017); Pai, M (2017). Processes of Care: Sreeramareddy, C. T (2009); Subbaraman, R., (2016); Naidoo, P (2017); Alsdurf, H (2016); MacPherson, P., (2014). Quality Impact: Tanimura, T (2014); Onyeonoro, U. U., (2015); Naidoo, P (2015). Health Outcomes: WHO (2018)

huge gaps in the care continuum, with only 33% of patients getting diagnosed and treated. To address these drop-outs during the cascade of TB care, Shete et al. evaluated the feasibility of a streamlined strategy called SIMPLE for improving TB diagnostic evaluation and treatment initiation among patients with presumed TB [28]. The SIMPLE strategy was developed using theory-informed design that accounted for predisposing, reinforcing and enabling factors, and sought to improve service quality while also improving efficient use of diagnostic resources. Despite this successful example, most NTPs do not have QI as an integral component. Nonetheless, some are starting to pilot QI programs in the public sector, notably South Africa [29]. QI programs have also been attempted in the public sector as implementation research projects [28], and included in private sector engagement projects in India with success [30,31]. In general, these QI pilots have tried to improve the cascade of care by addressing key gaps in healthcare facilities, some using a Plan Do Study Act (PDSA) cycle [32] to highlight where and how that quality of care can be improved.

4. Modeling impact of improving quality

What are the potential epidemiological implications of improving the quality of TB programs? Modelling analysis, commissioned for the Commission report, sheds light on the potential value of improving quality of care, as well as introducing high impact interventions to address country specific barriers to optimizing TB delivery in three archetypal countries: India (with a large private sector); Kenya (with HIV confection); and Moldova (with a high burden of MDR TB). As Fig. 3 illustrates optimizing the quality of TB programs, in addition to improving private sector engagement in India, access to antiretrovirals in Kenya and molecular diagnostics and second line drugs in Moldova, could have substantial impacts on TB mortality. Moreover, QI interventions would not be hugely expensive, particularly when weighed against the profound economic costs of failing to act.

5. Improving quality: Need for a research agenda

Making the case for incorporating QI methods to improve TB programs involves generating a body of evidence that documents the potential benefits. Establishing a research agenda for scaling up QI methods in TB programs is therefore essential. In particular, implementation research is needed to understand how to improve care cascades, i.e., find patients earlier, evaluate them quickly, and provide effective treatment resulting in a cure [33]. Moreover, research to assess whether differentiated strategies for providing patient-centered care and supporting treatment adherence must be a high priority and should occur in tandem with research strategies focused on improving the quality of TB services [34–36].

As the Commission report highlights, the economic rationale pursuing such strategies is compelling. The potential economic value is illustrated by modelling analysis in three different country-settings –India, Kenya and Moldova, illustrated in Fig. 3, leveraging an approach where the value of lives lost prematurely was derived using value of statistical life estimates [37–39]. The value of the loss associated with TB mortality is, on average, $32bn per year in India; $2.7bn in Kenya; and $35mn in Moldova. Weighed against these costs, the dividends of any investment in research to improve TB service quality are likely to be tremendous.

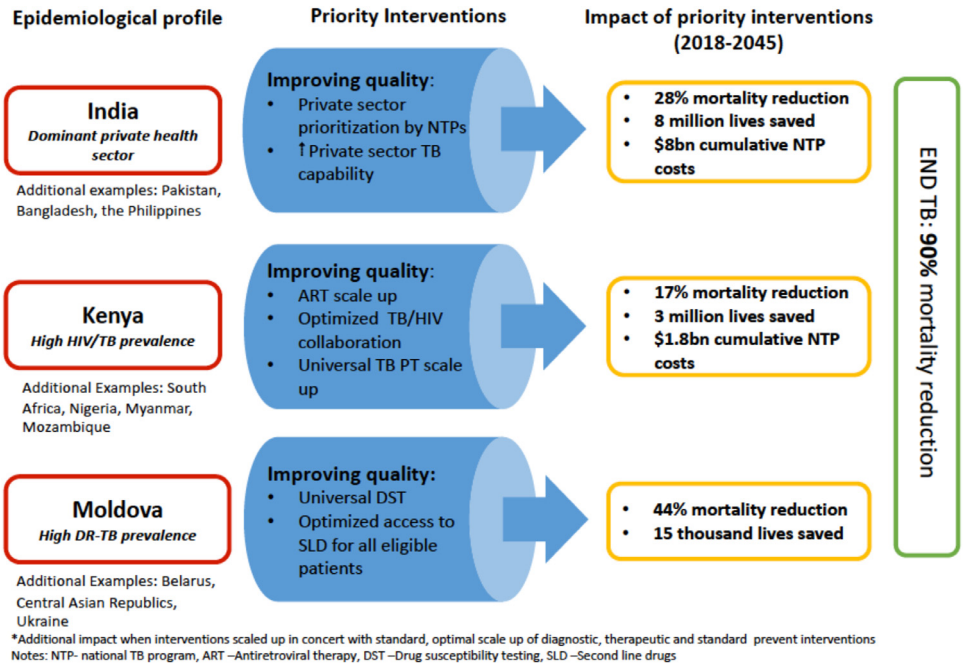


Fig. 3. Prioritizing policies to end TB, 2018–2045: Country case studies.

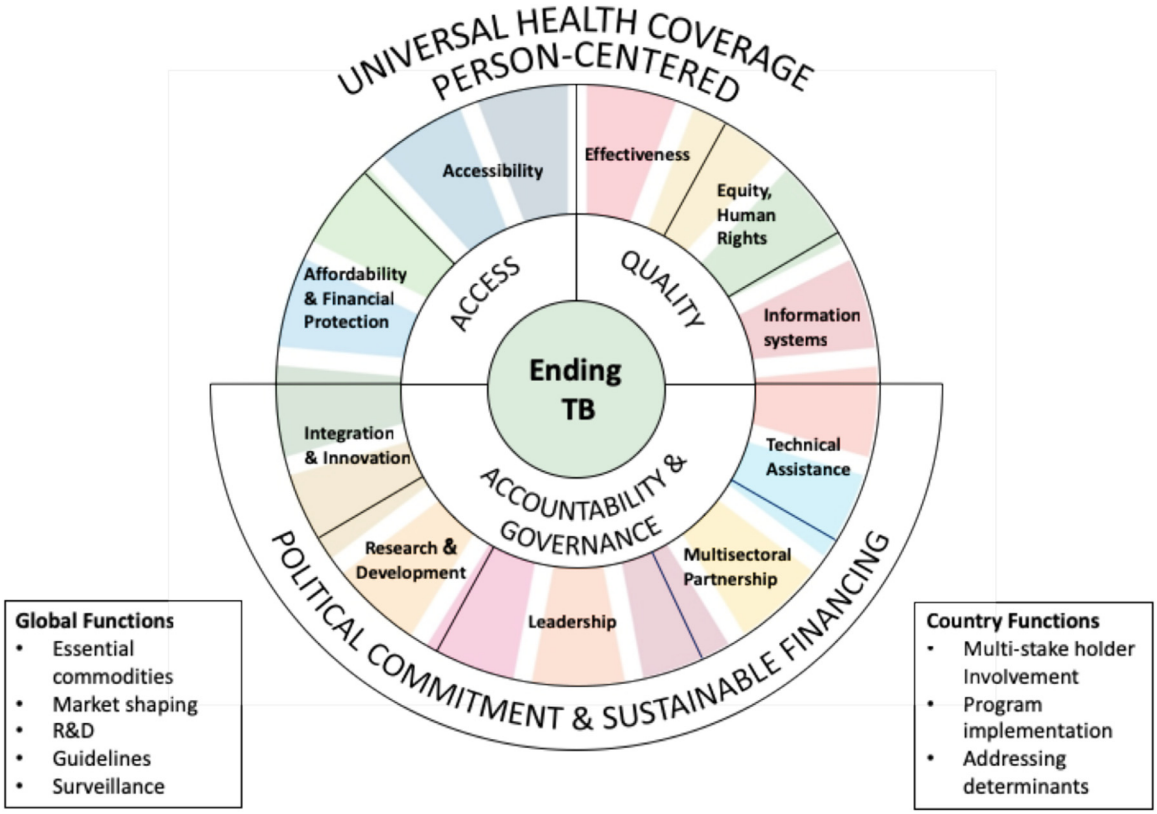


Fig. 4. Conceptual framework for ending TB, in the era of the sustainable development goals.

6. Next steps: Improving quality demands a multisectoral response

Fig. 4 provides a framework for operationalizing country-owned responses to drive progress towards ending TB and to leverage good practices in the TB response to advance other Sustainable Development Goals while ensuring that the quality of TB services is prioritized. This framework represents an idealized response and illustrates mutually reinforcing functions performed by state and global actors. These functions are person-centered, rights-based, and data-informed. The priority is ensuring high quality care for persons with TB who present followed closely by a focus on active case-finding strategies and TB prevention interventions targeted at high-risk groups. A strong TB response needs to be guided by country-owned, multisector and multi-

stakeholder coordination, accountability and good governance at all levels to achieve sustained long-term efforts. Civil society is a vital constituency to ensure that TB programs and stakeholders are held accountable at global, national and subnational levels. In addition, the framework underscores the importance of addressing TB as a core component in achieving Universal Health Coverage (UHC). While countries are in varying stages of progress towards UHC, for high TB burden countries, prioritizing investments in TB to realize UHC will be critical.

Effective leadership at the National Tuberculosis Program (NTP) level is a critical element of a successful and coordinated TB response. Empowering NTP managers to take the necessary steps to institute effective strategies will require increased financing and recognition that NTP leaders must play an inter-sectoral, convening role with stakeholders of other government ministries, including finance, justice, labor, social welfare, housing, mining, and agriculture. It will also demand multisectoral accountability to ensure that TB programs are of the highest quality.

As the Lancet Commission on TB highlights, an important lesson from HIV/AIDS response is that partnering with stakeholders from the civil society and the private sector is necessary to enable social accountability to demand high quality programs. Civil society dramatically changed the global response to HIV/AIDS, making it a top priority at all levels and driving improvements in quality and uptake of evidence-informed interventions [40,41]. TB survivors and their advocates can play an essential role in creating incentives for political leaders to advocate for improvements in the quality of TB programs, by generating public support for those decisions, and in holding leaders and service providers accountable for how resources, commitments, and services are delivered.

7. Summary

In summary, the institution of structured QI programs as an integral part of all TB programs, supported by clear metrics that take into account setting-specific contexts is an essential pre-requisite of ensuring patient-centered programming and realizing a path towards ending TB. Promoting communities of practice through QI learning networks can also have important spillover impact on other clinical programs. At a global level, WHO can promote improved quality through providing quality indicators for reporting and supporting delivery of QI-specific technical assistance. As the Lancet Commission highlights, many countries – even many low- and middle-income countries – have demonstrated that that it is achievable, despite the limitations of existing tools. The prospect of a TB-free world is not a distant aspiration. It is a realistic objective that can be achieved with the right combination leadership and resources aligned with laser-focus on delivering high quality TB programs.

Ethical statement

This review article does not include any primary data collection or research that warranted Institutional Review Board review

Declaration of Competing Interest

We have no conflict of interests.

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J Clin Tuberc Other Mycobact Dis 19 (2020) 100157

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

What quality of care means to tuberculosis survivors

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ARTICLE INFO

Keywords:
Tuberculosis
Patient-centric care
Quality of care
Accessibility
Availability

ABSTRACT

Quality of care for patients of TB suffers in India as well as in other countries, because the commonly accepted definitions of high quality care, rarely goes beyond correct diagnosis, treatment and adherence. The problem with the existing definitions and metrics of quality careis that they leave out patients, and when high quality care is defined without patients' perspectives, their needs and expectations are not addressed. Thispaper, based on a workshop held by TB survivors, attempts to examine the current state of quality of care extended to patients of TB, and to improve the scope of this care for the affected individuals, by the government, the healthcare system, and the society. The aim of the workshop and this paperis to arrive at a comprehensive, inclusive, and most importantly, a patient-centric definition of what quality of care looks like – to them.

1. Introduction

What quality of care looks like, depends on who is defining it. Healthcare must follow evidence-based guidelines, pose minimal risks and minimal delays for service users, and must be delivered equitably, regardless of factors like race, gender, geography, and socioeconomic status. It calls for healthcare that is people-centric, and takes into account the preferences and aspirations of individual service users and their communities [1].

However, analysis of user narratives reveals actual quality of care suffers in India as well as in other countries, because the commonly accepted definitions of high quality care, rarely goes beyond correct diagnosis, treatment and adherence. This is based on extensive interviews and documentation of cases of Tb affected individuals by the SATB team and reflect quality of care challenges across urban rural geographies, regional and gender variations as also socio-economic variations. The problem with all these definitions and metrics is that they leave out patients, and when high quality care is defined without patients' perspectives, their needs and expectations are not addressed. This is particularly true in India where these definitions are often developed by international agencies and experts and become the basis of discussions for quality.

When speaking of healthcare, it is a given that the patient is the consumer – then why is it that healthcare services do not include the perspective of the patients? This represents an ethical, systemic but also epistemological contradiction where affected communities lack the agency either to shape, own or negotiate quality metrics for them.

Patients understand high quality care better than anyone else. Foregrounding their experiences and perspectives puts patients back at the centre of care, which is only logical but also ethical since they experience healthcare first hand. In order forall stakeholders within the health system to understand and know what patients need, Survivors Against TB – a patient-led movement to strengthen India's fight against TB – convened a meeting with TB survivors to identify challenges and solutions to quality care, asking a simple question: *As patients, what do you need?*

2. Methodology

Through a comprehensive workshop held in Mumbai, we used a 360-degree approach to look at how quality care can be defined and implemented in a people-centric manner in both public and private sectors. The objective of conducting a workshop was to essentially employ generative learning, narrative and textual analysis so as to evolve a patient led definition of quality, make the existing definitions of quality of care in Tb, more inclusive and sensitive and define key metrics to measure quality as defined by patients.

The workshop included 20 TB survivors, a healthcare provider and community workers, to evolve what high quality care means from the point of view of patients.

A bottom-up, participatory research [2] method was applied, wherein patients/survivors of TB, and community workers, were familiarized with each other and the context – this was done by having a focus groupdiscussion [3] where all the participants were given the opportunity to substantiate where they came from and what influenced their experience and perception of quality of care as a TB-affected

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https://doi.org/10.1016/j.jctube.2020.100157

individual, or TB health professional in India. Focus group discussion is frequently used as a qualitative approach to gain an in-depth understanding of social issues. The method aims to obtain data from a purposely selected group of individuals rather than from a statistically representative sample of a broader population.

Verbal as well as non-verbal observations and interactions were duly noted down as field notes through the process of the workshop. Key socio-economic nuances such as gender, class, caste, etc. were taken into consideration while analysing responses as well as the final data.

We performed a content analysis of the interactions, field notes and other verbal and non- verbal interactions. Content analysis is a research tool used to determine the presence of certain words, themes, or concepts within some given qualitative data (i.e. text). Using content analysis, researchers can quantify and analyse the presence, meanings and relationships of such certain words, themes, or concepts.

The idea was to evolve a more comprehensive and thoughtful definition of quality of care, and this was what emerged.

2.1. What does quality care mean to patients?

Based on the focus group discussion, content analysis of participant responses, a definition was evolved through consensus. Participants defined high quality care for TB-affected patientsmeant care which is affordable, easily available and accessible – to begin with; care which is delivered efficiently in settings that are convenient and comfortable for patients, and provided in a dignified, empathetic and stigma-free manner.

TB-affected individuals stated that ideally, high quality care would be rooted in patients' economic, social and cultural realities, and would respond to patients' needs, including the need to address stigma and other mental health issues, while respecting their dignity and privacy.

Keeping these broad expectations in mind, we have found the following indicators of high quality care for TB patients:

High Quality Care is available, accessible and free. If a healthcare facility offers free tests or treatment but is located miles away, without convenient and affordable transportation, it is neither free nor high quality's affected in individuals and their familiesexperience hardships in procuring drugs, availing healthcare facilities, and paying for long-drawn treatment [4]. This was included as the role of family and caregivers, and they were seen as critical to facilitating access. If the quality of care is only high in terms of its effectiveness, and not so much with respect to its affordability, availability or accessibility, then that is not care to begin with.

High Quality Care is evidence based and best in class, involving access to the best diagnostics and drugs, and a transparent drug supply chain. Patients and survivors of TB demanded that they receive point-of-care accurate diagnostics that adhere to the relevant WHO guidelines [5], and necessitate drug-susceptibility testing. Patients must have access to the best quality medicines, regardless of whether they seek care in the public or the private sector. In other words, both sectors should offer equitable and fair access, pricing, and quality of drugs to all patients. An argument made by survivors about the need to include this in quality metrics is to ensure the best technologies and most suitable regimens where governments and private may use sub-optimal technologies or toxic drug regimens.

High Quality Care is efficient. A rather ignored aspect of quality care, is efficient timely and flexible care; TB affected individuals are also workers and often the only breadwinners in their homes. Efficiency may seem relatively simple though here it should also be viewed as the right of the consumer. A broader content analysis throws multiple issues from economic support to affordability and related poverty and debt. To that end, healthcare facilities should be open according to patients' work schedules, so as to not impede their employment chances. Tests must be available promptly, so that patients are not forced to continue taking medicines just because of delays in test results. More importantly, efficiencyshouldbe a core value in the conceptualisation and delivery of care.

High Quality Care must be transparent, and provide patients with information about their disease and the treatment. Respect for patients' autonomy is a cornerstone of high quality care. As patients, they deserve to know what their diagnosis means – what kind of TB they have and what drugs they are given, or not given, and why. TB survivors recounted their difficult experiences of having to spend a fortune on their treatment, a major part of which was unforeseen. So they demand that patients must be made aware of what the hidden costs of their treatment will be – care without this information is neither free nor transparent. They also need to know all the possible side-effects they can expect, and how they can manage them [6]. Patients should be provided with information as and when they ask for it, in easily accessible or visual formats, in their local languages. They need this to make informed, well-considered decisions about their health care.

Finally, every affected individual must have the freedom to choose where they seek care – they need to know what options they have for their treatment and heir drugs, and how they choose to pay for and access them. Based on content analysis we may conclude that this specifically refers the lack of patient agency and choice between the public and private sectors particularly in India.

High Quality Care must address the mental health of patients. Over the course of the workshop, it was discovered that most patients, regardless of their socio-economic or medical differences, had at some point of their treatment, felt like their mental health was ignored, disregarded or often treatment caused these issues [7]. Treatment providers need to be alert to side-effects that impact mental health of the TB patient, along with the psychological and emotional toll that the disease and treatment can have on them. Proper counselling and mental health support must be made mandatory across all sectors – public or privateas part of TB care [8].

High Quality Care must protect the patients' privacy. A patient's TB status should never be revealed to others, including other patients at healthcare facilities. Treatment providers ought to be mindful of how they may be inadvertently violating the privacy of their patients. Divulging a patient's TB status not only exposes them to unnecessary stigma and discrimination, but is also likely to create unwanted panic in the community. With an increase in online health information systems, protecting the health data of patients is critical [9].

High Quality Care is care with dignity. As a patient, one needs to feel reassured and respected during treatment. During the workshop, an overwhelming majority of patients claimed that they felt discouraged or dissuaded from asking their healthcare providers legitimate questions related to their treatment. This was based on extensive content analysis and recurring use of phrases. Patients must be made to feel comfortable asking their doctors questions and voicing their concerns, not just in general, but also about taboo topics like sex and menstruation. This was cited as a particular challengeby female members of the group. Healthcare settings need to be conducive to patients with diseases like TB, that are generally stigmatized, and these patients must be treated with respect and dignity by health workers. Care with dignity means care that is free of stigma. Patients cannot be stigmatized by the very people who are supposed to be caring for them, especially doctors and healthcare workers.

Other associated issues: An important aspect highlighted was the lack of agency or ability to give feedback to modify or improve the current paradigms of care and its associated behavioral practices. Another important issue was the lack of indigenous paradigms of quality –referring to most discussions dominated by international expert and agencies. The insufficient focus on punitive action for poor quality care, especially inadequate clinical practice, open discrimination and

2.2. So how can we achieve high quality of care?

While this is by no means a comprehensive set of solutions to achieve high quality care, here are suggestions developed by TB survivors themselves on what India can do to achieve high quality TB care for everyone.

Create new and more flexible forms of service delivery, increased private sector engagement in TB management and care, and more flexible timings to ensure improved access in the public sector.

Governments must invest in high quality diagnostics and powerful stakeholders must actively work on ensuring the availability of important drugs to avoid stock-outs –in both public and private sector.

More robust research and investment should go into drug development, so that patients can get newer, cheaper, and safer drugs, with shorter courses, and make them physically, socially, and financially accessible to the affected individuals.

Critically examine and address specific challenges that children affected by TB face, and then develop child friendly medicines and ensure their availability across India, in both private and public sector.

Create mandatory skill-building for the affected community and survivors, and continuous education program and refresher training using ICT for all health personnel in the public and private sectors on TB, on dealing with patients, their families, information on services available and necessary training on diagnostic and treatment guidelines, mental health, and stigma. Here, skill building is referring to reskilling for those unable to go back to work they were doing especially manual labour in the informal sector. An important aspect that is germane to high-quality care though has remained largely neglected in foundational work on quality. Every single member of the healthcare community must be aware of these fundamental aspects of disease and treatment, without which they cannot deliver high quality care to patients who need it most.

Build peer and mentor support networks to help provide patients with care that informs and educates them; here, patients will have access to a community that listens to them, has had similar experiences and can therefore act as each other's support system and sounding board, in addition to extending logistical or medical help based on their own personal experience. While the Indian government has begun initial efforts in this regard they remain unclear and need a proper community directed strategic focus for them.

These networks must be funded, formalized, strengthened and integrated with the rest of the healthcare system.

Create patient education and information programs in local languages which are rolled out as soon as a patient seeks diagnosis and care. This will allow them to be informed about what's to come, and they will not be forced to rely on someone else to understand their own disease and its treatment.

Expand and strengthen the 24 × 7 toll-free helpline that will actually providepatients with help and information. Texting options should be made available so that the helpline is accessible to individuals with hearing impairments as well.

The wider community will also need to be sensitized through information sessions at workplaces, schools, social and cultural gatherings, and targeted marketing on social media. In the absence of support from one's own community, patients may feel further isolated from the rest of the world, thus aggravating the stigma and mental health condition and making it harder for them to recover from the disease and its attendant problems.

Provide for legal punitive action against discrimination against TB patients in workplaces, families, healthcare settings and in communities.

Build the capacity of healthcare providers to provide realistic care that addresses issues of class, caste, gender especially marginalized gender identities. This remains a broader issue across the health system one that has been neglected up till now. Patients' social and economic identities often intermingle with their health, and the treatment that is then offered to them. Therefore it is crucial that healthcare professionals be aware of these nuances while dealing with patients from different socioeconomic backgrounds.

Create systems of feedback and information collection for government and private doctors, so as to ensure long-term accountability and continuous improvement, referring to the lack of agency or ability to give feedback to modify or improve the current paradigms of care and its associated behavioral practices.

These systems should be people-centric, and include patient interviews and reviews of doctors, for the reference and safety of other patients to protect their interests.

Ensure legal provision for paid leave and job assurances for TB patients; this should be a part of all workplace policies, public or private. While it is relatively unclear the form this can take as its both law and institutional practices-workplace policies were a clear pathway as was a non-discrimination policy.

For the huge percentage of Indians working in the informal sector, create economic support programs and provisions for skill-building, so that they can gain an income while undergoing treatment, as well as after the treatment is completed.

Create expanded mental health counselling services that are available and accessible to TB patients throughout the course of their treatment, to eliminate self-stigma and help with depression and other mental health issues that the patients may face or be predisposed to. Also train all healthcare staff in basic mental health awareness screening and stigma reduction so that they can support patients appropriately.

Ensure that TB helpline responders receive training in mental health issues, and the helpline is connected to peer support groups and suicide help lines.

Create robust systems that safeguard privacy in the public and private sectors. Ensure legal repercussions for privacy violations to deter healthcare providers from divulging personal information of patients.

Finally, never forget – the TB patient is the most important stakeholder in the fight against TB.

3. Conclusion

Discussions, definitions and metrics of quality, clearly need strong patient and community led inputs. A lack of such participative and sufficiently inclusive efforts would, from the perspective of patients, in quality definitions and programs that are neither owned, nor beneficial. In a more pragmatic and implementation sense, a lack of patient led definitions would result I creating programs that are top down and have an insufficient understanding of patient needs and ground realities.

This, in the long-term, would create poor quality care, and acerbate the health system and its consumers. It can also limit the autonomy of communities to intervene and engage with the health system and other key stakeholders. This together with increased investment in such programs would increase inequality and inequity.

A renewed discussion on high quality care led by survivors, patients and affected communities, presents a clear window of opportunity to redress power imbalances, improve quality of care and create a people focussed paradigm of high quality care that is currently missing in both the public and private sectors. This could be leveraged effectively by national programs in high burden countries like India as spring board to recasting approaches to TB care and addressing the epidemic in a more comprehensive, people—focussed and community centric way .For this, to happen, the conversation must be inclusive and also equal-paradigms that have remained missing in earlier conversations on TB care.

Ethical statement

Hereby, I, Chapal Mehra, consciously assure that for the manuscript WHAT QUALITY CARE MEANS TO US: SURVIVORS SPEAK, the following is fulfilled:

(1) This material is the authors' own original work, which has not been previously published elsewhere.

(2) The paper is not currently being considered for publication elsewhere.

(3) The paper reflects the authors' own research and analysis in a truthful and complete manner.

(4) The paper properly credits the meaningful contributions of co-authors and co-researchers.

(5) The results are appropriately placed in the context of prior and existing research.

(6) All sources used are properly disclosed (correct citation). Literally copying of text must be indicated as such by using quotation marks and giving proper reference.

(7) All authors have been personally and actively involved in substantial work leading to the paper, and will take public responsibility for its content.

Declaration of Competing Interest

None

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J Clin Tuberc Other Mycobact Dis 20 (2020) 100171

Contents lists available at ScienceDirect

J Clin Tuberc Other Mycobact Dis

journal homepage: www.elsevier.com/locate/jctube

Quality of tuberculosis care in the private health sector☆

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ARTICLE INFO

Keywords:
Public-private mix
Quality care

ABSTRACT

As countries move towards achieving universal health coverage, efforts to engage all care providers have gained more significance. Over a third of people estimated to have developed TB in 2018 were not detected and notified by national TB programs (NTPs). This gap is more pronounced in countries with large private sectors, especially those with a high burden of TB. Health care providers outside the scope of NTPs, including the private and informal sector, are often the first point of care for TB patients. However, these providers are not fully engaged despite evidence from country experiences and projects that demonstrate increased detection and good treatment outcomes through publicprivate mix (PPM) approaches. While there are often concerns about quality of care in public facilities, there is also increasing evidence that quality of TB care in the private sector falls short of international standards in many places and urgently needs improvement. Failure to engage the full range of health care providers for TB has serious consequences in terms of access to quality care, resulting in increased transmission as a result of delayed diagnosis and treatment; excess mortality and morbidity as a result of inappropriate treatment; and increased drug resistance as a result of incomplete treatment. Recent attention to this issue has led to significant increases in private TB notifications, especially in India, Indonesia and the Philippines, but the gap between notification and the extension of quality program services for provision of treatment and care appears to be growing.

1. Private healthcare utilization and TB in low- and middle-income countries

There is extensive literature on private healthcare in low- and middle-income countries [1,2]. In most low- and middle-income countries, private providers are an important source of healthcare for all socio-economic strata: typically, the less-poor tend to make more use of formal and qualified providers, while the poor often turn first to informal and unqualified providers. Private providers often account for 50–70% of care, especially outpatient primary care and especially in urban areas (Table 1).

The provider types listed last (informal providers, drug shops, independent qualified providers) in Table 2 are both far more numerous and more important for early care-seeking, especially for lower-income populations, and therefore for interruption of transmission. They are also more difficult to engage because of their large numbers, the relatively low case yield per provider, low administrative capacities, and the fact that in many cases they operate on the borders of legality. In contrast, specialists and hospitals are fewer in number, are easier to engage, can take on more complex tasks and may often have relatively high case-loads, but they also tend to serve high socio-economic groups and are unlikely to be the first providers consulted.

Globally, WHO estimates that 3 million of the 10 million people who fell ill with TB in 2018 were “missed”, i.e. were not detected and notified by government programmes [3]. Three countries – India, Indonesia and Nigeria – account for 46% of all missing people with TB, while a further 7 countries accounted for a further 34%. The absolute number of missing people with TB is determined by population size, TB incidence and the treatment coverage rate. The treatment coverage rate (which also influences TB incidence) is itself determined by the strength of the public programme, the size of the private healthcare market, and the quality of the TB program’s engagement with private providers.

While some people with TB are asymptomatic and delay seeking care, most of the missing people with TB are thought to seek some kind of treatment from public or private healthcare providers, including those that do not fall under the purview of national TB programmes. There is some considerable degree of under-reporting of publicly-managed cases (particularly in public hospitals, which often fall under another section of the Ministry of Health that is administratively distant from the NTP), and there are many missed diagnostic opportunities in

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https://doi.org/10.1016/j.jctube.2020.100171

Table 1
Percent of population that used private sources of care for childhood diarrhea, cough and/or fever, 2000–2011.[1]

Region	Total	Poorest 20%	Least poor 20%
South-east Asia	66%	63%	81%
South Asia	79%	80%	85%
Sub-Saharan Africa	51%	52%	52%
Latin America, Caribbean	34%	23%	61%

[1] UCSF analysis of data from Demographic and Health Surveys 2000–2011. Population-weighted averages of respondents with children under 5 who sought care within prior two weeks for diarrhea and fever/cough. Survey data from 40 countries: http://www.ps4h.org/globalhealthdata.html.

routine consultations in both public and private facilities. But in many high-burden countries the majority of the missing people with TB are likely to seek treatment from private providers at one or more points in their care seeking – and this private provider role is particularly critical in the countries at the very top of the high burden list.

As Table 3 indicates, dominant and largely unregulated private health sectors are characteristic of seven of the top 10 countries ranked by TB incidence (the exceptions being China, South Africa and Democratic Republic of the Congo). In these seven countries, home to 57% of global TB incidence and over 62% of missing cases:

- Private providers are the destination for an average of 75% (range: 67–84%) of initial care-seeking;
- Private expenditure represents 61–74% of total expenditure on health;
- Private markets deliver 15–54% of total anti-TB drugs;
- Yet private for-profit notifications represent just an average of 23% (range: 12–28%) of total notifications and 16% (range: 3–21%) of estimated incidence.

Whereas DHS and TB prevalence surveys provide data on the role of un-engaged private providers in initial consultations, data on their role in TB treatment is scarce. In recent years, attempts have been made to analyze data on private sector sales of anti-TB drugs in 10 high-burden countries for which such data are available (Table 5) [12,13]. There are considerable methodological challenges in converting sales units to number of patients who were, or could be, treated. Data suggest that private TB drug sales represent more than half of all TB drugs distributed in India and Indonesia, and between one third and one half in the Philippines and Pakistan. The private TB drug sales in India alone represent more than 60% of total private TB drug sales in these 10 countries. Private retail channels are relevant but less important in China, Bangladesh, Thailand, and Vietnam (with a large decrease in private sector volume in Bangladesh from 2003 to 8) [12]. Private retail sales seem to be of little significance in South Africa and in Brazil, which was not included in the analysis and is an exception in that private TB drug sales are effectively prohibited by the regulatory authorities. TB drug sales data are not yet available for Nigeria, where a TB prevalence survey found 20% of cases were being treated in the private sector [14], or Myanmar, where a prevalence survey found 22% private treatment[1], down from 38% in 2009 [15].

The data on missing people with TB and private TB drug sales suggest that a failure to effectively engage private providers may not be the main constraint to TB care in some countries, notably South Africa, China, Ethiopia and Zambia. Ethiopia and Zambia have dominant public sector health systems, although Ethiopia's private sector is growing along with urbanization. South Africa has a polarized health system in which a strong private sector serves a minority and the majority of the population is served by a strong public health infrastructure; the principal challenge for the TB program is to reduce delays and losses within the public system. China is a special case: it has made considerable progress in reducing the burdens of TB, with publicly-owned hospitals that act like private providers.

2. What do we know about quality of care in the private sector?

While there are often concerns about quality of care in public facilities, there is also increasing evidence that quality of TB care in the private sector falls short of international standards in many places and urgently needs improvement [4]. The evidence comes from systematic reviews on the quality of TB care or surrogates of quality (e.g. TB diagnostic delays) [5], analyses of TB patient pathways and care cascades [6], and newer simulated patient studies that directly measure quality of TB care [7]. Specific issues identified include:

- Low rates of TB testing by private providers, even when patients present with typical TB symptoms;
- Low rates of referral to the national TB programme, even when patients present with typical TB symptoms;

Table 2
Types of private providers.

Private provider type	Examples	Comments
Specialists (pulmonologists, chest physicians)	450 in Bangladesh; PDPI (Indonesia Pulmonologists' Society) in Indonesia	Very high case load but usually late in patient pathway and higher income; often challenge national protocols; key opinion leaders
High-end corporate hospitals	500 in India (eg. Fortis, Care, etc.) Private medical colleges: 67 in Bangladesh 1–2 in major cities of smaller lower-income countries	Often reluctant to address TB because of stigma and image Serve higher socio-economic groups Pathology, imaging, administrative capacity
Mid-size hospitals	~ 30 k nursing homes in India	Access in secondary cities and major towns
Laboratories	9 k in Bangladesh; 30 k in India (including 5 large networks)	Increasingly organized in networks
Pharmacies	25 k Indonesia; 8,200 in Kenya	Mainly in urban areas Chains emerging in some countries
Independent qualified GPs	60 k Bangladesh; 97 k Pakistan; 8 k Myanmar; ~70 k Indonesia	Still mainly fragmented Represented by medical associations
Drug shops	200 k in Bangladesh; 10 k ADDO[1] in Tanzania; 40 k-200 k PPMV[2] in Nigeria	Often regulatory controversy about what they can and can't sell. May provide consultations.
Independent less-than-fully-qualified practitioners	300 k in Pakistan; 3–4 unqualified providers per village (77% of all providers) in India	Often first point of care, especially in rural areas Often controversial Considerable overlap with the category of drug shops

[1] Accredited Drug Dispensing Outlets.
[2] Patent and Proprietary Medicine Vendors.

[1] N. Yamada, personal communication, 31/5/19

Table 3
Basic data on TB, private providers and health finance, 10 countries with highest TB incidence, 2018.

Country	TB Burden					Notifications from for-profit providers			Private provider share			Health finance
	Population (millions)	Incidence rate per 100,000	Incidence (thousands)	Treatment coverage	Missing patients (thousands)	MDR cases (thousands)	Number per year	No. per 100 k population	% of estimate incidence	% of TB notifications	Initial care-seeking	TB Treatment		Private % of total health expenditure (2017)
												Prevalence Survey	Private TB drug sales	
India	1,350	199	2,690	74%	696	130	542,233	40	20%	25%	74%	46%	54%	72%
China	1,430	61	866	92%	71	66								43%
Indonesia	268	316	845	67%	281	24	101,839	38	12%	18%	74%	46%	51%	51%
Philippines	107	554	591	63%	219	18	94,163	88	16%	25%	70%	21%	43%	65%
Pakistan	212	265	562	64%	202	28	86,402	41	15%	23%	85%		45%	67%
Nigeria	196	219	429	24%	325	21	12,625	6	3%	12%	67%	22%		78%
Bangladesh	161	221	357	75%	90	6	74,524	46	21%	28%	84%	30%		77%
S. Africa	58	520	301	76%	73	11							15%	44%
DRC	84	321	270	63%	100	6					43%			48%
Myanmar	54	338	181	76%	43	11	19,242	36	11%	14%	78%	21%		76%

Sources: WHO Global TB Report (2019) except: private for-profit notifications from each NTP; % of initial care-seeking from DHS surveys and TB prevalence surveys; 2017 private health expenditure from WHO Global Health Expenditure Database; private drug sales data from Malhotra (2018).

- Private providers prefer to empirically manage with antibiotics and order tests later, resulting in multiple rounds of broad-spectrum antibiotics and other non-specific therapies, multiple patient visits and providers seen, and diagnostic delays;
- Chest x-rays are the preferred tests for TB; sputum tests such as smear microscopy or GeneXpert or cultures are rarely used; Xpert is also not widely available in the private sector at subsidized rates as in the public sector;
- Use of drug susceptibility testing (DST) in the private sector is very low, even among patients with history of anti-TB therapy;
- What providers know and what they do in practice are often very different ('know-do gap');
- Limited capacity to support patients with adherence and treatment completion;
- High costs of care, with 50% of the total costs incurred before TB is diagnosed [8].

There is very wide variation in the quality of TB-related care amongst private providers, and some of it of course is very good. It should also be acknowledged that practices common amongst private providers have sometimes become more accepted by public programmes, such as chest radiography as a screening tool or, daily regimens with fixed dose combinations.

Table 4, below, shows the proportion of 'correct management'[2] of simulated patients with classic TB symptoms by private (non-NTP) providers in three countries, using the same standardized patient cases.

3. Published evidence of effectiveness of private provider engagement

Published literature on public-private mix for TB has increased considerably over the last few years, but it remains dominated by evidence from India.

Evidence on the effectiveness of PPM was strengthened by three studies in 2006:

- A review of small pilot projects in India found that 27% of new smear-positive patients were attributable to private practitioners in 7 projects, while outcomes for privately-treated patients in 12 projects exceeded the program target of 85% treatment success; the projects were all small [16].
- A review of data from 15 public-private mix projects in 8 countries found a treatment success rate of 89.6% for new smear positive cases and an increase in case detection of between 10% and 36% over periods ranging from 9 months to 3 years [17].
- An economic analysis compared costs and cost-effectiveness of two pilot PPM projects in India with public sector DOTS and non-DOTS treatment in the private sector. The average cost-effectiveness of PPM DOTS and public sector DOTS was similar and roughly half that of non-DOTS private treatment [18].

In 2011, a systematic assessment of public-private mix for TB control identified 45 studies documenting 22 projects in 12 countries. The authors concluded: "*PPM has improved case detection and treatment outcomes among patients seeking care with private providers. Evidence on reducing patient costs is inconclusive, and there is scope for increasing equity in access to care by systematically engaging those providers who are the primary agents for poor people seeking health care.*" [19] A systematic

[2] For patients with symptoms indicating presumptive TB, correct management included recommendation of sputum testing or chest radiograph or referral to a public TB service center; for patients with evidence of microbiologically confirmed TB, referral or initiation of treatment with a standard, four-drug, first-line therapy; for suspicion of drug resistance, referral or recommendation of drug susceptibility test.

Table 4
Proportion of patients with TB symptoms who are correctly managed or referred by private providers, according to Standardized Patient studies.

Location	% Correctly managed	% Referred	Reference
Mumbai, India	37%	15%	Kwan et al. [9]
Patna, India	33%	10%	
Nairobi, Kenya	33%, private for-profit 40%, private FBO	4%, for profit 10%, FBO	Daniels et al. [7]
3 provinces in China – village and township clinics	28%, village clinics 38%, township clinics	28%, village clinics 18%, township clinics	Sylvia et al. [10]
1 province in South Africa	35%	26%	Boffa et al. [11]

Table 5
Estimates of annual first line treatment course-equivalents sold through non-NTP channels and the percent of total market (private sales plus NTP notifications) that they represent.

Source	Wells et al. [12]		Malhotra et al. [25]	
Country	2008		2015	
India	2,320,110	64%	2,069,667	54%
Indonesia	498,487	63%	347,244	51%
Pakistan	265,850	52%	272,135	45%
S. Africa	14,310	4%	52,978*	15%
Bangladesh	25,200	14%	n/a	n/a
China	299,230	23%	n/a	n/a
Thailand	15,640	22%	12,507	15%
Philippines	221,220	61%	217,925	43%
Vietnam	12,250	11%	11,266	10%
Russia	19,630	13%	72,556	36%

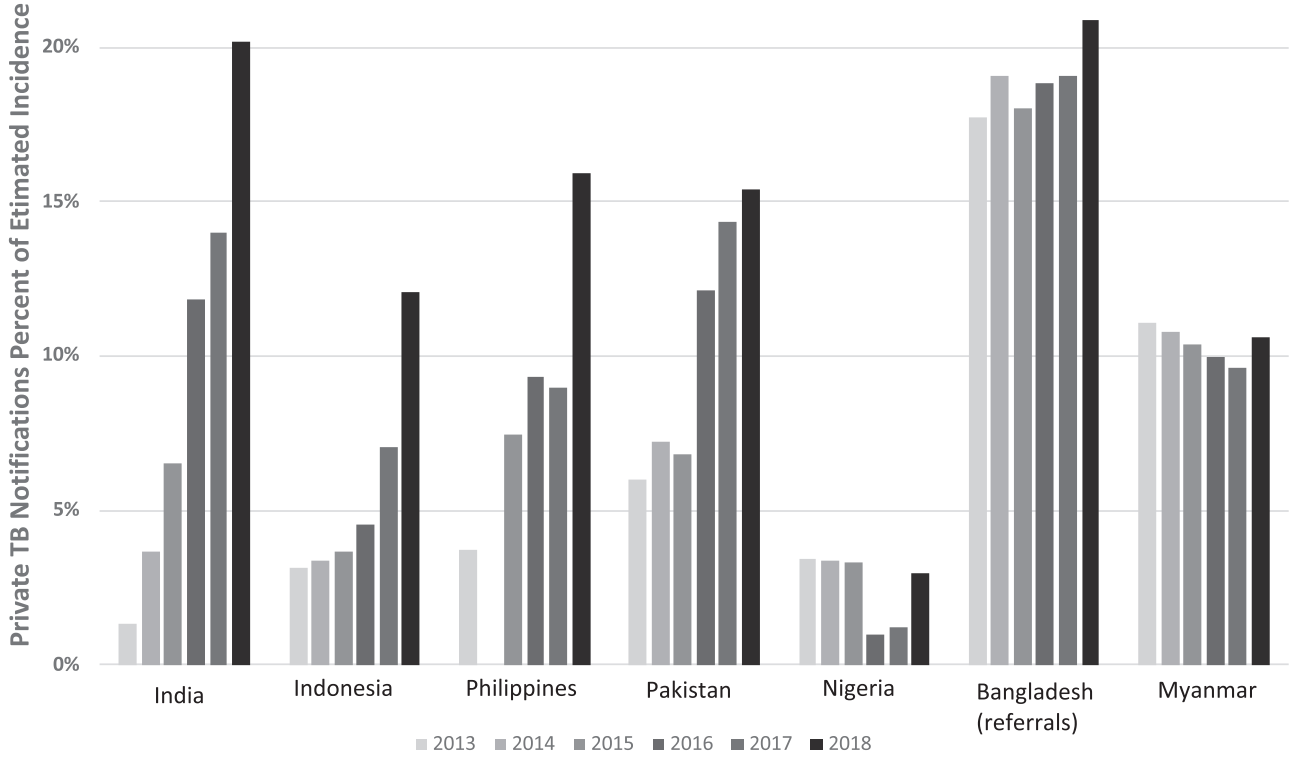
*Estimate excludes INH because of the large volumes believed to be used in preventive therapy.

review of literature published through May 2014 included 78 studies of 48 programs in 16 countries [20].

More recent articles have focused on the need to go beyond donor-funded pilot projects scale up systematic engagement of private providers and integrate such activities into the core operating model of national TB programs [21]. A modelling analysis published in 2019 suggested that scaling up private provider engagement for TB in India, through subsidized diagnostics and adherence support, could avert 28% of deaths between 2018 and 2045 [22]. The 2019 Lancet Commission on Tuberculosis highlighted the need to engage private providers: "*Given the dominance of private health care in countries with the largest share of missing patients with tuberculosis, private providers must be engaged to provide high-quality, person-centered care on a scale equal to their role in primary care to meet national and global goals*" [23].

4. Recent progress and challenges

Between 2015 and 2018, four of the highest burden countries with



[9] Author analysis of NTP data, distinguishing notifications from for-profit providers from those of the non-profit sector to the extent possible.

Fig. 1. TB notifications from private for-profit providers as a proportion of estimated TB incidence, 2013–2018, in selected high-burden countries with dominant private healthcare sectors Author analysis of NTP data, distinguishing notifications from for-profit providers from those of the non-profit sector to the extent possible.

dominant private healthcare sectors (India, Indonesia, Philippines and Pakistan) increased their annual private TB notifications by more than half a million, to 911,786. In Bangladesh over the same period, referrals from private for-profit providers increased by just 20%, while in Nigeria they fell slightly from a very low level and in Myanmar they have fallen steadily from a higher level. For the 7 countries as a whole, the proportion of total notifications contributed by private providers increased from 13% to 23%, while as a proportion of estimated incidence they increased from 7% to 16% (Fig. 1).

However, the recent increase in notifications may be driven by global targets and commitments made recently at the UN High Level Meeting on TB and as part of initiatives such as the WHO Director General flagship initiative Find.Treat.All.EndTB (with the Global Fund and Stop TB), the Global Fund Strategic Initiative to reduce the number of "missing" TB patients and initiatives by the US Agency for International Development in countries.

These increases in notifications, while a positive step towards closing gaps in care, are often not bacteriologically confirmed, may not always indicate an increase in quality service provision and do not provide information on treatment outcomes for the patients notified. These challenges need to be addressed. For instance, from 2017 to 2018:

- In India, only 16% of all private notifications in 2018 were bacteriologically confirmed, 4% received program drugs, 6% got DST and 15% received at least one of three nutritional support payments[3]
- In the Philippines, 90% of the increased private notifications were generated through a "mandatory notification" app that provides no data on bacteriological confirmation, adherence or outcomes.[4]
- In Indonesia, 71% of the increase on private notifications came from "mopping up", in which they searched hospital records for additional closed cases that hadn't been reported before, and only 41% of all private cases had any outcome reported.[5]

These trends reinforce the need to ensure quality of TB care amongst private healthcare providers, to improve the validity of data systems, and to hold countries and programmes accountable for indicators of effective coverage.

5. A Roadmap for engaging private providers to improve quality of TB care

Experience with a very wide range of formal and informal providers and facilities in widely varying health systems contexts suggests that it is possible to engage all providers in productive and effective partnerships that enhance TB prevention and care. Constraints are many, and mostly common across contexts, but they can all be overcome with sufficient commitment and investment. Public-Private Mix approaches can be a pathway to ensure quality monitoring and collaboration to ensure TB patients access quality care, wherever they seek it along the care pathway.

In 2018, WHO, the Public-Private Mix Working Group of the Stop TB Partnership, and global partners released a "Roadmap" to guide the scale-up private provider engagement in efforts to end TB [24]. The Roadmap recommends ten actions at national and global levels to scale up the engagement of all care providers towards universal access to care:

(i) Build understanding about patient preferences, private sector dynamics and the rationale for engaging all providers;
(ii) Establish a supportive policy and regulatory framework;
(iii) Set appropriately ambitious targets for Public-Private Mix;
(iv) Adapt flexible models of engagement applicable to local contexts;
(v) Advocate for political commitment, action and investment in PPM;
(vi) Harness the power of digital technologies;
(vii) Allocate adequate funding for engaging all providers, including by capitalizing on financing reforms for universal health coverage;
(viii) Deliver a range of financial and non-financial incentives and enablers;
(ix) Partner and build the capacity of intermediaries and key stakeholders; and
(x) Monitor progress and build accountability.

6. Conclusion

As countries race ahead to close gaps in care and reach targets, the engagement of private providers on a scale commensurate with their importance will be critical. However, it is imperative that quality considerations both for diagnosis and care provision are enforced. New partnerships, modern data systems, new payment mechanisms, new skills, and different attitudes will need to be harnessed even more to facilitate this, and to ensure that patients access quality care wherever they seek it. This is the true measure of universal health coverage.

Acknowledgements

This article draws heavily on two documents published by the World Health Organization and partners in October 2018: "*Engaging private healthcare providers in TB care and prevention: a landscape analysis*" (material from which was included in the final report of the 2019 Lancet Commission on Tuberculosis) and "*Public-private mix for TB prevention and care: a roadmap*".

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Contents lists available at ScienceDirect

Journal of Clinical Tuberculosis and Other Mycobacterial Diseases

journal homepage: www.elsevier.com/locate/jctube

Improving the quality of tuberculosis care in the post-pandemic world

In 2019, recognizing the importance of quality in TB care, the *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases*, launched a series on this topic [1]. The series included 19 published papers [2–20], and covered a diverse range of topics. The entire series is open access and available at: https://www.sciencedirect.com/journal/journal-of-clinical-tuberculosis-and-other-mycobacterial-diseases/special-issue/10JL8LN0VVT.

In this concluding article, we cover the key messages from papers in the series. We also outline some strategies for improving quality of TB care. Given the Covid-19 pandemic and its negative impact on TB services, the topic of quality of TB care has become even more pertinent.

1. Impact of Covid-19 pandemic on TB services

Progress in TB control was stalling, even before the Covid-19 pandemic. The 2020 Global TB report shows little change since the previous year [21]. Nearly 1.4 million people died from TB in 2019. Of the estimated 10 million people who developed TB that year, some 3 million were either not diagnosed, or were not officially reported to national authorities.

Progress towards SDG, End TB and UN High Level TB meeting targets is lagging. For example, while the target for TB preventive therapy is 30 million by 2022, only 6.3 million people have been treated during 2018 and 2019. While the target for funding TB care and prevention is $13 billion annually, only $6.5 billion were raised during 2020.

As predicted, the Covid-19 pandemic is making things worse. In September, several civil society organizations working on TB released the results of a large survey done to document the impact of the pandemic on TB care, research and funding [22]. Around the world, policy and program officers reported significant drops in TB notification. Over 70% of healthcare workers and advocates reported a decrease in the number of people coming to health facilities for TB testing. In Kenya, 50% of people with TB reported having trouble finding transport to care and in India, 36% of people with TB reported health facilities they normally visit closed.

The 2020 Global TB Report shows big reductions in TB notifications. The data show 25–30% reductions in TB notifications reported in 3 high burden countries – India, Indonesia, the Philippines – between January and June 2020 compared to the same 6-month period in 2019. TB services are similarly disrupted in many countries, and the disruptions extend over several months, rather than just weeks.

In India, the world's highest burden country, TB services are seriously disrupted, and the disruptions extend over several months, rather than just weeks [23]. India is dealing with a large-scale *syndemic* of TB and Covid-19.

A model by WHO [21] suggests that the global number of TB deaths could increase by around 0.2–0.4 million in 2020 alone, if health services are disrupted to the extent that the number of people with TB who are detected and treated falls by 25–50% over a period of 3 months.

The first pressing priority is to catch-up on all the missed patients and offer them TB treatment, in both public and private health sectors. It is also critical to ensure that everyone on TB therapy is adequately supported to complete the full duration of treatment. In this context, the key messages in the 19 articles in our series are highly relevant.

2. Key messages from the articles in the series

Table 1 attempts to summarize the key messages in the 19 articles in the series. The articles clearly demonstrate that poor quality of TB care is a major issue in all subgroups (adults, children), in all forms of TB (childhood, latent and DR-TB), and in a variety of countries and settings [2,3,5,10,12,15]. Standardized patient (SP) studies in 4 high-burden countries showed that few patients were offered appropriate diagnostic tests but many were offered empirical therapies, including broad-spectrum antibiotics and steroids [2]. Several articles described the so-called "know-do" gap in which healthcare workers can describe best practices in theory but don't necessarily implement them in practice [2,4]. Other articles highlighted the importance of high-quality health systems (as part of universal health coverage [UHC]) in improving the quality of TB care, arguing for a shift in focus from the quality of individual providers to the strength of the health system at every level of care in both public and private sectors [5,6,8,11,14,18]. The series also highlights the importance of the private health sector in many high TB burden countries, and the importance of engaging private providers to improve quality of TB care [13,20].

3. How can we improve quality of care?

In addition to pointing out key gaps in care quality, some of the articles outline several potential solutions (Fig. 1 provides a high-level summary). A clear consensus is that improving the quality of TB care cannot be accomplished in a vacuum – it requires UHC and approaches that target the foundational strength of robust health systems [5,6,8,11,14,18]. Quality in TB care needs to be better defined so it can be measured [5,11], and it must be centered on patients' perspectives to ensure that their needs and expectations are addressed [19]. Efforts to improve quality of TB care can be designed with lessons learned from other disciplines as a guide [6]. Promising approaches proposed in these articles included using existing tools and approaches for quality improvement [7,14] and pursuing a research agenda that investigates

https://doi.org/10.1016/j.jctube.2021.100212

Available online 7 January 2021

Please cite this article as: Jacob Bigio, *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases*, https://doi.org/10.1016/j.jctube.2021.100212

Table 1
Key messages from the articles in the series on quality of care.

Focus (reference)	Authors	Abstract
Lessons on quality of TB diagnosis from standardized patients [2]	Benjamin Daniels, Ada Kwan, Madhukar Pai, Jishnu Das	Standardized patient (SP) studies in India, China, South Africa and Kenya show that in general quality of TB care is low: relatively few SPs were offered appropriate diagnostic tests but 83% of interactions resulted in prescription of medication, frequently inappropriate broad-spectrum antibiotics, fluoroquinolones and steroids
Quality of drug-resistant tuberculosis care: Gaps and solutions [3]	Zarir Udwadia, Jennifer Furin	There is a quality crisis in the field of drug-resistant tuberculosis (DR-TB) care. DR-TB care is unsafe, inequitable, not patient-centred, and ineffective. The paper posits strategies to improve quality of care and advocates for a human-rights based approach to DR-TB care
In the eye of the multiple beholders: Qualitative research perspectives on studying and encouraging quality of TB care in India [4]	Andrew McDowell, Nora Engel, Amrita Daftary	Three qualitative case studies on TB diagnosis in India. (1) "Know-do" gap: GPs know best practices but don't implement them. (2) Quality of care is limited by health system issues, even with easy-to-use diagnostics. (3) Patients in private pharmacies expect to receive tangible products. Pharmacists can "dispense" free vouchers for TB screening tests
Measuring and improving the quality of tuberculosis care: A framework and implications from the Lancet Global Health Commission [5]	Catherine Arsenault, Sanam Roder-DeWan, Margaret E. Kruk	Expanding diagnosis and treatment coverage alone will not create a TB-free world; high-quality health systems are essential. Efforts should focus on governing for quality, redesigning service delivery, transforming the health workforce and igniting demand for quality TB services
Implementing quality improvement in tuberculosis programming: Lessons learned from the global HIV response [6]	Daniel J. Ikeda, Apollo Basenero, Joseph Murungu, Margareth Jasmin, … Bruce D. Agins	Lessons learned from successful QI programs for HIV can guide improvements in TB care quality. QI programs should be NTP-coordinated. NTPs should develop comprehensive frameworks for QI capacity building, specifying curricula and standards for training at all health system levels in both public and private sectors, with scalability planned from the outset
Quality of TB services assessment: The unique contribution of patient and provider perspectives in identifying and addressing gaps in the quality of TB services [7]	Charlotte Colvin, Gretchen De Silva, Celine Garfin, Soumya Alva, … Jeanne Chauffour	The quality of TB services assessment (QTSA) aims to identify gaps in TB services and prioritize ways to improve care. A recent QTSA in the Philippines showed that providers report having counselled patients on TB more than patients report having received the information
The high-quality health system 'revolution': Re-imagining tuberculosis infection prevention and control [8]	Helene-Mari van der Westhuizen, Ruvandhi R. Nathavitharana, Clio Pillay, Ingrid Schoeman, Rodney Ehrlich	TB infection prevention and control (IPC) implementation should be linked with health system strengthening, moving it from the silo of NTPs, with IPC viewed as a system-wide goal rather than the responsibility of individual healthcare workers. Patient experience should be added to the definition of high-quality care
Quality of life with tuberculosis [9]	Ashutosh N. Aggarwal	Diminished capacity to work, social stigmatization, and psychological issues worsen quality of life (QOL) in TB patients. Governments and program managers need to step up socio-cultural reforms, health education, and additional support to patients to counter impairment in QOL
Quality of TB care among people living with HIV: Gaps and solutions [10]	Kogieleum Naidoo, Santhanalakshmi Gengiah, Satvinder Singh, Jonathan Stillo, Nesri Padayatchi	Gaps within HIV-TB care cascades must be systematically analysed. HIV-infected patients often present asymptomatically with TB and are under-evaluated with routinely available diagnostics. HIV-TB patients can have poor treatment outcomes due to unmanageable side effects of concomitant TB therapy and ART and the financial expense of multiple health visits
Closing gaps in the tuberculosis care cascade: an action-oriented research agenda [11]	Ramnath Subbaraman, Tulip Jhaveri, Ruvandhi R. Nathavitharana	Many people with active TB suffer poor outcomes at critical points in the health system, highlighting poor quality of TB care. The proposed research agenda asks: 1) Who is falling out of the TB care cascade?, 2) Why are patients falling out of the cascade?, and 3) What interventions are needed to reduce gaps in the care cascade?
Quality matters: Redefining child TB care with an emphasis on quality [12]	Farhana Amanullah, Jason Michael Bacha, Lucia Gonzalez Fernandez, Anna Maria Mandalakas	Child TB often presents like non-TB pneumonia or with difficult-to-diagnose extrapulmonary TB. Bacteriological confirmation is challenging. Children are rarely included in Phase 3 trials so have delayed access to new medications. Child TB cascade data is rarely

(*continued on next page*)

Table 1 (*continued*)

Focus (reference)	Authors	Abstract
		available. The authors present a framework to improve the quality of child TB care
Quality of tuberculosis care by pharmacies in low- and middle-income countries: Gaps and opportunities [13]	Rosalind Miller, Catherine Goodman	The quality of pharmaceutical TB care has historically been poor. Interventions should expand beyond case detection to improve counselling of patients and appropriate medicine sales. Key areas for attention include pharmacy-specific global guidelines and the regulatory environment
Implementation science to improve the quality of tuberculosis diagnostic services in Uganda [14]	Adithya Cattamanchi, Christopher A. Berger, Priya B. Shete, Stavia Turyahabwe, … Achilles Katamba	System-level barriers lower the quality of care in Uganda, despite Xpert availability. Only 20% of patients with presumed TB received Xpert testing and nearly half with positive Xpert results were not rapidly linked to treatment. The authors conclude that Xpert scale-up should be accompanied by health system cointerventions to facilitate effective implementation
Identifying gaps in the quality of latent tuberculosis infection care [15]	Hannah Alsdurf, Dick Menzies	Quality care for LTBI must address key challenges including low prioritization of LTBI, provider knowledge gaps about testing and treatment, and patient concerns about side effects of preventive treatment. TB programmes need to ensure that these issues are addressed in a patient-centred manner
User experience and patient satisfaction with tuberculosis care in low- and middle-income countries: A systematic review [16]	Danielle Cazabon, Tripti Pande, Paulami Sen, Amrita Daftary, … Madhukar Pai	Most patients reported high satisfaction, despite widespread evidence of low-quality TB care. This could be due to acquiescence response bias, low expectations or because patients fear loss of services if they express dissatisfaction. The authors note the lack of standardized tools for measuring patient satisfaction and recommend their development.
Tuberculosis deaths are predictable and preventable: Comprehensive assessment and clinical care is the key [17]	Anurag Bhargava, Madhavi Bhargava	Comprehensive assessment and clinical care are required to reduce TB morbidity and mortality. TB programs need to define criteria for inpatient care referral, address the paucity of hospital beds, and develop and implement guidelines for the clinical management of seriously ill patients with co-morbidities
Improving quality is necessary to building a TB-free world: Lancet Commission on Tuberculosis [18]	Michael J.A. Reid, Eric Goosby	The Lancet Commission on TB states that strategies for improving quality must be hard-wired into the organization of NTPs. It calls for implementation research to understand how to improve care cascades, highlights the compelling economic rationale for ending TB and describes addressing TB as a core component in achieving Universal Health Coverage
What quality of care means to tuberculosis survivors [19]	Chapal Mehra, Debshree Lokhande, Deepti Chavan, Saurabh Rane	When high quality care is defined without patients' perspectives, their needs and expectations are not addressed. High quality care for TB-affected patients is affordable, easily available and accessible, delivered efficiently, and provided in a dignified, empathetic and stigma-free manner
Quality of tuberculosis care in the private health sector [20]	Guy Stallworthy, Hannah Monica Dias, Madhukar Pai	In many high TB burden countries, the private healthcare sector manages a large share of all patients. However, quality of TB care in the private sector falls short of international standards in many places and urgently needs improvement

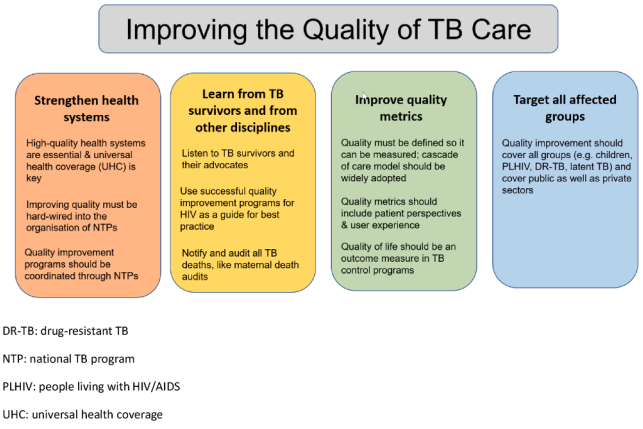

Fig. 1. Strategies to improve quality of TB care. DR-TB: drug-resistant TB. NTP: national TB program. PLHIV: people living with HIV/AIDS. UHC: universal health coverage.

reasons for losses at each stage of the TB care cascade [11].

When the series was launched in 2019, we had hoped it would result in a robust and sustained conversation about quality TB care, a topic that has heretofore been woefully neglected. At the start of 2021, we find ourselves in a crisis, where the TB epidemic has worsened because of the Covid-19 pandemic. Given the massive setback to progress in reaching any of the TB targets, it's time for the TB community to leverage Covid-19 innovations and systems (e.g. home-based and tele-health care, rapid and easy access to testing, digital adherence tools, real-time data tracking, sick pay and social benefits) to improve TB care and get back

on track [24]. In fact, there cannot be a more opportune moment for the TB community to leverage Covid-19 innovations to reimagine TB care, and make universal health coverage a reality.

Ethical statement

The manuscript is an editorial with no original data. Ethics approval is not applicable.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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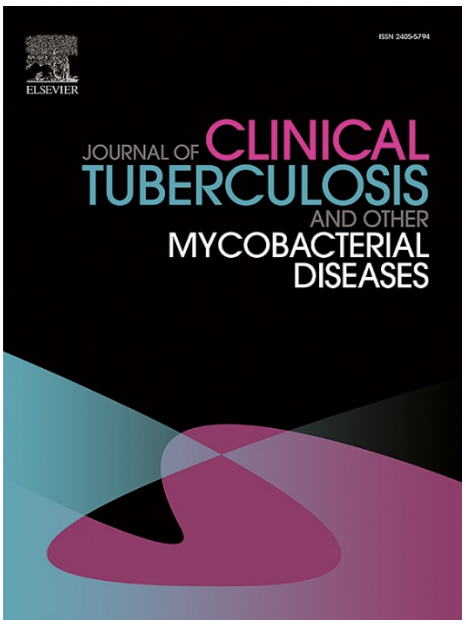

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