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

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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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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.

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