Title: Quality of tuberculosis care in high burden countries: the urgent need to address gaps in the care cascade

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PII: S1201-9712(16)31200-0
DOI: http://dx.doi.org/doi:10.1016/j.ijid.2016.10.016
Reference: IJID 2747

To appear in: *International Journal of Infectious Diseases*

Received date: 13-10-2016
Revised date: 14-10-2016
Accepted date: 18-10-2016

Please cite this article as: Cazabon D, Alsdurf H, Satyanarayana S, Nathavitharana R, Subbaraman R, Daftary A, Pai M, Quality of tuberculosis care in high burden countries: the urgent need to address gaps in the care cascade, *International Journal of Infectious Diseases* (2016), http://dx.doi.org/10.1016/j.ijid.2016.10.016

Highlights

Quality of tuberculosis care in high burden countries: the urgent need to address gaps in the care cascade

- Despite the high coverage of DOTS, tuberculosis (TB) continues to affect 10.4 million people each year, and kills 1.8 million.
- High TB mortality, the large number of missing TB cases, the emergence of severe forms of drug-resistance, and the slow decline in TB incidence indicate that merely expanding the coverage of TB services is insufficient to end the epidemic.
- Quality of tuberculosis care in both the public and private sectors falls short of international standards in many high burden countries
- National TB programs will therefore need to systematically measure and improve quality of TB care, and invest in quality improvement programs.

Quality of tuberculosis care in high burden countries: the urgent need to address gaps in the care cascade

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Abstract

Despite the high coverage of DOTS, tuberculosis (TB) continues to affect 10.4 million people each year, and kills 1.8 million. High TB mortality, the large number of missing TB cases, the emergence of severe forms of drug-resistance, and the slow decline in TB incidence indicate that merely expanding the coverage of TB services is insufficient to end the epidemic. In the era of the End TB Strategy, we need to think beyond coverage and start focusing on the quality of TB care that is routinely offered to patients in high burden countries, in both public and private sectors. In this review, we describe current evidence on the quality of TB care in high burden countries, major gaps in the quality of care, and some novel efforts to measure and improve the quality of care. Based on systematic reviews on the quality of TB care or surrogates of quality (e.g. TB diagnostic delays), analyses of TB care cascades, and newer studies that directly measure quality of care, we show that the quality of care in both the public and private sectors falls short of international standards and urgently needs improvement. National TB programs will therefore need to systematically measure and improve quality of TB care, and invest in quality improvement programs.

Keywords: tuberculosis, quality of care, cascade of care, quality improvement, standards for TB care

In May 2014, the World Health Assembly approved the End TB Strategy, which proposes the ambitious target of ending the global tuberculosis (TB) epidemic by 2035.[1] The goal will be met when TB-related deaths and active TB incidence are reduced by 95% and 90%, respectively, compared with the 2015 values. Are we on track to reach these goals?

Background

During the Directly Observed Treatment Short course (DOTS) era in the 1990s and early 2000s, high burden countries (HBCs) focused on achieving "coverage", defined as the availability of free TB diagnostic and treatment services in all regions or districts of a country. While nearly all countries have managed to substantially improve geographic coverage, the 'quality' of services received little attention. As a result, TB continues to be a major infectious threat and remains the largest cause of infectious disease mortality worldwide, with 10.4 million new TB cases and 1.4 million TB deaths estimated in 2015[2]. The WHO estimates the global burden of multi-drug-resistant TB and rifampicin-resistant TB (MDR/RR-TB) to be 3.9% of new cases of active TB disease and 21% of previously treated cases. Of the 10.4 million TB cases, 4.3 million patients are either not diagnosed or not notified to national TB programs. Further, TB incidence is declining at a very low rate of 1.5% per year.[2]

These data suggest that the current approach to global TB control, in which the onus has been on expanding coverage of TB services, needs to be reconsidered. In the era of the End TB Strategy, we need to think beyond coverage and start focusing on the quality of care that is routinely provided to patients in HBCs, in both public and private sectors.[3,4] Quality TB care is patient-centric care that is consistent with international standards, delivered in an accessible, timely, safe, effective, efficient and equitable manner. In this narrative review, we describe current evidence on quality of TB care in HBCs,

major gaps in quality of care, and some novel efforts at measuring quality of care, primarily through examples of recent work conducted in India. Where available, we appraise the findings of systematic reviews on quality of TB care or surrogates of quality (e.g. TB diagnostic delays), analyses of TB care cascades, and newer studies that directly measure quality of care using simulated patients.

Quality of care for latent TB infection

The WHO recommends treating latent TB infection (LTBI) in populations at high risk of progressing from LTBI to active TB disease.[5] These include patients with specific immunosuppressive conditions, notably HIV, and adults and children who have had contact with patients with active pulmonary TB cases. However, few HBCs implement these recommendations, even among people living with HIV, where the need is most urgent.[2] Some TB experts have recently argued for expanded and more aggressive implementation of LTBI screening and treatment programs in HBCs to mitigate incidence of active TB disease.[6]

There have been several reviews conducted on LTBI screening, diagnosis, and treatment but few have appraised the quality of LTBI care. In the most recent systematic review of 58 studies, Alsdurf and colleagues examined patient losses from the cascade of care for LTBI from the identification of those intended for screening to those who completed treatment (Figure 1)[7]. The authors identified areas where LTBI care has been successfully delivered (patients receiving tuberculosis skin test results, a referral for further evaluation if a test is positive, starting therapy after it was recommended), but they also identified important gaps in care in need of improvement. These gaps include the initial linkage to screening for LTBI, completing a medical evaluation after being referred, being recommended for treatment after a medical evaluation and completing treatment once started.

The authors also found that higher proportions of people tested positive for LTBI in low- and middle-income countries (LMICs) versus high-income countries, 61.3% and 24.8% respectively.[7] Treatment completion rates also differed between LMICs and high-income countries. Of people who started preventive therapy, only 52% of people in LMICs completed treatment, as compared to 70% in high-income countries. When comparing treatment completion among those who were eligible, less than 17% in LMICs, and 23% in high-income countries completed treatment; not nearly as large of a difference as among those starting treatment.[7] A variety of factors contributing to these gaps were highlighted, Including low TB risk perceptions and financial hardships among patients to the lack of provider knowledge regarding LTBI treatment.[7]

This review highlights that studies on LTBI management that focus on LTBI diagnosis (usually as a result of contact investigations) and adherence to treatment, need to recognize the various interim steps where patient attrition can occur in order to improve the quality of LTBI care in its entirety. The authors found fewer losses to occur among high-risk populations (i.e., close contacts or patients with serious medical disorders) likely as a result of intensified follow-up, supporting the need for improved quality of care to ensure successful completion of preventive TB therapy.[7]

Quality of care for active TB

We identified only one systematic review, from India, that explicitly reviewed studies on quality of TB care. Satyanarayana and colleagues conducted a systematic review of Indian studies on healthcare providers' knowledge and self-reported practices regarding TB, and used the International Standards for

TB Care (ISTC) to benchmark quality of care.[8] Of the 47 studies identified in the review, 12 used medical records, and 35 were based on questionnaires. None assessed actual practice using standardized (simulated) patients. Ten of 22 studies evaluating provider knowledge about TB diagnosis found that less than half of providers had correct knowledge using sputum microscopy for persons with typical TB symptoms. Of the four studies that assessed self-reported practices by providers, three found that less than one-fourth reported ordering sputum smears for persons with typical TB symptoms. In 11 of 14 studies that assessed treatment, less than one-third of providers knew the standard 4-drug (HRZE) regimen for drug-sensitive TB. Across all standards, providers had better knowledge as compared to self reported practices. In this review, 11 studies included both public and private providers; in general, public sector providers had relatively higher levels of appropriate knowledge as well as practice.

Other systematic reviews have focused on TB diagnostic delays, which is a surrogate of quality of TB care. In a systematic review of 39 studies, including data from 45 countries, Sreeramareddy and colleagues estimated the median time interval between the onset of symptoms suggestive of pulmonary TB (PTB) and the patient's first contact with a health care provider was 31.7 days (patient delay).[9] The median time interval between the first health consultation and the date of diagnosis was 28.4 days (health system delay). The median time interval between the onset of PTB symptoms and the initiation of anti-tuberculosis therapy was 67.8 days (total delay).

A subsequent systematic review, that focused on 23 studies from different parts of India, identified that the medians of patient, diagnostic and total delay were 18.4 days (IQR 14.3 to 27 days), 30 days (IQR 24.5 to 35.4 days), and 55.3 days (IQR 46.5 to 61.5 days) respectively.[10] This review also found that Indian TB patients, on average, are diagnosed after three healthcare provider visits. These studies show

that TB diagnosis may be delayed, even when patients present with overt TB symptoms, and underscores the need to address this major diagnostic gap.

The HIV community has actively used the cascade of care analysis to identify and address major gaps in the continuum and quality of HIV care, from diagnosis to successful virological suppression after anti-retroviral therapy.[11] This helps assess progress towards the UNAIDS '90-90-90 targets', which aim to diagnose 90% of all HIV positive people, provide antiretroviral therapy (ART) for 90% of those diagnosed and achieve viral suppression for 90% of those treated. Figure 2 illustrates a global HIV care cascade and highlights the current gaps at each step of the cascade.[11]

While published analyses of TB care cascades are scarce, a recent analysis from India provides useful insights on how this approach can help identify gaps in quality of TB care.[12] Subbaraman and colleagues conducted a cascade of care analysis for TB in India using data from the Revised National TB Control Programme (RNTCP), the WHO and targeted systematic reviews.[12] The study estimated that over 25% of prevalent TB cases in 2013 were not being evaluated at governmental TB diagnostic centers (Figure 3). Of the 1.9 million cases that made contact with the public health facilities, about half a million cases were either not correctly diagnosed or were not put on treatment once diagnosed. The study used recurrence free survival as the endpoint of the cascade rather than treatment completion (used by National TB Programmes). The authors suggested that routine follow-up with patients after treatment ends may be equally as important as monitoring adherence to treatment, due to considerable rates of post-treatment TB recurrence. This will facilitate early detection of relapse cases. Of note, setting specific context is important for understanding the cascade of care as in some settings re-infection is common and thus recurrence free survival may be less likely to reflect the quality of TB care received.

Traditionally, studies of quality of TB care have mostly relied on knowledge-assessment questionnaires (e.g. "vignettes"), direct observation of providers, recall-based patient surveys, and chart abstraction (e.g. prescription audit). However, these methods may not reflect actual practice.[13,14] Consequently, standardized or simulated patients (SPs) are increasingly used in low-income countries to assess quality of care for a variety of conditions.[15-18] Relative to other methods of measuring quality of care, data from SPs yield an assessment of provider practice that is free from observation bias, less vulnerable to recall bias, and more complete than medical records. Furthermore, SPs permit estimates of case detection rates since illnesses are fixed by design. Finally, because cases are standardized, the methodology allows for quality comparisons across different care providers (e.g. public vs. private).

Das and colleagues recently published the first validation study on the use of SPs for assessing quality of TB care.[16] Four prototypical cases, two for presumed TB and one each for confirmed TB and suspected multi-drug resistant TB (MDR-TB), were presented by 17 simulated patients, with 250 SP interactions with 100 consenting healthcare providers in Delhi. The researchers also used vignettes to assess provider knowledge of presumed TB. Correct case management was benchmarked using Standards for TB Care in India (STCI).[19] The proportion of SPs correctly detected to have TB was strikingly low at 5%, with a high correlation noted between SP recall and audio recordings. Across all cases, only 52 out of 250 (21%; 95% CI: 16-26%) were correctly managed. Correct management was higher among qualified doctors (adjusted OR=2.41, 95% CI: 1.17-4.93) as compared to all informal providers and practitioners of alternative forms of medicine. Provider knowledge based on responses to the vignettes was markedly more consistent with the recommendations outlined in the STCI than their practice. For example, while 73% said they would order a sputum test or X-ray for suspected TB, only 10% actually did so when SP visited them.

Based on the success of this pilot project in identifying gaps in quality of TB care, a similar methodology was used in three Indian cities to assess how pharmacists managed persons with TB symptoms. Indian pharmacists are frequently consulted by patients for over-the-counter medications.[20] Satyanarayana and colleagues trained simulated patients to present as two cases. Case 1 was a simulated patient presenting with 2–3 weeks of cough and other typical TB symptoms. Case 2 was a simulated patient presenting with a laboratory test report which confirms pulmonary TB. SPs completed 1200 interactions in 622 pharmacies in Delhi, Mumbai, and Patna cities. The researchers defined ideal management for both cases a priori as referral to any health care provider without antibiotics or steroids being dispensed. Ideal management seen in only 13% of pharmacies that received Case 1 SPs. But for Case 2 SPs, ideal management proportion increased to 62%. The use of broad spectrum antimicrobials was nearly half in Case 2 interactions as compared to Case 1 interactions. Referrals were significantly more common when simulated patients carried with them evidence of TB (i.e. positive sputum test report), thus making the diagnosis apparent to pharmacists.

Thus, the use of the SP methodology allowed the researchers to show that Indian pharmacists can delay the diagnosis of TB by dispensing broad-spectrum antibiotics (including fluoroquinolones), and not referring persons with typical TB symptoms for testing. However, the study also showed that, contrary to popular belief, none of the pharmacists in three cities were dispending first-line anti-tuberculosis medications over-the-counter. These findings are highly relevant to India, could help prevent antibiotic abuse, and increase referrals from pharmacists.

These novel simulated patient studies present direct evidence that improving the quality of care in HBCs with complex health systems such as India must be a priority. The SP methodology can feasibly be replicated in other HBCs, as they can inform quality improvement (QI) programs to address gaps at different stages of the continuum of TB care.

Quality of care for drug-resistant TB (DR-TB)

Mounting evidence demonstrates the primary transmission of drug-resistant TB (DR-TB) strains, but the emergence and persistence of TB drug-resistance also highlights the shortcomings of the current quality of TB care. Data demonstrate frequent delays in the diagnosis of MDR/RR-TB and globally less than one quarter of the estimated MDR/RR-TB patients are detected and reported to national surveillance systems.[2] Empirical management of TB without drug susceptibility testing (DST), inappropriate drug regimens, and insufficient attention to concurrent social support for patients to facilitate treatment completion are major drivers of DR-TB. The WHO has proposed five priority actions to tackle the global DR-TB crisis: 1) prevent the development of drug-resistance through high quality treatment of DS-TB; 2) expand rapid testing and detection of DR-TB cases; 3) provide immediate access to effective treatment and proper care; 4) prevent transmission through infection control; and 5) increase political commitment with financing. Unfortunately, HBCs are yet to address these priority actions to tackle DR-TB. In many countries, fewer than half of all patients with MDR-TB are on second-line drug therapy.[2]

While there have been no systematic reviews on the quality of care for DR-TB, reviews discussed earlier show critical gaps in service delivery among studies involving patients with DR-TB. Satyanarayana and colleagues found one study that examined quality of care for DR-TB, which identified that only 39% of healthcare providers reported conducting DST for eligible TB cases.[8] Moreover, using SPs, Das and colleagues found that that even among qualified, trained doctors in India, a DST was rarely ordered for a SP with classic TB symptoms and a clear history of previous, incomplete therapy.[16]

In the Indian cascade of TB care analysis by Subbaraman and colleagues, data for MDR-TB patients were analyzed separately.[12] As shown in Figure 4, the cascade suggests that the vast majority of MDR-TB patients who present to public sector diagnostic facilities are not diagnosed with drug resistance, highlighting an urgent need to move towards universal DST, as recommended by the End TB Strategy.[12] Of note, outcomes for MDR-TB patients were considerably worse than for DS-TB patients, with only 10.6% of MDR-TB patients achieving recurrence-free survival.

Suboptimal care for DR-TB is not limited to India. The WHO reported that in 2015, there were an estimated 480 000 cases of MDR-TB globally and 100 000 cases of rifampicin-resistant TB (RR-TB). Of these, only 130 000 (~23%) were detected and reported.[2] Unless this gap is addressed, MDR-TB will continue to be a major challenge. Even after diagnosis, only about half of these patients with DR-TB were successfully treated. This means access to second-line therapy is suboptimal, and patients are not getting the support they need to complete the long treatment for DR-TB.[2]

Policy and implementation gaps

Patient-centric, quality TB care is critical for reaching the End TB targets, and yet, it is clear that many patients do not receive such care in HBCs. While the ISTC[21] has laid out the expectations for quality standards, our review shows that the quality of care in both the public and private sectors does not meet these standards, serious implementation gaps continue to be a concern in many settings.

In 2015, MSF and Stop TB Partnership published a report called “Out of Step”. This was based on a survey of 24 high TB burden countries, to assess policy adoption in these settings.[22] Serious implementation gaps were identified in the survey. The study showed heavily reliance by countries on

inaccurate smear microscopy, while only 8 countries had revised their national diagnostic algorithms to include Xpert MTB/RIF (Cepheid Inc, USA) as the frontline test for individuals with suspected TB (instead of sputum microscopy). While intermittent therapy for drug-sensitive TB is suboptimal, compared to daily therapy, six countries still offered them. So, it is important for the TB community to acknowledge these implementation gaps and find ways to raise the resources that are necessary for providing quality care that is consistent with international standards.[23] Achieving political will and consensus on this issue will be critical.

Quality Improvement (QI) interventions

TB programs must start to systematically analyze gaps in their care cascades, and work towards measuring and incorporating quality of care indicators, in addition to routine coverage indicators. This can be achieved using the established framework of QI, which is a proven, effective way to improve care for patients and to improve practice for healthcare providers. Healthcare systems are inherently complex but using a systematic approach enables the optimization of processes and interventions. QI should be a continuous process and an integral part of adding value to patient care and to the healthcare delivery system.[3,4]

In TB, there is a paucity of projects that specifically aim to establish and test QI interventions. However, there are many examples of interventions that have improved quality of TB care in both public and private sectors. As an example, Davis and colleagues prospectively evaluated TB diagnostic services at five primary health-care facilities in Uganda over 1 year, after introducing a real-time, electronic performance-monitoring system.[24] They collected data on every clinical encounter, and measured quality using indicators derived from the ISTC. In 2009, there were 62,909 adult primary-care visits at

the facilities included in the study. During the first quarter of 2009, clinicians referred only 21% of patients with cough greater than or equal to 2 weeks for sputum smear microscopy and only 71% of patients with a positive sputum examination for TB treatment. These proportions increased to 53% and 84%, respectively, in the fourth quarter of 2009. The cumulative probability that a smear-positive patient with cough greater than or equal to 2 weeks would be appropriately evaluated and referred for treatment rose from 11% to 34% ($P = 0.005$). The quarterly number of tuberculosis cases identified and prescribed treatment also increased four-fold, from 5 to 21.

A subsequent follow-up study in Uganda evaluated the benefits of a multi-component health system strengthening intervention for improving quality of care.[25] Same-day smear microscopy was implemented at six health centers, and a performance feedback initiative was implemented in which healthcare providers were given a monthly "report card" on their adherence to specific ISTC indicators. These included the proportion of adults with cough referred for sputum examination, the proportion completing sputum examination, and the proportion of smear-positive patients initiating treatment. Same-day sputum microscopy increased the proportion of patients receiving ISTC-adherent care by 14% (95%CI:10-18), and performance feedback increased the proportion of patients receiving ISTC-adherent care by 15% (95%CI:10-20). Thus, these studies show that real-time performance monitoring and targeted health system strengthening interventions can improve adherence to internationally accepted standards of TB care.

In the private sector, where quality of TB care can deviate considerably from expected standards, several public-private partnerships have attempted to improve quality of care, with varying degrees of success, as reviewed elsewhere.[26] India's Revised National TB Control Program (RNTCP) and state and municipal governments have recently reported success with innovative models of private sector

engagement.[27] In urban pilots in Mumbai, Patna and Mehsana, the Indian TB program has engaged a large number of private providers, and greatly increased the numbers of private TB case notifications. In addition, the Indian TB program has improved diagnosis of TB by offering free vouchers for tests such as GeneXpert, provided patients free daily fixed dose combinations, and improved adherence support to patients managed in the private sector, with good treatment completion rates.[27]

Conclusions

In order to improve TB care, with a view to achieving the ambitious targets set out in the End TB Strategy, we need to increase access to TB care and simultaneously ensure that the care provided is of sufficiently high quality.[3,4] Healthcare systems and national TB programs will therefore need to think beyond access and coverage of healthcare services, and start systematically measuring and improving quality of TB care. Routine evaluation of delays in TB diagnosis and SP studies can help to identify and monitor deficiencies in health systems and provider behavior that may compromise the diagnostic evaluation of TB patients. As shown in Table 1, regular analysis of the cascade of care can help shift metrics away from the focus on coverage of health services and towards a focus on engagement and retention of patients to ensure that all TB patients achieve an optimal outcome of treatment completion and recurrence-free survival. The institution of structured QI programs as an integral part of all national TB programs, supported by clear metrics that take into account setting-specific contexts, will be an important step to achieve the goal of providing high quality TB care to all patients.

Conflicts of interest:

None of the authors have financial or industry conflicts to disclose. MP serves as a consultant to the Bill & Melinda Gates Foundation, and on advisory committees of FIND, Geneva, and TB Alliance, New York. These agencies had no involvement in this manuscript.

Funding:

SS is supported from an operations research fellowship grant from the Center for Operations Research, Paris, France. RS is supported by a Harvard Catalyst KL2/Catalyst Medical Investigator Training award (KL2 TR001100) and a grant from the Bill & Melinda Gates Foundation. AD is supported by a grant from IC-IMPACTS and TB REACH (Stop TB Partnership). MP is supported by a Canada Research Chair Award from CIHR, and grants from IC-IMPACTS, TB REACH, FIND, Geneva, and Bill & Melinda Gates Foundation. None of the funding sources had any involvement in the production or submission of this manuscript.

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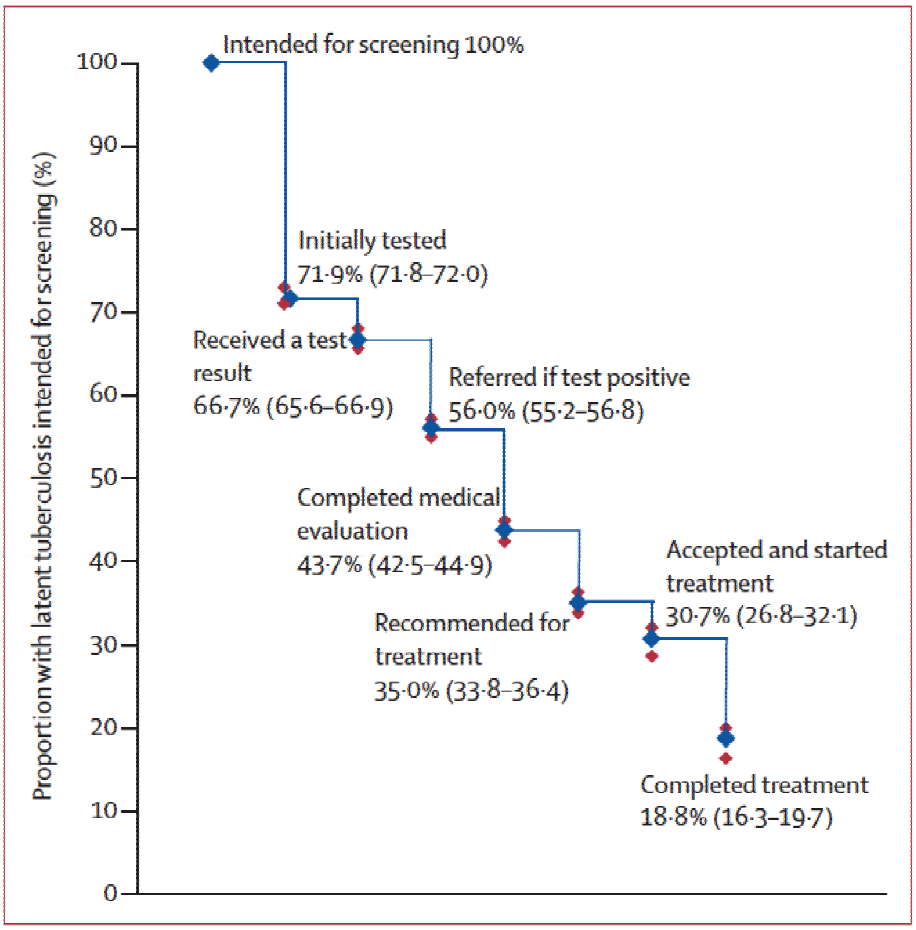
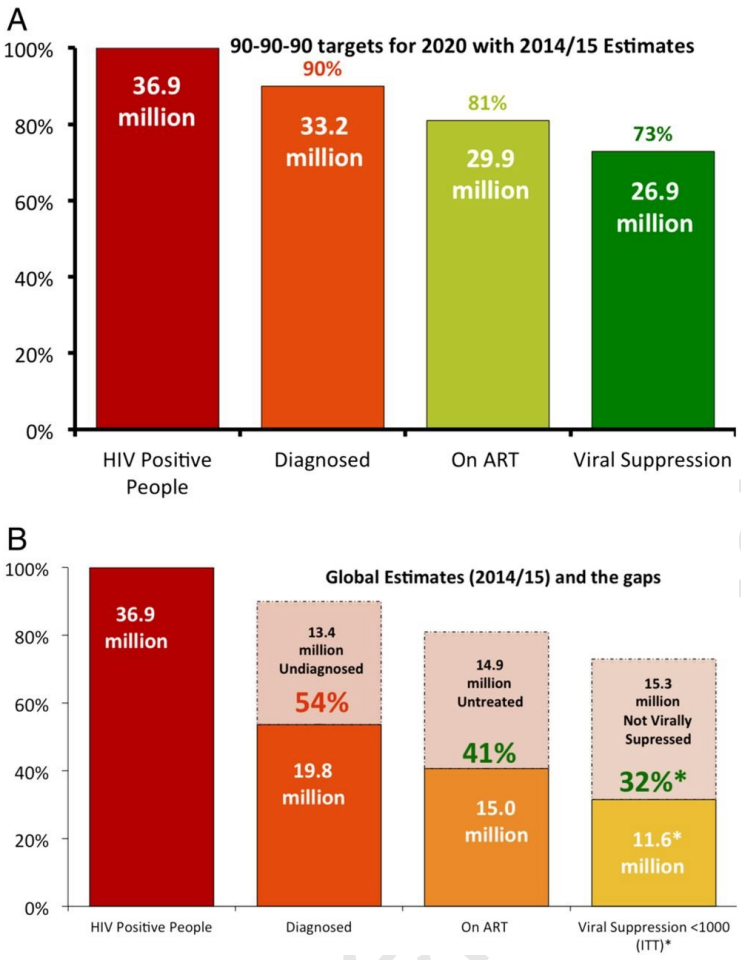
Figure 1: Losses and drop-outs at each stage of the cascade of care in latent tuberculosis infection (LTBI). Numbers in parentheses are 95% CIs. The value for each level is calculated as the product of the value from the preceding step, multiplied by the pooled estimate for that step (from fixed-effects analysis).



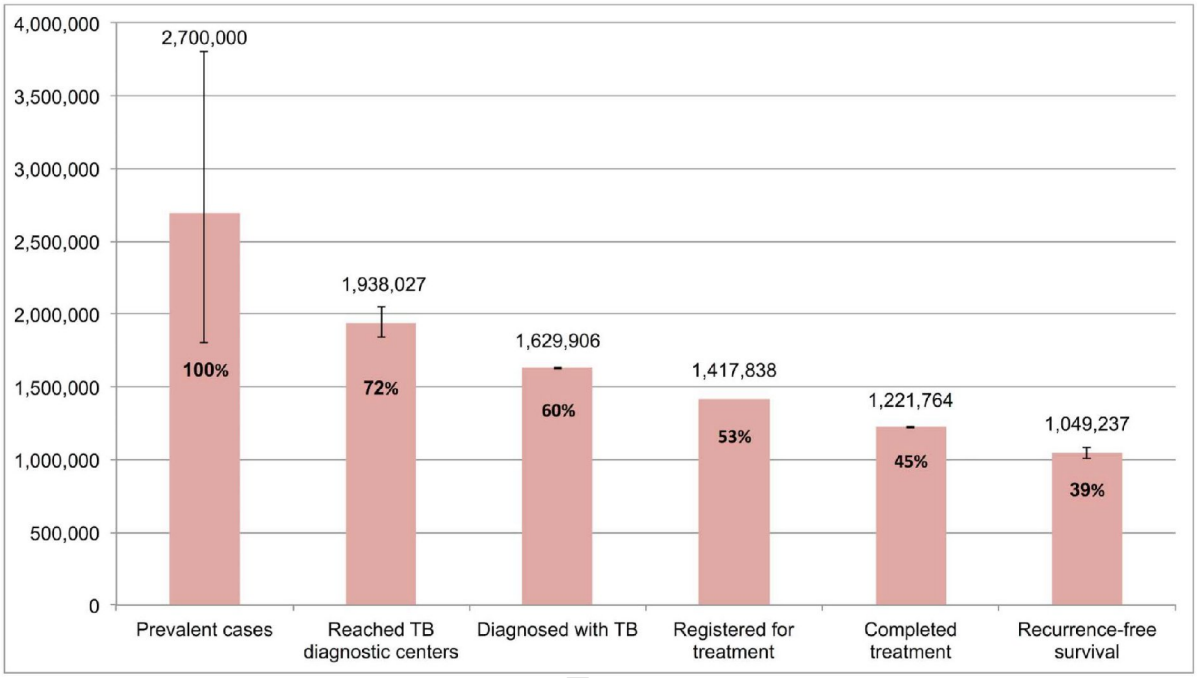
Source: Alsdurf H et al. Lancet Infect Dis 2016[7] (reproduced with permission)

Figure 2. Analysis of the HIV cascade of care, comparing the UNAIDS targets for 2020 with global estimates for 2014/15.



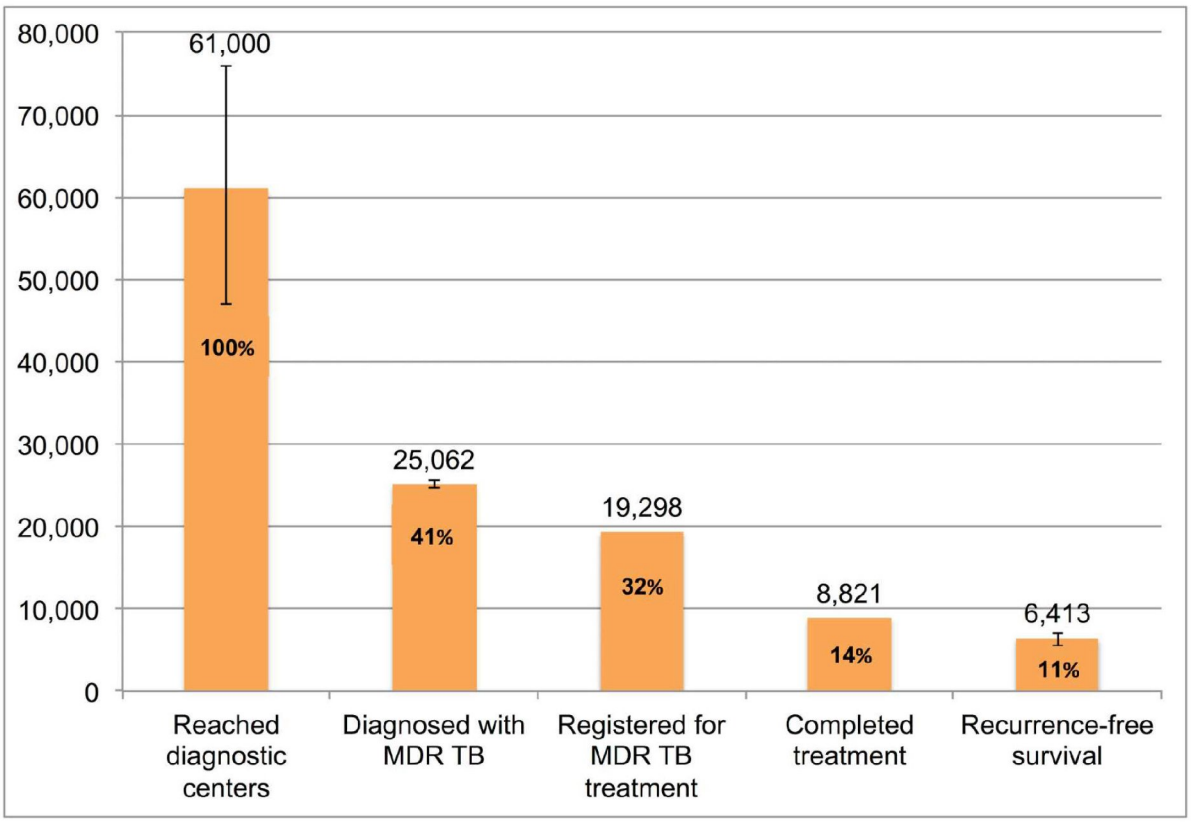
Source: Levi et al. BMJ Global Health 2016[11] (Open Access, under Creative Commons License)

Figure 3: The cascade of care for all forms of tuberculosis in India's Revised National Tuberculosis Control Programme (RNTCP) in India, 2013. Error bars depict 95% confidence 739 intervals.



Source: Subbaraman R et al. PLoS Med 2016[12] (Open Access, under Creative Commons License)

Figure 4. The tuberculosis cascade of care for multidrug-resistant tuberculosis (MDR-TB) patients detected and treated by the Revised National Tuberculosis Control Programme (RNTCP) in India, 2013. Error bars depict 95%confidence intervals for each estimate.



Source: Subbaraman R et al. PLoS Med 2016[12] (Open Access, under Creative Commons License)

Table 1: Advantages of the cascade of care model for monitoring tuberculosis (TB) programs

• Helps policymakers and program staff to visualize the largest gaps in care delivery to facilitate design of targeted interventions to reduce those gaps
• Shifts program goals away from "coverage" of a population with TB health services and towards engagement and retention of all TB patients at each step of care
• Places "notified" TB patients in the larger context of the overall TB population or the TB population reaching care, which helps reveal new gaps in care
• Shifts program metrics away from case notification and treatment completion to more rigorous outcomes such as one-year TB recurrence free survival
• Cascades for TB sub-populations (e.g., smear-negative or multidrug-resistant patients) may identify unique points of attrition requiring different interventions from the overall TB population
• Sub-population cascades have also been used in HIV to identify high-risk and vulnerable demographic groups, such as adolescents and incarcerated individuals
• Incorporation of the cascade into routine monitoring of TB programs may allow development of unified metrics and global targets, as UNAIDS has done for the "90-90-90" HIV/AIDS strategy