AN EVALUATION OF PRIVATE SECTOR PATHWAYS TO DIAGNOSIS OF TUBERCULOSIS IN CHENNAI, INDIA

by
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A dissertation submitted to Johns Hopkins University in conformity with the requirements for the degree of Doctor of Philosophy.

Baltimore, Maryland
October, 2015

Abstract

Setting

Private practitioners are frequently the first point of healthcare contact for patients with tuberculosis (TB) in India. However, inappropriate TB management practices among private practitioners may contribute to delayed TB diagnosis. As new TB diagnostic tests are developed and the national TB control program seeks to better engage the private sector, it is important to understand pathways to TB diagnosis in urban India.

Design

A cross-sectional study was conducted among patients and practitioners in Chennai city from January 2014 to February 2015. Patient participants were diagnosed with TB in the private sector and referred for TB treatment through a public-private mix program in Chennai. Practitioners practicing in the private sector, who saw at least one TB patient per year, were randomly selected from both the general community and a list of practitioners who referred patients to the public-private mix program. Cross-section interviews were conducted with 289 patients and 228 practitioners using standardized questionnaires.

Results

Among 212 patients with pulmonary TB, 90% first contacted a formal private provider, and 78% were diagnosed by the first or second provider seen after a median of three visits per provider. Median total delay was 52 days (Mean 69). Consulting an informal (rather than formally trained) provider first, was associated with an increase in risk of prolonged total delay >90 days (aRR 2.5, 95%CI: 1.3-4.5). Among 228 private practitioners, only 52% of practitioners sent >5% of patients with cough for TB testing, 83% used smear microscopy for diagnosis, and 22% notified TB cases to authorities. For new patients with pulmonary TB, 30% of practitioners reported referring all patients for treatment, while 70% (160/228) listed 27 different regimens; 78% (125/160) of these prescribed a regimen classified as consistent with ISTC. Under half (48%, 110/228) of all practitioners utilized any point-of-care (POC) tests in their clinics. Providers using POC tests were more likely to work in hospitals (56% vs. 43%, P=0.05) and less likely to be chest specialists (21% vs. 54%, P<0.001). When asked about using a hypothetical, novel POC test for TB that was accurate, took 20 minutes, and required no equipment, only half (51%, 117/228) of all providers would use the test in-house.

Conclusion

Even among patients seeking care in the formal private sector in Chennai, diagnostic delays are substantial. TB management practices in India's urban private sector are heterogeneous and often suboptimal. Novel strategies are required to engage private providers and integrate new diagnostics into the private system to improve diagnostic capacity and decrease TB transmission in India.

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Acknowledgements

I chose to pursue advanced training in epidemiology to gain further experience with research study design, implementation, and analysis, and translational research for programmatic planning. To achieve this objective through my dissertation research, I developed and implemented a cross-sectional study to evaluate pathways to tuberculosis diagnosis through in the private health sector in Chennai, India. This work would not have been possible without the collaboration and support of a number of dear mentors, colleagues, and friends.

First, I would like to express my heartfelt gratitude to my advisor, David Dowdy, and co-advisor, Jonathan Golub, who have guided and supported my development through the doctoral program in complementary roles that genuinely enhanced my experience at Johns Hopkins. David is an inspiring and devoted mentor who encouraged my academic growth and believed in my ability to persevere even in the most challenging of times, always supporting me as a student, colleague and friend. Jonathan's mentorship provided me with invaluable insights, expertise, confidence, and opportunities for personal and professional growth. To say the influence of these two mentors has been instrumental to my development is an understatement. Further, I am thankful for my colleagues in the TB Research Center and Modeling Group at Johns Hopkins for their thoughtful support, questions, and feedback.

I am also deeply grateful for the knowledge, support, and introduction to India provided by Madhukar Pai, Ramya Ananthakrishnan, and the entire team at REACH in Chennai; their efforts and dedication made much of this work possible. Additionally, I would like to acknowledge Shruti Mehta, my thesis committee advisor, who provided valuable feedback and support throughout the academic and dissertation process. I would also like to recognize Susan Sherman, who served on my departmental oral exam committee and became a mentor and friend, providing me with both inspiration and an opportunity to branch into new areas of infectious disease research. I am also thankful for the support of the Department of Epidemiology and the Center for Global Health.

Finally, I would like to express my gratitude to my friends and family, without whom I would not have survived the doctoral program. My "super" friends and fellow students kept me going with their laughter, encouragement, and occasional distraction. Megan Clarke-Corso, Rebecca Pierce, Kristen Little, Shan Anderson, Shaun Truelove, and Katie Mues were cherished consultants and partners in crime and academia. Furthermore, I would like to thank Laura Podewils for always believing in me and providing the spark that led me to pursue a doctoral degree. To my adoring family, Dad, Wendy, and Ali, I could never ask for a more loving or supportive family; thank you for all that you do to enable me to follow my professional dreams. To my Mom, your love, strength and ambition helped carry me these past three years and made me who I am today. Lastly to my beloved husband, Michael, you have followed me around the world with your love; and while I may not have made it look easy, I could not have gotten through all of the blood, sweat, and tears without you and your encouragement.

Table of Contents

List of Tables

List of Figures

Chapter I: Introduction

Tuberculosis and the Burden in India

Although tuberculosis (TB) is a curable disease, it remains a major public health problem throughout the world. TB is the second leading infectious disease cause of death after human immunodeficiency virus (HIV) worldwide.[1] In 2013, there were 9 million incident cases of TB and 1.5 million deaths from TB according to the World Health Organization (WHO).[1]

In India today, it is estimated that two deaths occur every three minutes from TB.[2] India had an estimated 2.1 million incident TB cases (171 per 100,000) occurring in 2013; a TB case burden that accounts for 24% of the world's incident cases.[1,2] WHO ranks India as the top country for TB burden with its total population over 1.2 billion people, 2.6 million prevalent TB cases (211 per 100,000), and 240,000 TB-related deaths (19 per 100,000).[1] Additionally, 2.2% of all new cases and 15% of all retreatment cases in India were diagnosed with multidrug resistant TB (MDR TB) in 2013.[1,3] India also ranks as the top country accounting for 31% (2.9 million) of the global "missed" TB cases that are either not diagnosed or diagnosed but not notified to the national TB program.[3]

The Indian Healthcare System: Role of the Public and Private Sectors

The Indian Healthcare System is complex and heterogeneous.[4,5] Disease-specific, vertical health programs play a central role in strengthening components of India's health system by sharing human and material resources, increasing demand for health services, and encouraging civil society's involvement in service delivery.[6] Vertical programs, such as the Government of India's Revised National Tuberculosis Control Programme (RNTCP), also aid in improving patient confidence and perceptions in facilities for diseases of high public health significance.[6] The RNTCP is located within the Department of Health and Family Welfare. It is sponsored by the central health ministry and receives little (<1%) outside funding support from international donors for its health resources.[6] The vertical design and structure of the RNTCP are more functionally integrated with the Indian health system, aiding its contribution towards strengthening the overall health systems.[6,7]

In 1998, the RNTCP began implementation of the WHO's global TB control strategy of directly observed therapy short-course (DOTS) and expanded to countrywide coverage by 2006.[8,9] The RNTCP currently provides decentralized access to free diagnostic and treatment services for patients with TB in approximately 13,000 sputum smear microscopy centers and 650,000 DOTS centers within the public healthcare system.[2] Although this access to public healthcare is widely available, up to 80% of individuals with a cough lasting more than two weeks first seek care from private healthcare providers.[4,5,9–12] These private providers include both qualified and unqualified providers and practitioners of alternative health systems that outnumber qualified, allopathic doctors in some urban settings.[4,5,13] There is evidence that up to 25% of individuals classified as allopathic doctors working in the private sector have no medical training and thus are unqualified practitioners.[4,5,13,14] Further, while the Government of India has made TB case notification mandatory to improve case detection and TB control efforts, private practitioners rarely comply and notify the government of their patients with TB.[15]

The RNTCP's National Strategic Plan for 2012-2017 aims to achieve "universal access" to quality assured TB diagnosis and treatment for all patients with TB by 2017.[16–18] To achieve this vision, the RNTCP aims to reach the following targets: (i) early detection and treatment of at least 90% of estimated TB cases in the community; (ii) screening of all re-treatment smear-positive TB patients for drug-resistant TB and provision of treatment for MDR TB patients; (iii) HIV counseling and testing offered for all TB patients with linkage to HIV care support for those with HIV; (iv) successful treatment of at least 90% of all new TB patients and 85% of all previously-treated TB patients; and (v) RNTCP services extended to patients diagnosed and treated in the private sector.[16] The RNTCP seeks to achieve these objectives by sustaining the program activities and achievements to date, and by extending the reach and quality of services to all persons diagnosed with TB, including better engagement of the private sector in partnerships for TB diagnosis.[16]

Patients Accessing the Indian Private Sector

Patients with TB in India often see multiple healthcare providers prior to obtaining a TB diagnosis. Frequently, patients with TB symptoms begin seeking advice from informal private providers, then seeking medical care from formal private practitioners, and eventually end up getting free treatment under the RNTCP. [4,5,19–21] Thus, patients move from one provider to another until they are finally diagnosed with TB and initiated on TB treatment after substantial delays since symptom onset.[4,5,19] However, there is evidence that up to two-thirds[22] of patients seek care and are treated exclusively in the private sector, these practitioners include formally-trained, allopathic doctors and non-allopathic AYUSH (includes ayurveda, yoga and naturopathy, unani, siddha, homeopathy) practitioners[13], and informal traditional healers, unqualified or unlicensed practitioners, and chemists or pharmacists who practice in the private sector. Even given its prominent role in TB patient management, little is understood about the pathways to diagnosis and delays to TB treatment among these patients in the private sector.[4,20,23]

With little collaboration across the health sectors, navigating the Indian health system can be challenging for individuals with TB-related symptoms. A household survey in Chennai showed that 60% of the individuals with a long-standing cough first went to a private practitioner for care.[24] An older study previously reported that as many as 67% of patients are diagnosed and started on TB treatment by private healthcare providers and remained with the private sector, while 34% changed to the public sector within the first six months.[14] More recent research from Mumbai determined that only one-third of the private practitioners surveyed referred their patients with TB to government services for treatment.[10] Seeking care from a private practitioner as the first point of care is more common among patients living in urban areas, who are literate, and earning an income greater than 2,000 rupees (approximately US$31.00) per month.[4,11] Given this heavy private sector involvement, understanding the diagnostic pathways among patients who access and are ultimately diagnosed and treated in the private sector (without accessing the RNTCP) is critical to TB control in India.

TB Diagnosis in India: Importance of Diagnostic Tests for TB Control

Early diagnosis and effective treatment of TB are critical to mitigate the burden of TB transmission[1]; however, the most widely used TB diagnostic test globally, sputum smear microscopy for acid-fast bacilli, is over 125 years old and routinely fails to detect half of all TB cases.[25–27] Based on a negative policy recommendation from the WHO, in 2012 the Indian government banned the manufacture, sale and distribution of sero-diagnostic test kits for diagnosis of tuberculosis.[3,28–32] As a result, the diagnostic landscape in India is changing with the availability of novel automated TB diagnostic technologies, such as the Xpert MTB/RIF assay (Xpert) and the line probe assay. Owing to its high sensitivity to detect TB and rifampicin resistance in two hours, Xpert is recommended by WHO for diagnosis of individuals at risk of having MDR-TB or HIV-associated TB and as a follow-on test to microscopy.[3] Unfortunately, other serological tests (e.g., QuantiFERON Gold In-Tube), designed for diagnosis of latent TB infection, are also being used for active TB diagnosis in India.[33–35]

In accord with the RNTCP's National Strategic Plan to achieve "universal access" to TB diagnosis, the Initiative for Promoting Affordable Quality TB tests (IPAQT) has made WHO endorsed tests more affordable in the private sector, with an effort to address the gap left by the ban on serological tests.[3,36] NGO-led models[24] and Private Provider Interface Agency projects in select cities[37] are also working to engage private practitioners in guideline-based TB care. Nonetheless, for the utility of new diagnostics to be realized, the current practices, needs, and challenges of private providers in TB care must be addressed. To realize the goal of universal access to TB care, it is important to understand the patient pathways where delays and missed TB diagnoses occur in order to implement diagnostic algorithms to reduce these delays.[21]

Patient Pathways to Care for TB

Due to the complicated pathways to obtain care for TB in India, many patients experience a delay of two months or more from symptom onset to TB diagnosis and treatment initiation.[4,5,20,23] In a study conducted in Delhi among patients that first sought care in the private sector, 25% of patients saw four medical providers for TB-related symptoms prior to attending an RNTCP DOTS center for treatment.[5] In their complex pathways to care, 62% of patients with TB-related symptoms initially accessed health services from an informal private practitioner, 33% from a qualified private medical practitioner, and 7.4% from a retail chemist (pharmacist) (Figure 1).[5] Other studies of patients accessing the RNTCP TB services have reported mean delay durations up to five months from symptom onset to treatment initiation[5], and mean treatment delays from patient diagnosis with TB to initiation of treatment ranging from one to eight days[4,5,23], but up to 128 days in rural areas.[51] Factors associated with delays in diagnosis and treatment initiation in the public sector include: previous treatment, seeking a second opinion, drug delivery delays, and absence of TB diagnostic services in the local health facility.[5,11,12,23,51] Qualitative research has found that during this process of care seeking with multiple providers, patients lose considerable amounts of money and time as they are referred to private labs for multiple diagnostic tests to rule out non-TB diseases such as typhoid and malaria fevers.[52,53] Patients must then return to the private practitioners for interpretation of the diagnostic tests due the relationships between labs and providers, further contributing to their healthcare expenses. This arrangement can lead to distrust among patients causing them to switch providers, seek second opinions, and/or failure to trust lab results.[52]

Figure 1.1. Pathways undertaken by patients to reach the RNTCP (DOTS) Facilities in Delhi, India.

This figure, published by Kapoor et al.[9], illustrates the pathways taken by patients who were treated for TB under the RNTCP in Delhi, India in 2012. All of the patients initially sought care from informal and formal private providers with long delays before TB treatment initiation. Among these patients, 25% saw four healthcare providers prior to attending an RNTCP DOTS Center. All patients were sampled from the public sector where they were eventually treated at RNTCP DOTS Centers.

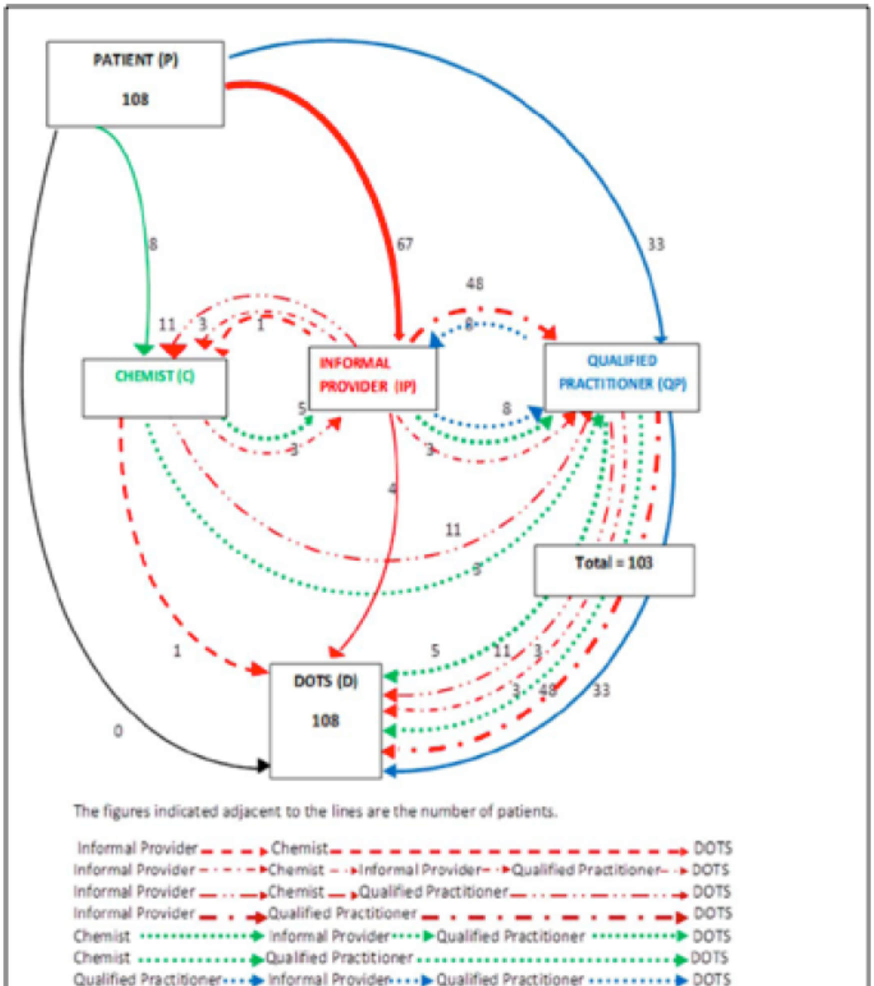


Figure 1. Pathways undertaken by the patients to reach the RNTCP (DOTS) Facilities, Delhi, India.
doi:10.1371/journal.pone.0042458.g001

Prolonged total delays to diagnosis after TB symptom onset occur frequently among patients who first seek care in the private sector, allowing for ongoing TB transmission in the community during the total symptomatic time.[4,20,23] Increased delays from symptom onset to treatment initiation are also associated with seeking additional medical counsel or second opinions, female gender, site of TB disease, and absence of local diagnostic services.[4,5,11] Additionally, multiple visits to a private practitioners required prior to TB diagnosis due to lack of TB symptom screening knowledge also contributes to prolonged diagnostic delays.[4]

It is widely recognized that TB control in India will not be achieved without engagement of the private healthcare providers.[16,33,54] By better integrating the private sector with the RNTCP, it may be possible to reduce the time patients spend seeking a diagnosis after onset of infectiousness, thus decreasing the burden of TB transmission in the community. However, the actual usage of specific TB diagnostic tests, TB patient volumes, capacity to achieve rapid TB diagnosis, and practitioner characteristics associated with prompt and appropriate diagnosis in the private sector are not well characterized.[10,14,45]

Private Practitioners' TB Diagnosis and Treatment Practices

The current RNTCP guidelines for pulmonary TB diagnosis rely on outdated technology including chest x-ray as a screening tool and microbiological confirmation of diagnosis with sputum smear microscopy.[38,39] Cartridge-based nucleic-acid amplification tests, such as Xpert, are recommended as a diagnostic test for children, persons with HIV-infection, and for suspected drug-resistance, but not for general diagnosis of pulmonary TB.[16,38,40] However, a recent systematic review found that only half of the healthcare providers from both the public and private sectors tested patients with long-lasting cough for suspicion of TB, and just two-thirds used smear microscopy for patients with presumptive TB.[24,41]

The existence of a significant private health sector (comprised of qualified and unqualified providers) in India that frequently serves as the first point of medical contact for patients with TB-related symptoms is one of the reasons for low case detection rates, wherein practitioners frequently diagnose TB using inadequate diagnostic tests.[1,33,41] For example, private healthcare providers commonly use serologic antibody tests to diagnose active TB in the Indian private sector, and inappropriate TB prescriptions are common. Poor treatment prescription practices are evidenced by the finding that only one third of private sector practitioners know the international standard treatment regimen for new patients with drug-susceptible TB.[10,22,41] Given the reports of poor treatment outcomes and emerging drug resistance in India, these findings are particularly concerning, especially in urban areas.[41–44]

The RNTCP and the Indian Medical Association have adopted the International Standards for TB Care (ISTC) and recently published the Standards for TB Care in India (STCI) to support quality TB control practices.[45–47] The ISTC include 21 standards of diagnosis, treatment, and other practices that describe a widely accepted level of TB care.[45,47] The standards are intended to be complementary to local and national TB control policies that are consistent with WHO recommendations to promote effective engagement of all providers in delivering high quality care fore patients.[47] Measures of adherence to the ISTC in primary care centers in rural in Uganda found that approximately 52% of patients received ISTC-adherent care for TB[48], higher than a study in Indonesia reporting just 21% adherence in public health centers[49], though still inadequate for TB control. Nevertheless, the lack of adherence to the ISTC and STCI continues to be documented among private practitioners in India where adherence ranges from 11% to 94% for key standards, including use of sputum smear for persons with presumptive TB.[10,22,45,50] The inadequate TB management practices reported among private practitioners contribute to delays in TB patient diagnosis, development of drug-resistance, and ongoing TB transmission.[17,41,45]

Delays in Pathways to Diagnosis of TB

Delays in diagnosis of patients with TB are a key driver of transmission worldwide and may be a reason why TB incidence has not substantially declined despite global scale-up of the DOTS strategy.[1,4,55,56] Patients seeking care for TB-related symptoms can experience delays at any point along their pathway to TB diagnosis and treatment. The *Conceptual framework of definitions of delays* presented by Sreeramareddy et al. in a systematic review of delays in diagnosis and treatment of pulmonary tuberculosis in India evaluates the diagnostic process for individuals seeking care for TB-related symptoms (Figure 1.2).[4] This framework provides a linear model of the intervals that define a patient pathway to care from the time of TB symptom onset to treatment initiation. Additionally, an adapted framework for *The Model of Pathways to Treatment* developed by Scott et al. is presented here to understand the complex and dynamic nature of patient pathways through the Indian private sector (Scott Pathways Model; Figure 1.3).[57] In the adapted Scott Pathways Model, time intervals may occur in any sequence between events with no starting point, including forward and backward movement, much like the pathways to TB treatment reported by Kapoor et al.[5,57]

Figure 1.2. Conceptual framework of definitions of delays.

The conceptual framework of definitions of delays characterizes the intervals from the time of TB symptom onset to diagnosis and treatment of pulmonary tuberculosis in India.[4] This duration represents the total symptomatic time and period of infectiousness for a patient with TB.

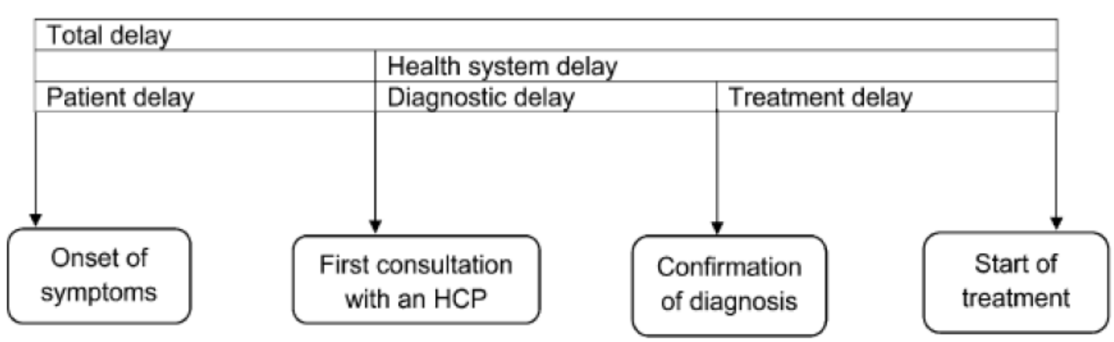
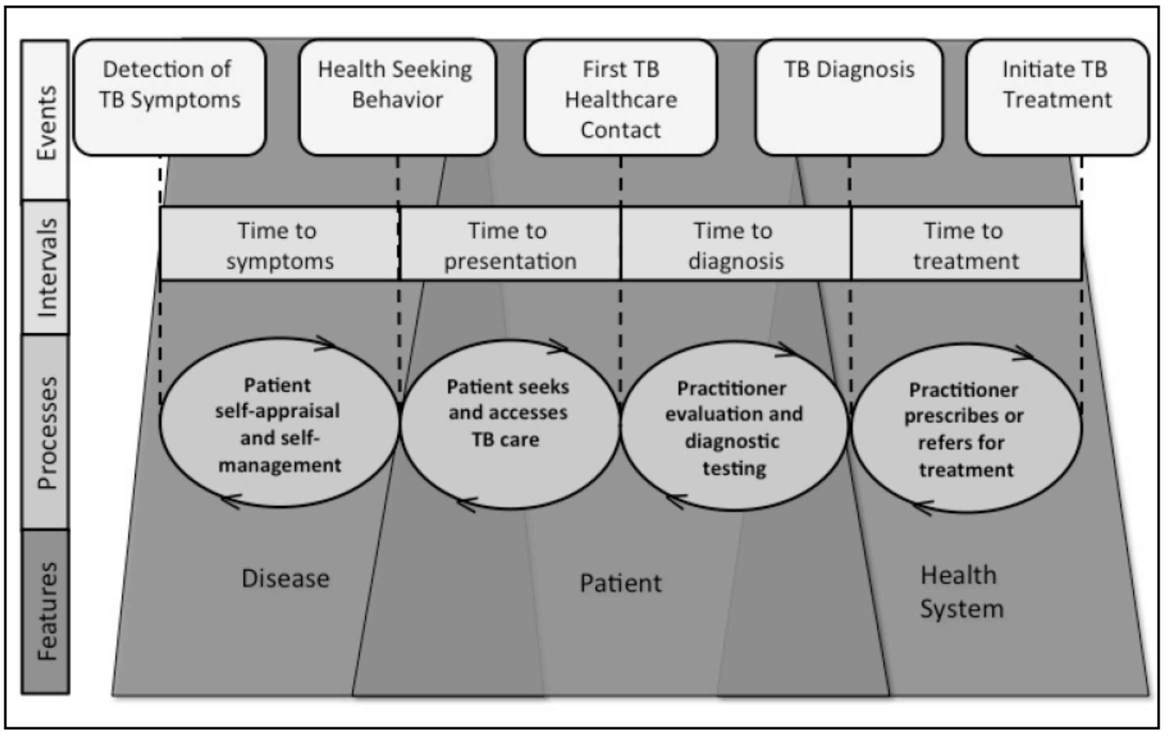


Figure 1 Conceptual framework on definitions of delays (NB: the size/length of components does not represent actual durations). Adapted from Yimer et al.[4] HCP = health care provider.

Figure 1.3: An adapted framework of *The Model of Pathways to Treatment* for Tuberculosis diagnosis.

The Model of Pathways to Treatment by Scott et al.[57] adapted for TB patients seeking care in the urban Indian private sector evaluates events occurring as features of the disease, patient, and health system. The framework illustrates processes that occur within intervals of the pathway that lead to potential event outcomes. The interval time periods may occur in any sequence between events with no starting point, allowing for forward and backward movement, as a patient navigates the health system to obtain diagnosis of TB and initiate anti-TB therapy.



The large number of patients who access the private sector as their first point of healthcare for TB-related symptoms, and the practitioners who see them, represent a key population for intervention to reduce TB transmission in the community. These models provide insight into the potential impact of intervention strategies for TB control by identifying independent features and intervals of pathways to care where a reduction in delay may improve diagnostic and treatment outcomes.

Impact of Novel TB Diagnostic Tools: Scale-Up of Xpert MTB/RIF and Point-of-Care Testing in India

Increased diagnostic capabilities to improve in TB case detection could substantially reduce the gap between notified cases and estimated incidence, while also reducing diagnostic delays.[1] The availability of a rapid, low cost, accurate diagnostic assay for TB that could be used at the point of care would be a major advance in efforts to reach the 2.9 million "missed" TB cases in India.[39] Such point-of-care (POC) tests offer rapid turn-around and communication of results to guide clinical decisions allowing diagnostic testing and follow-up actions to be completed in the same clinical encounter.[53] As TB control programs worldwide are beginning to prioritize molecular diagnostics that are more sensitive than smear microscopy[58], it is imperative to consider implementation of tests for TB that could be deployed at the point-of-care.[53,59] However, strategies for improving TB diagnostic practices in India need to be evidence-based and informed by data in the context of diagnostic pathways where they will be used.[60,61]

India has committed $100 million to scale-up of Xpert within the country[3], but the overall effect of implementing Xpert and other novel diagnostic tools will ultimately depend on deployment to improve the timeliness of effective treatment initiation.[60] Currently, India is using Xpert largely for diagnosing MDR TB among patients known to have TB rather than initial diagnosis of TB.[3] A recent study of Xpert use in decentralized public health settings in India found a 33% increase in the proportion of presumptive pulmonary TB patients with microbiologically confirmed TB and a 39% increase in TB case notification compared to using smear microscopy for initial diagnosis.[62] However, for Xpert and other POC TB diagnostics to reach those who need them, tests must be attractive, accessible, and practical to private practitioners who dominate the healthcare marketplace in India.[37]

Modeling analyses suggest that novel diagnostic tests can impact TB incidence in southeast Asia; however, their effect depends on sensitivity and the manner in which they are deployed.[63] The management of HIV and malaria was transformed by the availability of low-cost POC diagnostic tools, yet the need for POC tests for active pulmonary TB remains unmet contributing to delayed diagnoses that fuel the epidemic in high burden countries like India.[21,59,64] Research into Xpert use as a POC test for TB has demonstrated feasibility in African settings[65], but it remains a high-cost test that requires sophisticated equipment.[64] Further, the use of Xpert for TB diagnosis has not led to improvements in morbidity or mortality, though further research in additional settings is needed to determine the long-term impact[65], though modeling analyses suggest its use may decrease community TB transmission.[21,63] The urine lipoarabinomannan (LAM) lateral flow assay represents a simple, low-cost diagnostic test for TB that can be used at the point of care, but its niche use is limited to screening for HIV-associated pulmonary TB in patients with advanced immunodeficiency.[39,66] Additionally, other nucleic acid amplification tests are emerging in development pipelines building on the technology of Xpert, but with a range of options that allow for selection of tests that best suit local needs.[67] In the Indian setting, these include the portable PCR-based Truenat MTB assay (Molbio Diagnostics, Goa, India) that is intended for use in peripheral settings.[67,68] Nonetheless, an ideal, hypothetical, rapid test that can be deployed simply and closer to the point of care for active screening of TB in the private sector could have a projected 15% impact on reducing TB incidence.[63] Thus, as the RNTCP invests in deploying TB diagnostic tests capable of same-day diagnosis such as Xpert, and NGO-led models work to increase test availability in private laboratories[17,69], mechanisms of public-private cross-referral and regulation are essential to engage private practitioners to have a considerable population-level impact on TB in India.[21]

Conclusions

The RNTCP's plan for "universal access" to quality diagnosis and treatment for all patients with TB in the community recognizes the need to engage private sector providers in TB control efforts, to provide cost offsets to patients diagnosed and treated by private practitioners, and to improve national case notifications.[69] Additionally, as novel technology for diagnosis of active TB becomes increasingly available, it is expected to expand access to medical services, reduce delays in diagnosis, and improve health outcomes.[70] However, these improvements may not have a substantial population-level impact on the TB burden in India if they are not matched by innovation in the health system. A critical element of implementing any novel diagnostic test is to evaluate the existing mechanisms of patient access, as well as the capacity for, and acceptability of, the test among those healthcare providers who would be responsible for using it.[39,53] In this context, several important unanswered questions include the following:

(1) What is the impact of the first healthcare provider consulted on delay to diagnosis among patients diagnosed with TB in the urban Indian private sector?

(2) What are the TB management practices among urban Indian private practitioners and how do these compare to the International Standards for TB Care?

(3) What are the point-of-care testing practices and the priorities for novel point-of-care tests for TB among private practitioners in Chennai, India?

A cross-sectional survey of patients accessing the private sector for TB diagnosis and practitioners who saw at least one patient with TB in the past year was conducted in Chennai, India in collaboration with the Resource Group for Education and Advocacy for Community Health to answer these questions.

Chapter II: How do patients access the private sector in Chennai, India? An evaluation of delays in tuberculosis diagnosis

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This chapter has been accepted as a manuscript and is pending publication with the International Journal of Tuberculosis and Lung Disease.

Abstract

Setting: Diagnosis and treatment of tuberculosis (TB) in India are characterized by heavy private-sector involvement. Delays to treatment remain poorly characterized among patients seeking care in the Indian private sector.

Objective: To assess delays in TB diagnosis and treatment initiation among patients diagnosed in the private sector, and pathways to care in an urban setting.

Design: Cross-sectional survey of 289 consecutive patients who were diagnosed with TB in the private sector and referred for TB treatment through a public-private mix program in Chennai from January 2014 to February 2015.

Results: Among 212 patients with pulmonary TB, 90% first contacted a formal private provider, and 78% were diagnosed by the first or second provider seen after a median of three visits per provider. Median total delay was 51 days (mean 68). Consulting an informal (rather than formally trained) provider first, was associated with a significant increase in total delay (absolute increase: 25.8 days, 95%CI: 9.9-41.7) and in risk of prolonged delay >90 days (aRR 2.5, 95%CI: 1.3-4.5).

Conclusion: Even among patients seeking care in the formal (vs. informal) private sector in Chennai, diagnostic delays are substantial. Novel strategies are required to engage private providers who often serve as the first point of contact.

Introduction

Delays in diagnosis of patients with tuberculosis (TB) are a key driver of transmission worldwide.[1,55] In India, where one thousand people die of TB every day, excessive delays often occur between the onset of TB symptoms, diagnosis of disease, and initiation of anti-TB therapy.[1,2,4] Early diagnosis and effective treatment are critical to reduce TB mortality and stop ongoing transmission.[1,4,17] The Government of India's Revised National Tuberculosis Control Programme (RNTCP) aims to achieve "universal access" to quality diagnosis and treatment for all patients with TB by 2017.[16] To realize this goal, it is important to understand where delays and missed TB diagnoses occur and how to implement diagnostic algorithms to reduce these delays.[21]

India has a complex and heterogeneous healthcare system.[1,4,5] The RNTCP provides access to free TB diagnostic and treatment services in the public sector.[9] However, up to 80% of individuals with long-lasting cough first seek care from the private sector, where unqualified providers and practitioners of alternative health systems outnumber qualified, allopathic doctors.[4,5,13,14] With little collaboration across health sectors, many patients with TB see multiple healthcare providers (HCPs) as they first seek advice from informal private providers, then medical care from formal private HCPs, and eventually get treated under the RNTCP.[4,5,19–21] Other patients seek care exclusively in the private sector; yet, we know very little about the pathways and delays to TB diagnosis and treatment among these patients.[4,20,23] Although the Government of India has made TB case notification mandatory, this practice is rarely followed by private practitioners.[15]

Currently, the RNTCP seeks to better engage the private sector in partnerships for TB treatment (a "public-private mix", or PPM model), offering the opportunity to explore pathways to TB diagnosis among patients who seek care in the private sector.[4,14,18] We therefore undertook a study to evaluate delays in TB diagnosis and treatment initiation among patients who were diagnosed with TB in the private sector and started on treatment in a PPM program in Chennai, India.

Methods

Setting

This study was conducted in Chennai in Tamil Nadu state in India. Chennai was the sixth largest city in India with a population of 4.6 million in 2011, making it the most densely populated city in Tamil Nadu.[71]

Study design and study population

In collaboration with the Resource Group for Education and Advocacy for Community Health (REACH), we conducted a cross-sectional survey of patients accessing the private sector for TB diagnosis. REACH is a non-governmental PPM organization established in 1999 operating in collaboration with Corporation of Chennai to involve private HCPs in the RNTCP.[24] REACH operates four PPM centers located in private hospitals working with a network of private HCPs in Chennai to support patients with TB. In the REACH PPM model, private HCPs refer patients with TB to PPM Centers to receive free DOT under supervision of REACH staff.

Sample selection and data collection

We recruited patients who were diagnosed with TB and referred to REACH PPM Centers in Chennai by private HCPs (i.e., not referred by pharmacists or government/RNTCP practitioners). From January 2014 through February 2015, we consecutively enrolled consenting patients from all four REACH PPM Centers and conducted interviews using a structured questionnaire. All adult patients with pulmonary (PTB), extra-pulmonary, or drug-resistant TB receiving treatment for six months or less at a REACH PPM Center were eligible for interview. Trained study staff performed interviews privately at REACH PPM Centers or via telephone at the patients' discretion. The patient interviews collected information on patient socio-demographics and clinical TB disease; intervals between symptom onset, TB diagnosis, and treatment; and used multiple prompts to understand the characteristics, sequence and type of providers consulted. The type of provider and dates of symptom onset, health-seeking encounters, diagnosis, and treatment initiation were collected by patient recall using multiple questions and/or from patient treatment cards when available from the patient. Family members frequently accompanied patients during the interview though they were not the subjects of the interview.

Definitions

We utilized the conceptual framework proposed in a systematic review by Sreeramareddy and colleagues to shape our definitions of delay.[4] Our primary outcome was total symptomatic time, or total delay, defined as the interval from patient-reported symptom onset to TB treatment initiation. We defined prolonged total delay as duration >90 days, which was the 75th percentile in our sample, and extremely prolonged delay as duration >150 days, which was the 90th percentile in our sample.

For this analysis, we classified an HCP as any person or facility approached by the patient for relief from their health problem.[20] Formal HCPs include allopathic doctors and non-allopathic AYUSH (includes ayurveda, yoga and naturopathy, unani, siddha, homeopathy) practitioners[13] with formal training who practice in the public or private sector. The public sector comprises all formal HCPs working in government facilities. The private sector includes all formal HCPs practicing in a private clinic or hospital, and informal HCPs including traditional healers, unlicensed practitioners without formal medical training, and chemists or pharmacists. Patients diagnosed in a private hospital who then began treatment at the REACH PPM Center within the hospital were counted as diagnosed by a formal private HCP. Patients diagnosed by a formal private HCP in a separate clinic and then referred to a REACH PPM Center for treatment were considered to have PPM as a separate, final provider. Patients were classified as having ≤2 visits per HCP if the number of visits was unknown.

Statistical analysis

We performed univariate analyses to assess differences in proportion for categorical variables using Pearson's chi-squared and Fisher's exact test. Among patients with PTB, we examined patient pathways to TB treatment by HCP type, sector, and sequence using the median [interquartile range]. We assessed differences in median total delay, measured continuously in days, using the non-parametric Wilcoxon test. We explored patient pathway characteristics specified a priori for differences in mean total delay using generalized linear models with a gamma distribution, identity link function, and robust standard errors. We adjusted for potential clustering of health-seeking behaviors by PPM Center location. We investigated risk factors for prolonged delay comparing patients with total delay >90 days in multivariable Poisson regression models with robust standard errors (as log-binomial models failed to converge).[72]

Results

Socio-demographic and clinical disease characteristics

Among the 479 patients initiated on treatment through REACH PPM services during the study period, 289 patients were referred from private practitioners and thus eligible for the study. No patients declined the interview. Of these 289 patients interviews, the median patient age was 42 years. The majority of patients interviewed were men (56%), literate (87%), employed (54%), and lived in households earning <8,000 rupees per month (52%, approximately US$130). There were 212 patients with pulmonary TB, among them 67% reported cough lasting ≥30 days prior to presentation to an HCP. Only 16% of patients were previously treated for TB, and 29% reported a family member having received TB treatment. (Table 1).

Health seeking characteristics

Of all patients, 243 (84%) first sought care in the formal private sector (240 allopathic and 3 AYUSH providers), 28 (10%) in the informal private sector (15 pharmacists and 13 traditional healers or other providers), and 18 (6%) in the public sector. Patients saw a mean of 2 HCPs prior to TB diagnosis; only 10% saw more than 4 HCPs. However, patients visited their first and second HCPs a median of 3 times each prior to being diagnosed with TB. For the first HCP, median distance traveled was one kilometer and median total cost incurred was 1000 rupees (approximately US$16). In univariate analysis, employment, cough duration, first healthcare sector consulted, first HCP type, number of HCPs seen, and total cost were significantly associated with total delay >90 days from symptom onset to treatment initiation. Cough duration, site of TB disease, and number of HCPs seen prior were significantly associated with total delay >150 days. (Table 1).

Patient pathways to care for pulmonary TB

Of 212 patients with PTB, we identified 34 unique pathways through the private sector to TB diagnosis and treatment (Figure 1). Over three-quarters (165/212) of patients were diagnosed with TB after two or fewer providers. Diagnostic tests performed included chest x-ray (57%), blood test (46%), sputum smear (31%), others (16%), and CT scan (13%). The majority (167/212) of patients sought care exclusively from formal private HCPs. Over one-quarter (60/212) of patients were diagnosed by the first provider accessed and then referred to REACH PPM for TB treatment for a median total delay of 50 days, and a median of 3 visits per provider as above. The median interval between health seeking encounters with the first and second HCP was 10 days [IQR 5-30]. Only 5% (11/212) of patients first sought care in the public sector and were subsequently diagnosed with TB by a private HCP before being referred to REACH for treatment. Over half (119/212) of the patients reported the provider they first contacted was their contact for all medical needs. Additionally, 65% (138/212) of patients were not aware that free TB services were available at government health centers.

Patient and Health system delays

Among those with PTB, the median patient delay was 10 days (mean 25, range 0-339) from patient-reported symptom onset to first HCP contact; 23% waited >30 days to seek care after symptom onset. Median diagnostic delay from the first HCP encounter to confirmation of TB diagnosis was 28 days (mean 44, range 0-322). Median treatment delay from confirmation of TB diagnosis to TB treatment initiation was 2 days (mean 5, range 0-75). The median combined health system delay from first HCP contact to TB treatment initiation was 30 days (mean 46, range 0-323); 63% of patients experienced delays >14 days and 45% experienced delays >30 days.

Total delay

The median total delay from symptom onset to TB treatment initiation for patients with PTB was 52 days (mean 69, range 3-341). In adjusted analyses, patients who first consulted an informal HCP experienced a significant increase in mean total delay (mean increase: 25.8 days, 95%CI: 9.9-41.7). Mean total delay also increased if patients sought care from >2 HCPs (20.3 days) or were unemployed (17.9 days). (Table 2).

Predictors of prolonged total delay

Among patients with PTB who first consulted the formal private sector, a longer mean patient delay was noted, while the health system delay was longer among patients in the informal sector (Figure 2). Mean total delay for patients who first sought care in the public sector was 66 days (95%CI: 39-94; median 64 [IQR 47-77), similar to patients accessing the private sector (mean 65, 95%CI: 57-74; median 48 [IQR 31-82]). For patients who first sought care in the informal private sector, mean total delay (96 days, 95%CI: 66-126; median 73 [IQR 63-111]) was longer compared to those seeking care in the formal private sector (difference in mean total delay: 31 days, 95%CI: 14.2-47.6, $P<0.001$) and public sector (difference in mean total delay: 30 days, 95%CI: 1.5-58.4, $P=0.04$).

Nearly one-quarter of patients with PTB (46/212) experienced prolonged total delay >90 days and 7% (15/212) experienced extremely prolonged delay >150 days. In adjusted analyses, patients who first sought care from an informal HCP had 2.5 times the risk of having delay >90 days compared to formal HCPs (aRR 2.5, 95%CI: 1.3-4.5) (Table 3). Additionally, unemployment, no family history of TB, seeing >2 HCPs, and total spent with first HCP significantly increased the risk of delay >90 days.

Discussion

This study of patients diagnosed with TB in India's private sector demonstrates that prolonged delays are more common among patients accessing informal, rather than formal, providers as the first contact in their pathways to care. Among patients with PTB, first seeking care from an informal provider is associated with an almost four-week increase total symptomatic time prior to treatment initiation. Although prolonged delays in diagnosis are often attributed to patients seeking care from multiple HCPs in the private sector, 78% of patients in this study were diagnosed with PTB by the first or second provider they saw after relatively few visits per HCP. Nonetheless, delays remain substantial even among those who only saw formal providers; patients had a mean of three visits prior to TB diagnosis and health system delay exceeding 40 days, suggesting that even qualified HCPs may utilize non-specific or empiric therapies prior to testing for TB.

Our study is among the first to characterize patients diagnosed with TB in the Indian private sector. The majority of previous research assessing delays in pathways to care was conducted among patients treated under the RNTCP in government health centers as their first action in seeking care or after referral from other (private) practitioners.[4,5] However, more than three-quarters of our patient sample sought care exclusively from formal private HCPs, and only 11% (24/212) ever accessed RNTCP services. We found 84% of patients first consulted a formal private HCP, greater than the 30-78% in previous studies in urban settings and lower than the 0-47% of patients that first consulted a government provider.[4,5,12,20,23] Compared to patients treated at RNTCP Centers, these patients treated under PPM had higher levels literacy[20,23], household income[4,23], and lived in closer proximity to their first providers.[4,20,23]

Among these patients who were treated via PPM, the total delays reported were substantially lower than those (>90 days) among patients first seeking private-sector care in a previous study of patients ultimately treated by the RNTCP.[5] Relative to prior estimates in the literature, health system delay in our study was shorter among patients who first consulted formal private HCPs but longer among patients who first consulted government HCPs.[4,20,23] The majority of these PPM patients only saw one or two HCPs, fewer than the median of nearly three in a recent systematic review[4], suggesting PPM may have reduced the number of providers required to be seen before diagnosis.[5,73] However, the prolonged delays and multiple visits required prior to TB diagnosis are consistent with a recent systematic review on quality of TB care in India[41], which showed approximately half of HCPs knew that persons with cough lasting 2-3 weeks should be evaluated for TB, and two-thirds used smear microscopy for patients with presumptive TB. Although smear microscopy and chest x-ray were commonly used in diagnosis, the Indian system of patient referral to private labs for testing causes substantial delays during the diagnostic process.[52] Usage of inappropriate TB diagnostic tests documented among private practitioners in India may further contribute to delays in TB diagnosis, development of drug resistance, and ongoing TB transmission.[17,41,45] A recent study of standardized patients seeking care for TB symptoms in the private sector found that only 5% of private practitioners ordered any sputum testing.[74] While improved diagnostic tests, including Xpert MTB/RIF, are being scaled up in both public[62] and private sectors[18], use is still limited. A parallel study of private practitioners in Chennai found that only 15% ordered Xpert MTB/RIF for TB diagnosis in the past year.[75]

Our findings highlight the need to improve diagnostic capacity to reduce delays in the private sector as the first point of patient care. Our study was not designed to evaluate specific interventions for reducing delays, but modeling analyses suggest that both increased access to improved diagnostic tests, such as Xpert MTB/RIF, and increased cross-sector referrals could substantially reduce the number of visits by TB patients that fail to result in TB diagnosis and treatment in India.[21] Additionally, a demonstration study implementing Xpert MTB/RIF as the initial TB diagnostic test in decentralized public health settings throughout India increased case-notification rates of all bacteriologically confirmed TB.[62] The RNTCP and Initiative for Promoting Affordable Quality TB Tests are working to increase availability of WHO-approved TB diagnostic tests in both public-sector microscopy centers and private laboratories used by formal HCPs.[17,69] The RNTCP also seeks to engage the private sector through innovative PPM schemes, which have increased TB case notification by 12-98% in previous studies of public-private partnerships in India.[8,76,77] By implementing a referral system for informal HCPs and giving formal private HCPs access to WHO-approved diagnostics, it may be possible to reduce diagnostic delays and thus decrease the burden of TB transmission in the community. Future studies should investigate the impact of specific interventions.

As an early investigation into patient pathways to TB diagnosis in the Indian private sector, this study has a number of limitations. First, this patient population may not be representative of other patients who access the private sector for TB care but are not referred to PPM. Patients that are not referred to PPM remain under private TB treatment may have higher income, greater privacy concerns, or less TB knowledge, or providers that are not aware of REACH PPM and thus they undergo private treatment. Additionally, we limited inclusion to patients referred to PPM by private practitioners (practicing in standalone private clinics, private hospitals, or private hospitals containing REACH PPM Centers) to evaluate patients accessing the private sector in Chennai, though REACH receives PPM referrals from other sources. Our findings may also not generalize to patients diagnosed in the public sector [5]. Second, similar to most other studies of diagnostic delay, our study relied on patient recall for data collection.[4] We conducted patient interviews within six months of starting TB treatment potentially affecting patient recall and biasing results to over or underestimate the effect of the first provider consulted on total delay, though we used calendars and interview reference cards to reduce recall bias in our data. Finally, we did not collect data on smoking or alcohol usage, two known confounders of delay, as our interviewers felt this was an invasion of patient privacy that would damage interviewer-patient rapport. Future studies should address the challenges in accessing the private sector to gather more representative data on this patient population.

Conclusion

Our study provides insight about delays in TB diagnosis and treatment among patients who received TB care in the Indian private sector. The pathways to care for TB in India are diverse, but most patients treated in PPM are linked to care after two HCPs or less in the private sector. However, total delays to diagnosis remain substantial. Patients who first seek care in the informal private sector do so quickly after symptoms develop, but then experience prolonged health system delays. Engaging informal and formal private HCPs to improve their capacity to rapidly diagnose TB is critical to reduce total symptomatic time and thus TB transmission.

Acknowledgements

We express our deepest thanks to the entire staff at REACH for their collaboration and assistance in conducting this study. We are also thankful to the patients who agreed to be interviewed for this study. This study was supported in part by a grant by the Bill & Melinda Gates Foundation (grant OPP1061487). Madhukar Pai is a recipient of a Tier 1 Canada Research Chair from the Canadian Institutes of Health Research. David Dowdy is supported in part by the B. Frank and Kathleen Polk Assistant Professorship in Epidemiology at the Johns Hopkins Bloomberg School of Public Health.

Tables and Figures

Table 2.1. Socio-demographic and care-seeking characteristics of patients with pulmonary and extra-pulmonary TB in the private sector in Chennai, India.

Characteristic	Total (n=289) n (%)	Total Delay >90 days (n=70) n(%)	*P**	Total Delay >150 days (n=28) n(%)	*P**
Age, median [IQR]	42 [28-53]	42 [27-53]	0.76	38 [28-50]	0.46
≥ 45 years	127 (44)	29 (41)	0.63	10 (36)	0.36
Male	163 (56)	36 (51)	0.35	12 (43)	0.13
Education					
Illiterate	38 (13)	11 (16)	0.69	2 (7)	0.60
Literate, less than Primary	40 (14)	7 (10)		4 (14)	
Primary and/or Secondary	135 (47)	33 (47)		12 (43)	
Senior Secondary and/or Graduate	76 (26)	19 (27)		10 (36)	
Employment					
Unemployed	43 (15)	13 (19)	**0.05**	4 (14)	0.60
Other	89 (31)	28 (40)		11 (40)	
Employed	157 (54)	29 (41)		13 (46)	
Ave. household income/month					
< Rs. 4000	38 (13)	9 (13)	0.82	1 (3)	0.31
Rs. 4001 - Rs. 8,000	112 (39)	30 (43)		10 (36)	
Rs. 8,001 - 10,000	64 (22)	13 (19)		7 (25)	
> Rs. 10,001	75 (26)	18 (25)		10 (36)	
Cough duration prior to diagnosis, median [IQR]	30 [28-90]	90 [45-120]	**<0.001**	105 [30-165]	**0.01**
Cough ≥30 days	156 (54)	41 (59)	**<0.01**	14 (50)	0.11
History of previous TB treatment	38 (13)	7 (10)	0.42	4 (14)	0.77
Family member ever treated for TB	80 (28)	13 (19)	**0.05**	9 (32)	0.66
Site of TB Disease					
Extra-Pulmonary TB	77 (27)	24 (34)	0.10	13 (46)	**0.01**
Pulmonary TB	212 (73)	46 (66)		15 (54)	
First Healthcare Sector Consulted					
Government	18 (6)	6 (8)	0.07	4 (14)	0.18
Private	243 (84)	53 (76)		21 (75)	
Informal or Pharmacy	28 (10)	11 (16)		3 (11)	
First Healthcare Provider Type					
Informal	28 (10)	12 (17)	**0.02**	24 (86)	0.33
Formal Allopathic or AYUSH	261 (90)	58 (83)		4 (14)	
HCPs seen prior to diagnosis, median [IQR]	2 [1- 2]	2 [2-3]	**<0.001**	2 [2-3]	**<0.01**
1 HCP	117 (40)	16 (23)	**<0.001**	5 (18)	**0.01**
2 HCPs	106 (37)	27 (39)		11 (40)	
3 HCPs	36 (13)	12 (17)		6 (21)	
≥4 HCPs	30 (10)	15 (21)		6 (21)	
Visits to 1st HCP, median [IQR]†	3 [1-5]	3 [2-5]	0.14	4 [3-6]	0.23
>2 visits	88 (30)	26 (37)	0.16	11 (39)	0.29
Distance to 1st HCP, median [IQR]	1 [0- 3]	1 [1-4]	0.26	1 [1-4]	0.43
>2 km	73 (25)	23 (33)	0.09	10 (36)	0.18
Total cost incurred with 1st HCP, median [IQR]	1000 [300-3000]	1500 [500-5000]	**0.04**	1500 [500-5500]	0.20
Less than Rs. 400	88 (30)	16 (23)	0.10	6 (21)	0.36
Rs. 401 to Rs. 1000	77 (27)	15 (22)		6 (21)	
Rs. 1001 to Rs. 3000	57 (20)	17 (24)		6 (21)	
Greater than Rs. 3000	67 (23)	22 (31)		10 (36)	

*Pearson's chi-squared (or Fisher's exact) test for categorical variables comparing those with ≤90 and >90 days, and 150 days; Wilcoxon test for continuous variables. †Patients were classified as having ≤2 visits to the first HCP if the number of visits was unknown.

Figure 2.1. Pathways and days of total delay from symptom onset to TB diagnosis and treatment initiation among patients being treated for pulmonary TB at a PPM Center in Chennai.

PTB Patients n (%)	Provider Number 1 →	2 →	3 →	4 →	5	Median Total Delay [IQR]	Range
Total n=212						52 [33-83]	(3-341)
60 (28)	PD	PPM				50 [28-72]	(3-341)
38 (18)	PD	PD				57 [40-88]	(14-316)
22 (10)	PD					37 [20-83]	(7-180)
21 (10)	PD	PD	PPM			46 [34-69]	(13-150)
10 (5)	PD	PD	PD			54 [30-108]	(17-199)
6 (3)	GD	PD	PPM			56 [31-73]	(8-77)
5 (2)	PD	PD	PD	PD		35 [27-71]	(21-163)
5 (2)	PD	PD	PD	PPM		54 [51-71]	(36-83)
4 (2)	PH	PPM				68 [60-117]	(60-117)
3 (1)	GD	PD				77 [63-170]	(63-170)
3 (1)	PD	PD	GD	PD		49 [37-58]	(37-58)
3 (1)	PH	PD	PPM			41 [31-69]	(31-69)
2 (1)	PA	PD				41 [4-78]	(4-78)
2 (1)	PD	GD	PD	PPM		75 [40-110]	(40-110)
2 (1)	PD	GD	PD			174 [25-322]	(25-322)
2 (1)	PD	GD	PPM			31 [22-40]	(22-40)
2 (1)	PD	PD	PD	PD	PPM	116 [97-135]	(97-135)
2 (1)	PH	PD	PD	PD		104 [98-111]	(98-111)
2 (1)	PH	PD				92 [73-110]	(73-110)
2 (1)	T	PD	PPM			235 [147-323]	(147-323)
2 (1)	T	PD				109 [73-145]	(73-145)
2 (1)	T	PPM				25 [19-31]	(19-31)
1 (0.5)	GD	PD	PD			72	--
1 (0.5)	GD	PPM				47	--
1 (0.5)	PA	PPM				59	--
1 (0.5)	PD	PD	GD	PD	PPM	48	--
1 (0.5)‡	PD	PD	PD	PD	PD	98	--
1 (0.5)	PD	PD	PD	PD	PD	144	--
1 (0.5)	PD	PH	PD	PD	PD	34	--
1 (0.5)	PH	GD	PD	PPM		70	--
1 (0.5)	PH	PD	PD	PPM		176	--
1 (0.5)‡	T	GD	PD	PD	PD	92	--
1 (0.5)	T	GD	PD	PPM		63	--
1 (0.5)	T	PD	PD	PD	PPM	108	--

Legend: Each line represents a unique pathway taken by patients to arrive at health facilities with REACH PPM Centers. Each box represents a different healthcare provider seen by patients, though each box may represent more than one provider encounter. For each provider, multiple encounters were often performed. Patients who were diagnosed in a private hospital and then began treatment with the REACH PPM Center within the hospital are noted as PD for the final encounter. Patients who were diagnosed by a PD in a separate clinic who were then referred to a REACH PPM Center for treatment are noted as PPM for the final encounter. Abbreviations: PD= Formal Qualified Private doctor, PPM= REACH Public-Private Mix, GD= Formal Qualified Government doctor, PH= Informal Pharmacy, PA= Formal Qualified Private AYUSH, IN= Informal unqualified non-medical, Traditional, Other.

‡Patient pathways show only first 5 HCP encounters for these patients; full paths were 8 HCPs = PD→ PD→ PD→ PD→ PD→ PA→ PD→ PPM; and 6 HCPs = T→ GD→ PD→ PD→ PD→ PPM.

Table 2.2. Predictors of differences in duration of total delay days to diagnosis and treatment initiation among patients with pulmonary TB (n=212) in Chennai.

Characteristic	Total PTB n (%) (n=212)	Median Total Delay [IQR]φ	Mean Total Delay (SD)	Unadjusted Difference in Mean Total Delay (95% CI)	*P*	Adjusted Difference in Mean Total Delay (95% CI)‡	*P*
Age <45 years	111 (52)	48 [30-83]	68.3 (61)	Ref		Ref	
≥45 years	101 (48)	58 [34-86]	69.1 (55)	0.8 (-6.8 - 8.4)	0.83	-4.1 (-16.1 - 7.9)	0.50
Female	73 (34)	53 [36-90]	69.7 (55)	Ref		Ref	
Male	139 (66)	51 [32-82]	68.2 (60)	-1.5 (-23.4 - 20.4)	0.89	6.1 (-14.3 - 26.6)	0.56
Education up to Primary	118 (56)	49 [31-78]	66.3 (59)	Ref		Ref	
Secondary or greater	94 (44)	54 [37-93]	71.7 (56)	5.4 (-4.3 - 15.0)	0.28	1.5 (-8.3 - 11.2)	0.77
Unemployed	80 (38)	64 [36-100]*	79.2 (63)	Ref		Ref	
Employed	132 (62)	48 [31-73]	62.4 (54)	-16.7 (-39.8 - 6.3)	0.15	**-17.9 (-32.1 - -3.7)**	**0.01**
Ave. monthly household income <Rs. 8,001	114 (54)	51 [32-88]	68.3 (57)	Ref		--	
≥Rs. 8,001	98 (46)	54 [33-78]	69.2 (60)	0.9 (-17.5 - 19.3)	0.92	--	
History of TB treatment	34 (16)	54 [36-86]	73.4 (62)	5.6 (-16.7 - 27.9)	0.62	11.1 (-1.3 - 23.5)	0.08
No previous TB treatment	178 (84)	51 [32-83]	67.8 (57)	Ref		Ref	
Family member treated for TB	61 (29)	46 [32-71]	62.2 (61)	-9.1 (-19.1 - 1.0)	0.08	-4.0 (-16.1 - 8.1)	0.52
No family treated for TB	151 (71)	54 [33-94]	71.3 (57)	Ref		Ref	
First healthcare provider informal	22 (10)	73 [63-111]**	96.4 (66)	**30.9 (14.2 - 47.6)**	**<0.001**	**25.8 (9.9 - 41.7)**	**<0.01**
Formal allopathic or AYUSH	190 (90)	49 [32-78]	65.5 (56)	Ref		Ref	
HCPs seen prior to diagnosis ≤2	165 (78)	48 [31-77]**	63.8 (56)	Ref		Ref	
>2 HCPs	47 (22)	71 [37-108]	85.8 (63)	**22.1 (8.8 - 35.4)**	**<0.01**	**20.3 (5.4 - 35.2)**	**<0.01**
Visits to 1st HCP ≤2 or unknown†	153 (72)	51 [34-78]	65.8 (53)	Ref		Ref	
>2 visits	59 (28)	59 [30-94]	76.3 (69)	10.5 (-7.3 - 28.3)	0.25	7.2 (-7.5 - 22.0)	0.34
Distance to 1st HCP ≤2 km	159 (75)	53 [33-82]	67.0 (57)	Ref		Ref	
>2 km	53 (25)	49 [33-93]	73.5 (62)	6.5 (-1.5 - 14.6)	0.11	0.6 (-9.2 - 10.3)	0.91
Total cost for 1st HCP <Rs. 1000	109 (51)	53 [33-77]	63.1 (48)	Ref		Ref	
≥Rs. 1000	103 (49)	51 [31-97]	74.5 (67)	11.4 (-5.5 - 28.3)	0.18	5.3 (-11.8 - 22.3)	0.54

‡Adjusted for all other variables with data in this column.
φMedians assessed using non-parametric Wilcoxon test for equality where *P <0.05, and **P<0.01.
†Patients were classified as having ≤2 visits to the first HCP if the number of visits was unknown.

Figure 2.2. Distribution of mean patient, health system, and total delays by the first healthcare sector consulted after symptom onset among patients with pulmonary TB (n=212) in Chennai.

Legend: Patient delay was defined as the interval between onset of symptoms suggestive of PTB and patient's first contact with an HCP; Health system delay is time from the patient's first contact with any HCP to the initiation of anti-TB treatment; Total delay is time from symptom onset to the initiation of anti-TB treatment. Crossbars represent 95% confidence intervals for mean delays. Median patient, health system, and total delay for patients first seeking care from: public sector practitioners were 10, 44, and 64 days; formal private providers were 10, 26, and 48 days; informal private providers 9, 72, and 73 days; overall was 10, 30, and 52 days, respectively. The 11 patients who first sought care in the public sector were eventually diagnosed by private practitioners; patients diagnosed by public sector providers were not included in this study.

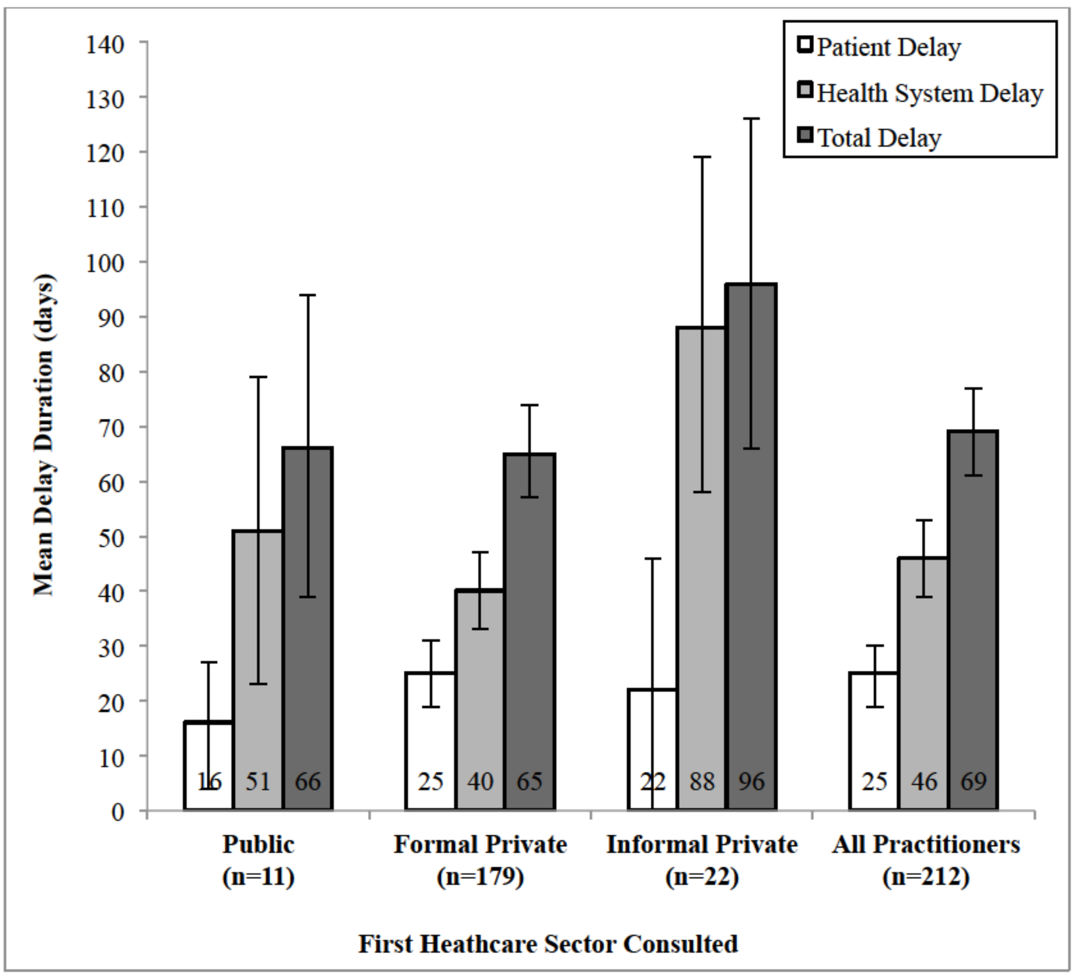

Table 2.3. Risk factors for prolonged delay >90 days to diagnosis and treatment initiation among patients with pulmonary TB in Chennai.

Characteristic	Total Delay >90 days n (%) (n=46)	>90 Days Unadjusted RR (95% CI)	*P*	>90 Days Adjusted RR (95% CI)*	*P*
Age ≥ 45 years	22 (48)	1.1 (0.6 - 1.8)	0.86	0.9 (0.5 - 1.6)	0.66
Male	29 (63)	0.9 (0.3 - 2.4)	0.83	1.4 (0.5 - 4.3)	0.56
Education Secondary or greater	23 (50)	1.3 (0.8 - 1.9)	0.25	1.2 (0.7 - 1.9)	0.51
Employed	22 (48)	0.5 (0.3 - 1.1)	0.09	**0.5 (0.2 - 1.0)**	**0.04**
History of previous TB treatment	7 (15)	1.0 (0.5 - 1.8)	0.94	1.2 (0.9 - 1.5)	0.18
Family member ever treated for TB	7 (15)	**0.4 (0.3 - 0.7)**	**<0.001**	**0.5 (0.3 - 0.9)**	**0.02**
Informal first HCP	10 (22)	**2.4 (1.6 - 3.8)**	**<0.001**	**2.5 (1.3 - 4.5)**	**<0.01**
Saw >2 HCPs prior to diagnosis	17 (37)	**2.0 (1.4 - 3.0)**	**<0.001**	**1.7 (1.3 - 2.3)**	**<0.001**
Visited 1st HCP >2 times†	15 (33)	1.3 (0.9 - 1.8)	0.18	1.0 (0.7 - 1.4)	0.97
Distance to 1st HCP >2 km	14 (30)	1.3 (0.9 - 1.8)	0.17	1.1 (0.7 - 1.8)	0.68
Total cost for 1st HCP ≥Rs. 1000	29 (63)	**1.8 (1.3 - 2.5)**	**<0.001**	**1.9 (1.4 - 2.5)**	**<0.001**

*Adjusted for all other variables with data in this column.

†Patients were classified as having ≤2 visits to the first HCP if the number of visits was unknown.

Transition to Chapter III

The previous manuscript demonstrates the extensive diagnostic delays that patients experience even when seeking care in the formal private sector in Chennai. Notably, patients who consulted an informal provider as their first healthcare contact experienced a significant increase of more than three weeks of total delay from symptom onset to TB treatment initiation. The risk of a prolonged total delay exceeding 90 days was also significantly increased when an informal provider was the first point of care consulted. However, the specific practitioner practices that contributed to delays in diagnosis among patients eventually treated in a public-private mix program remain unclear among both informal and formal practitioners in the private sector. A further limitation of the previous study is that it fails to link patients with the specific practitioners that were consulted on the patient's pathway to care, thus prohibiting an evaluation of the practitioners' TB management practices. To address these concerns, we surveyed formal, qualified, allopathic practitioners practicing in the private sector in Chennai who had seen at least one patient with TB in the year prior interview. This cross-sectional study, described in the next chapter, examines practitioner-reported diagnostic and treatment practices for new patients with active pulmonary TB and benchmarks the appropriateness of these practices against the International Standards for TB Care.

Chapter III: How do urban Indian private practitioners diagnose and treat tuberculosis? A cross-sectional study in Chennai

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This chapter has had revisions requested and is under further peer review for publication with the journal PLOS ONE.

Abstract

Setting: Private practitioners are frequently the first point of healthcare contact for patients with tuberculosis (TB) in India. Inappropriate TB management practices among private practitioners may contribute to delayed TB diagnosis and generate drug resistance. However, these practices are not well understood. We evaluated diagnostic and treatment practices for active TB and benchmarked practices against International Standards for TB Care (ISTC) among private medical practitioners in Chennai.

Design: A cross-sectional survey of 228 practitioners practicing in the private sector from January 2014 to February 2015 in Chennai city who saw at least one TB patient in the previous year. Practitioners were randomly selected from both the general community and a list of practitioners who referred patients to a public-private mix program for TB treatment in Chennai. Practitioners were interviewed using standardized questionnaires.

Results: Among 228 private practitioners, a median of 12 (IQR 4-28) patients with TB were seen per year. Of 10 ISTC standards evaluated, the median of standards adhered to was 4.0 (IQR 3.0-6.0). Chest physicians reported greater median ISTC adherence than other MD and MS practitioners (score 7.0 vs. 4.0, $P<0.001$), or MBBS practitioners (score 7.0 vs. 4.0, $P<0.001$). Only 52% of all practitioners sent >5% of patients with cough for TB testing, 83% used smear microscopy for diagnosis, 33% monitored treatment response, and 22% notified TB cases to authorities. Of 228 practitioners, 68 reported referring all patients with new pulmonary TB for treatment, while 160 listed 27 different regimens; 78% (125/160) prescribed a regimen classified as consistent with ISTC. Appropriate Treatment practices differed significantly between chest physicians and other MD and MS practitioners (54% vs. 87%, $P<0.001$).

Conclusion: TB management practices in India's urban private sector are heterogeneous and often suboptimal. Private providers must be better engaged to improve diagnostic capacity and decrease TB transmission in the community.

Introduction

India accounts for approximately one-quarter of the world's 9 million incident tuberculosis (TB) cases every year.[1] The TB epidemic in India is complicated by the fragmented healthcare delivery system that includes practitioners in the public and private sectors.[1,4,5] Although the Government of India's Revised National TB Control Program (RNTCP) provides free TB healthcare services, up to 85% of patients experiencing TB-related symptoms in urban Indian settings first seek healthcare from private practitioners[4,78], and about 50% ultimately get TB treatment outside the RNTCP.[10,41]

Based on the International Standards for TB Care (ISTC)[47], India has recently published Standards for TB Care in India to ensure quality practices in both private and public sectors.[38] However, usage of inappropriate TB diagnostic and treatment practices, and lack of adherence to the ISTC continues to be documented among private practitioners in India[10,22,41,45,50], potentially contributing to delays in TB diagnosis, development of drug resistance, and ongoing TB transmission.[17,41,45]

Currently, there are several ongoing efforts to engage and improve the quality of TB care in the private sector. These include NGO-led models[24] and Private Provider Interface Agency projects in select cities[37] to engage private practitioners in TB care and the Initiative for Promoting Affordable Quality TB Tests (IPAQT) to increase availability of appropriate diagnostic tests in private laboratories.[17,69] In this context, it is helpful to assess urban private practitioners' practices for diagnosing and treating patients with active pulmonary TB.

Methods

Setting

Chennai is the sixth largest city in India with a population of 4.6 million.[71] There are an estimated 550 hospitals registered in Chennai and approximately 10,000 doctors working in the city, though the public-private affiliations are unknown.[79] We collaborated with the Resource Group for Education and Advocacy for Community Health (REACH) to conduct a cross-sectional survey of private medical practitioners (PPs) who saw at least one patient with TB in the past year. Established in 1999, REACH is a non-governmental public-private mix (PPM) organization collaborating with the Corporation of Chennai to involve PPs in the RNTCP.[24] REACH works with a network PPs that refer patients with TB to their four PPM Centers, located in private hospitals in Chennai, to receive free TB treatment under supervision of REACH staff or community supporters.

Sample selection and data collection

We recruited qualified, allopathic medical practitioners of all specialties working in the urban private sector. From January 2014 through February 2015, we enrolled consenting PPs from the ten 2011 census tract zones in Chennai and conducted interviews using a structured questionnaire. To identify PPs for recruitment, we used a listing of all city streets in Chennai to randomly select up to 50 street corners per zone. REACH staff started at each selected corner and used a structured movement algorithm until an eligible PP was located to recruit a maximum of five PPs per health facility and minimum of five PPs per zone. Additionally, we randomly selected PPs from REACH's database of PPM-referring PPs. All qualified PPs with formal medical training who diagnosed at least one patient with pulmonary TB (PTB) in the year prior to recruitment were eligible. After a PP agreed to be interviewed for the study, up to three attempts were made to complete the interview. Trained study staff performed the interviews privately in the PPs' offices. Structured interviews lasted approximately 15-20 minutes and collected data on PPs' socio-demographic information (excluding age, which was deemed potentially identifiable during ethical review), patient volume, TB disease knowledge, diagnostic and treatment practices, practitioner-reported intervals between patient presentation, diagnosis, and treatment, and their patient referral practices. PPs were asked about the drug regimen that they prescribed for their new adult patients of 60 kilograms with PTB using an open-ended format. PPs were subsequently asked to give the average total duration of treatment for PTB from a set of standardized responses. PP-reported education was used to assess level of training by comparing those with higher levels of training (i.e., medical doctor (MD) or master of surgery degree (MS)), to those with undergraduate bachelor of medicine and bachelor of surgery degrees (MBBS). We also compared chest specialists against those without such specialty training.

International standards for TB care (ISTC) 3rd Edition

The ISTC include 21 standards of diagnosis, treatment, and other practices that describe a widely accepted level of TB care.[45,47] We evaluated PP-reported practices against 10 ISTC standards (those for which comparative data were collected). An ISTC score was calculated by summing the total number of standards for which PP-reported practices agreed with ISTC recommendations. For example, a score of seven means the PP reported practices that were in accordance with seven of the 10 standards evaluated.

Statistical analysis

Our primary comparisons were of PPs seeing >12 TB patients per year (versus ≤12), and of MD and MS specialty physicians versus MBBS practitioners. We assessed univariate differences in proportion using Pearson's (or Fisher's exact) test and differences in medians for continuous variables using the non-parametric Wilcoxon test. Differences in mean patient volume and mean ISTC score were explored using linear regression models with robust standard errors to account for clustering within health facilities. We estimated multivariable associations with self-reported rapid TB diagnosis ($\leq$7 days after patient presentation) using Poisson regression models with robust standard errors to give relative risks, as the outcome was not rare and log-binomial models failed to converge.[72]

Ethical considerations

This study protocol was approved by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board, McGill University Health Center Biomedical Research Ethics Review Board, and REACH Independent Ethics Committee. Written informed consent was obtained from all practitioners prior to being interviewed for the study.

Results

Practitioner socio-demographic profiles

Of the 249 eligible private practitioners approached to participate, 228 were interviewed (92% participation rate). Among these, 161 (71%) were randomly selected within Chennai city and 67 (29%) from REACH's PPM database. The majority of PPs were men (70%) and median practice experience was 20 years (IQR 15-30) (Table 1). Over half (60%) of PPs had medical degrees and 36% had MBBS undergraduate degrees; 17% were chest specialist physicians. Overall, 56% of PPs worked in private standalone clinics, 34% in private hospitals, and 10% in both government and private healthcare settings. The mean annual patient volume in our sample was 6,387 (median 6,000 [IQR 4,000-8,000]) and 30 patients with TB (median 12 [IQR 4-28]). Chest physicians saw a mean of 92 (95%CI: 59-125) TB patients per year, versus 20 (95%CI: 15-25) among other MD/MS physicians, and 14 (95%CI: 8-20) among MBBS practitioners (Fig. 1). Providers who saw more than 12 patients with TB per year were more likely to be specialists, have more practice experience, work in a private hospital, know about Indian TB policies, initiate TB treatment without referral to the public sector, and obtain knowledge about TB from such sources as medical journals (Table 1).

Diagnostic testing practices

Sputum smear microscopy was commonly used for diagnosis of active TB (83% (188/228); 95%CI: 77-87), as was chest X-ray (97% (222/228); 95%CI: 95-99). Practitioners reported using non-microbiological tests not generally recommended for active TB diagnosis as part of their diagnostic processsuite including erythrocyte sedimentation rate (ESR) (54% (122/228); 95%CI: 45-60) and tuberculin skin testing (TST; 45% (103/228); 95%CI: 39-52) (Table 2). Nearly one-quarter (51/228, 22%) of practitioners reported using only smear and chest X-ray for TB diagnosis, while 17% (38/228) used only smear, chest X-ray, and ESR and 17% (39/228) reported using only the aforementioned tests plus TST. Molecular testing (e.g., Xpert MTB/RIF) and TB culture were much less commonly employed (15% (35/228); 95%CI: 11-20, and 15% (33/228); 95%CI: 10-19, respectively). Usage of serological antibody tests and IGRAs for diagnosis of active PTB was reportedly low among all practitioners (2% (5/228); 95%CI: 0-4, and 6% (14/228); 95%CI: 3-9, respectively). Among those practitioners that reported using Xpert and culture for TB diagnosis, 83% (29/35) and 55% (18/33) of practitioners, respectively, reported sending patients to private labs for diagnostic testing. The majority of practitioners reported sending patients to private labs for other diagnostic tests they used including: 57% (107/188) for smear, 65% (144/222) for chest X-ray, 70% (85/122) for ESR, 73% (75/103) for TST, and 93% (13/14) for IGRAs. Chest physicians and other MD/MS practitioners were more likely to report using smear microscopy (86% vs. 75%) and Xpert MTB/RIF (23% vs. 1%) for TB diagnosis than MBBS practitioners.

Health system delay and predictors of rapid TB diagnosis

The mean health system delay from patient presentation to TB diagnosis for patients with PTB was 7 days (median 6, range 1-22). Sixty-one percent of PPs reported rapid diagnosis within 7 days of patient presentation. PPs who used smear as the initial diagnostic test reported an average health system delay of 5 days, compared to 10 days among those who did not use smear at the first visit. In a comparison of shorter versus longer PP-reported delays (($\leq$7 days vs. >7 days) from patient presentation to TB diagnosis, the reported use of smear microscopy as the initial diagnostic test was the only variable associated with more rapid PP-reported diagnosis, with a relative risk of 3.2 (95%CI: 2.3-4.3) for diagnosis within one week.

ISTC and TB treatment practices

Adherence to the ISTC was generally inadequate (Table 3) with an overall median ISTC adherence score of 4.0 (IQR 3.0-6.0). Among PPs who saw patients with cough lasting >2 weeks in the week prior to being interviewed, only 52% sent more than 5% of these patients for TB laboratory testing. Only 25% of all PPs used culture or molecular testing for patients with clinical suspicion of TB, 33% monitored treatment response, and 22% notified TB cases to public authorities. There were no significant differences in use of smear microscopy by patient volume, health facility type, or health sector. Chest physicians and other MD/MS practitioners with higher levels of training reported greater adherence to all standards except for direct observation of treatment (Table 3). Median ISTC scores were significantly higher among chest physicians than other MD/MS practitioners (7.0 vs. 4.0, P<0.001), or MBBS practitioners (7.0 vs. 4.0, P<0.001), reflecting greater reported adherence (Fig. 2).

Of 228 responding PPs, 160 listed 27 different treatment regimens for PTB, while the other 68 referred all patients for TB treatment. Prescriptions inconsistent with ISTC included incorrect treatment durations (16/160), drug regimens lacking pyrazinamide and/or ethambutol (10/160) or including quinolones or injectable second-line agents (10/160). Of 160 PP's, only 78% prescribed a regimen consisting of (a) 6 to 8 months of isoniazid and rifampin, (b) at least one of pyrazinamide or ethambutol, and (c) no second-line agents for a hypothetical patient with new PTB. Appropriate prescription practices were significantly lower among chest physicians compared to MD/MS practitioners (54% vs. 87%, P<0.001), but not among providers that saw over 12 TB patients per year versus those who saw less (80% vs. 77%). Only 40% of PPs utilized DOTS-based approaches to ensure treatment adherence, including referral to RNTCP DOTS (55/228), REACH PPM (30/228), or both (7/228). One-third of all PPs reported using sputum smear, culture, or Xpert to monitor patients taking PTB treatment.

Discussion

Diagnostic and treatment practices were variable in this study of qualified private practitioners who diagnosed at least one patient with TB in the past year in the urban Indian private sector. As examples, less than half of surveyed practitioners tested patients with long-lasting cough for TB, nearly half used TST as part of their suite of diagnostic tests for active TB, less than one-quarter notified patients treated for TB to public health authorities, and over one-fifth used treatment regimens that were either too short, lacked critical drugs, or included second-line agents for patients with new pulmonary TB. NGO-led efforts to engage PPs in PPM partnerships in Chennai[24] have emphasized appropriate TB diagnostic practices, including usage of smear microscopy. Nonetheless, given that most patients with TB in urban India are diagnosed and treated in the private sector, the underutilization of Xpert and low adherence to ISTC highlights the need for widespread engagement of private practitioners for adequate TB control.

Prior studies of practitioners in India have consistently documented variable quality of TB care in the private sector.[10,22,24,41,45,50,80] In a recent systematic review, only half of the healthcare providers from both the public and private sectors tested patients with long-lasting cough for suspicion of TB, and two-thirds used smear microscopy for patients with presumptive TB.[41] Over three-quarters of providers in this study prescribed a treatment regimen potentially consistent with ISTC guidelines for new patients with PTB, higher than in other explorations of private sector TB treatment practices.[10,22,41] Our findings suggest that TB diagnostic, treatment, and notification practices in a randomly recruited sample of urban PPs remain inadequate. These findings are particularly concerning given reports of poor treatment outcomes and emerging drug resistance in India, especially in urban areas.[41–44]

This study is among the first to assess PP practices by patient volume and practitioner specialty.[42] We found that chest specialists and those seeing higher volumes of TB patients had somewhat more appropriate diagnostic, treatment, and notification practices, though critical gaps still remain, even with efforts by the RNTCP to make TB a notifiable disease.[14,17] We also describe a comprehensive evaluation of diagnostic practices and diagnostic delays among urban private practitioners, including a strong association between use of sputum smear microscopy for initial diagnosis and more rapid treatment initiation. These findings contribute to the growing body of evidence in support of stronger dissemination, implementation, and enforcement of the ISTC and Standards for TB Care in India for all Indian practitioners.

As a cross-sectional study of PP practices, this study has several important limitations. We included only formally trained qualified practitioners and providers referring to a public-private mix organization. While we were thereby able to attain a high response rate, our results are not representative of all urban private practitioners providing TB care (including unqualified providers and practitioners of alternative health systems) and likely overestimate the quality of care provided in Chennai as a whole. We restricted interviews to PPs who had diagnosed at least one patient with TB in the past year to reduce recall bias. Further, we used structured questionnaires for data collection, which allowed us to collect a larger volume of data in the short times available to interview PPs; however, for describing actual practices, vignette-based questions may be preferred.[42] Lastly, our survey captures PPs' knowledge and self-reported practices, but not actual practice. A recent study from India has used, for the first time, standardized patients to overcome this limitation, and has reported poor adherence to standards using this approach showing a wide gap between what providers know, and what they do in real practice.[74]

Our findings emphasize the TB burden and management challenges to practitioners in the urban private sector with several implications for policy. First, TB diagnosis and treatment patterns were variable, and while chest physicians and high-volume providers reported greater ISTC adherence in some aspects (e.g., use of microbiological tests), they reported lower adherence in others (e.g., prescription patterns). This widespread variability in practices highlights the need for broad-based education and involvement at all levels of the private sector. Practices in the informal sector and among lower-volume providers are expected to be substantially worse.[74] Second, practitioners who reported the shortest health system delays utilized smear microscopy as the initial TB diagnostic test, demonstrating the importance of performing TB-specific microbiological tests at the first patient visit to decrease diagnostic delay and TB transmission. Finally, as the RNTCP invests in deploying TB diagnostic tests capable of same-day diagnosis such as Xpert, and IPAQT works to increase test availability in private laboratories, mechanisms of public-private cross-referral and regulation are essential to engage PPs and link their patients to guideline-based TB care.[16,63] Modeling analyses suggest that such private-public mechanisms and availability of quality diagnostics can have a substantial population-level impact on TB in India.[32]

Conclusion

In conclusion, our study shows variability in TB diagnostic and treatment practices in India's urban private sector, including among qualified providers, high-volume providers, chest physicians, and those referring to public-private mix organizations for TB treatment. In particular, screening of individuals with persistent cough, use of TB-specific tests at the initial encounter, expanded use of molecular tests and treatment monitoring, and prescription of appropriate first-line regimens for PTB should be emphasized. Innovative approaches to TB control in India must include broad-based engagement of the private sector if TB elimination in India is to become a reality in the foreseeable future.

Acknowledgements

We express our deepest gratitude to the entire staff at REACH for their collaboration and assistance in conducting this study. We are also thankful to the practitioners who agreed to be interviewed for this study. This study was supported in part by a grant by the Bill & Melinda Gates Foundation (grant OPP1061487). Madhukar Pai is a recipient of a Tier 1 Canada Research Chair from the Canadian Institutes of Health Research. David Dowdy is supported in part by the B. Frank and Kathleen Polk Assistant Professorship in Epidemiology at the Johns Hopkins Bloomberg School of Public Health.

Tables and Figures

Table 3.1. Socio-demographic profile and management practices for all forms of TB among private practitioners in Chennai, India (n=228).

		Patients Diagnosed with TB in Past Year		
Characteristic	**Total (n=228) n(%)**	**≤12 Patients (n=110) n(%)**	**>12 Patients (n=118) n(%)**	***P****
Male	160 (70)	67 (61)	93 (79)	**<0.01**
Education				
MBBS	81 (36)	53 (48)	28 (24)	**<0.001**
MS	10 (4)	4 (4)	6 (5)	
MD	137 (60)	53 (48)	84 (71)	
Years practicing, *median [IQR]*	20 [15-30]	20 [12-30]	25 [15-30]	**0.03**
Practitioner specialty				
General medicine	153 (67)	83 (76)	70 (59)	**<0.001**
Chest/Pulmonary specialist	39 (17)	6 (5)	33 (28)	
Other**	36 (16)	21 (19)	15 (13)	
Type of facility				
Government with private practice in evening	22 (10)	13 (12)	9 (8)	**<0.001**
Private standalone clinic or polyclinic	129 (56)	76 (69)	53 (45)	
Private hospital or nursing home	77 (34)	21 (19)	56 (47)	
Action for pulmonary TB diagnosis				
Refer to RNTCP or PPM DOTS center	97 (42)	55 (50)	42 (36)	**0.03**
Treatment in private sector	131 (58)	55 (50)	76 (64)	
Knowledge of TB notification requirement***	214 (94)	99 (90)	115 (98)	**0.02**
Notification training	118 (52)	39 (36)	79 (67)	**<0.001**
Notified RNCTP of any TB patients	49 (22)	20 (18)	29 (25)	0.24
Knowledge of serological antibody test ban	126 (55)	48 (44)	78 (66)	**<0.001**
Awareness of PPM schemes via RNTCP	81 (35)	37 (34)	44 (37)	0.57
Source of information on TB***				
No sources/not PP's specialty	39 (17)	28 (16)	11 (9)	**<0.001**
Journals, books, newspaper, newsletters	82 (36)	36 (33)	46 (39)	0.33
Internet	71 (31)	33 (30)	38 (32)	0.72
CME or workshop	99 (43)	45 (41)	54 (46)	0.46
Medical representative or colleague	25 (11)	15 (14)	10 (9)	0.21

*Pearson's chi-squared (or Fisher's exact) test for categorical variables comparing practitioners who diagnosed 5 patients or less with TB to those who diagnosed more than 5 patients with TB in the past year; Wilcoxon test for continuous variables.

**Other MD and MS practitioner specialties included Obstetrics and gynecology (n=15), Pediatrician (n=5), Surgeon (General/Orthopedic/Ophthalmologic) (n=4), Diabetes Specialist (n=6), Ear nose and throat (n=2), Oncologist (n=1), and Radiologist (n=1).

***Categories are not mutually exclusive.

Figure 3.1. Mean annual volume of patients with tuberculosis (TB) in the past year according to practitioner training among private practitioners in Chennai.

Legend: Dark bars show the mean (with 95% confidence intervals shown as error bars) number of patients for whom a laboratory test was sent specifically to diagnose TB in the past year, as reported by private practitioners with each level of training. Light bars show the mean number of people reported to be diagnosed with TB in that year. Data table shows the mean number of total patients seen in the past year.

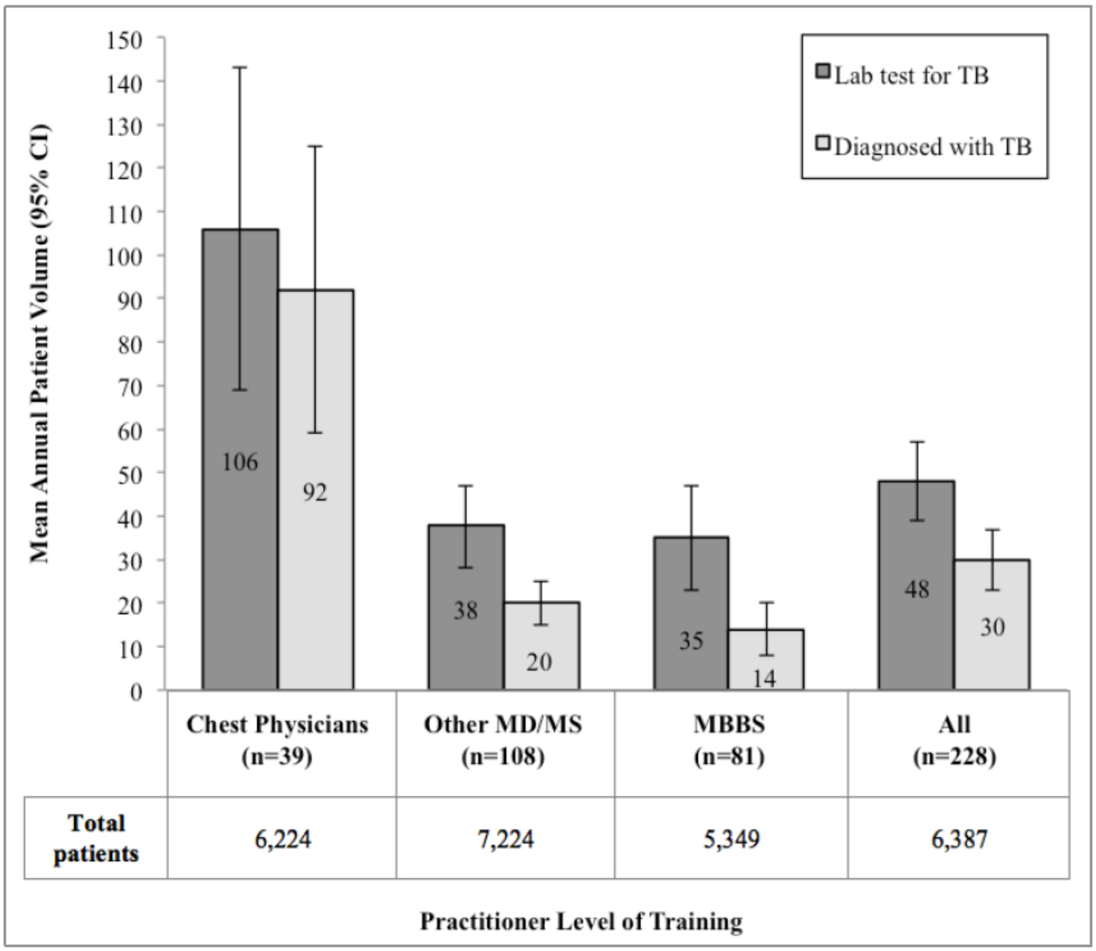


Table 3.2. Diagnostic testing practices according to practitioner specialty type among private practitioners in Chennai, India (n=228).

Diagnostic Test	Mean (SD) tests per month	Used in TB diagnosis n(%) All (n=228)	Practitioner Level of Training: Chest Physicians (n=39)	Other MD/MS (n=108)*	MBBS (n=81)	*P***	Ordered at first patient visit n(%) All (n=228)	Practitioner Level of Training: Chest Physicians (n=39)	Other MD/MS (n=108)*	MBBS (n=81)	*P***
Chest X–Ray	3.2 (4)	222 (97)	36 (92)	106 (98)	80 (99)	0.43	135 (59)	31 (80)	64 (59)	40 (49)	**0.03**
Sputum Smear	3.5 (4)	188 (83)	36 (92)	91 (84)	61 (75)	**0.04**	115 (50)	31 (80)	54 (50)	30 (37)	**<0.01**
Biopsy or FNAC	1.2 (3)	150 (66)	34 (87)	80 (74)	36 (44)	**<0.001**	108 (47)	31 (80)	53 (49)	24 (30)	**<0.001**
ESR	3.2 (4)	122 (54)	12 (31)	70 (65)	40 (49)	0.35	68 (30)	9 (23)	41 (38)	18 (22)	0.06
Mantoux Skin Test	2.4 (4)	103 (45)	12 (31)	50 (46)	41 (51)	0.22	61 (27)	12 (31)	29 (27)	20 (25)	0.60
Differential or Total Lymphocyte Count	4.1 (4)	71 (31)	8 (21)	45 (42)	18 (22)	**0.03**	45 (20)	7 (18)	28 (26)	10 (12)	**0.04**
MRI or CT Scan	1.1 (4)	53 (23)	17 (44)	26 (24)	10 (12)	**<0.01**	39 (17)	14 (36)	16 (15)	9 (11)	0.07
Molecular Test (Xpert or PCR)	1.0 (4)	35 (15)	23 (59)	11 (10)	1 (1)	**<0.001**	28 (12)	22 (56)	5 (5)	1 (1)	**<0.001**
Sputum Culture	1.4 (2)	33 (15)	9 (23)	9 (8)	15 (19)	0.20	25 (11)	7 (18)	7 (7)	11 (14)	0.35
Ultrasound	0.4 (1)	32 (14)	5 (13)	17 (16)	10 (12)	0.59	24 (11)	5 (13)	13 (12)	6 (7)	0.37
Drug Susceptibility Testing	0.8 (3)	19 (8)	16 (41)	2 (2)	1 (1)	**<0.01**	17 (8)	14 (36)	2 (2)	1 (1)	**<0.01**
Interferon Gamma Release Assays	2.8 (4)	14 (6)	3 (8)	7 (7)	4 (5)	0.78	5 (2)	1 (3)	3 (3)	1 (1)	0.66
Serologic Antibody Tests	1.0 (1)	5 (2)	1 (3)	1 (1)	3 (4)	0.35	2 (1)	0 (0)	1 (1)	1 (1)	0.99

*Other MD/MS practitioner specialties included Other/unknown (n=61), Obstetrics and gynecology (n=15), General internal medicine (n=11), Pediatrician (n=5), Surgeon (General/Orthopedic/Ophthalmologic) (n=4), Diabetes Specialist (n=6), Ear nose and throat (n=2), Oncologist (n=1), and Radiologist (n=1).
**Pearson's chi-squared (or Fisher's exact) test for categorical variables comparing chest physicians plus other MD/MS practitioners versus MBBS practitioners in the private sector.

Table 3.3. Evaluation of private practitioners' practices and concordance with the International Standards for TB Care, Chennai, India.

International Standards for TB Care	Mechanism for evaluation*	Concordance with ISTC n(%)				
			Practitioner Level of Training			
		All (n=228)	Chest Physicians (n=39)	Other MD/MS (n=108)	MBBS (n=81)	*P***
Diagnostic Practices						
ISTC 1: Evaluation of cough lasting ≥2 weeks to suspect TB†	*Sends >5% patients with cough >2 weeks for lab testing*	93 (52)	23 (73)	38 (44)	32 (53)	**0.03**
ISTC 2: Evaluation of sputum specimens for those with CXR findings suggestive of TB	*Uses smear and chest x-ray for PTB diagnosis*	185 (81)	35 (90)	89 (82)	61 (75)	0.09
ISTC 3: Assessment of ≥2 sputum specimens for microbiological examination	*Uses smear for PTB*	188 (83)	36 (92)	91 (84)	61 (75)	**0.04**
ISTC 4: Examination of appropriate specimens (and diagnostic tests) for presumptive EP TB	*Uses biopsy/FNAC to obtain specimens for EP-TB diagnostic testing*	150 (66)	34 (87)	80 (74)	36 (44)	**<0.001**
ISTC 5: Diagnosis of smear-negative TB based on bacterial culture or molecular testing	*Uses culture or Xpert MTB/RIF for TB diagnosis*	57 (25)	25 (64)	16 (15)	16 (20)	0.17
Treatment and Management Practices						
ISTC 8: Treatment with 2HRZE and 4HR fixed doses for new TB patients*Ŧ	*Regimen of H, R, and either Z or E for 6-8 months for hypothetical patient with new PTB*	125 (78)	20 (54)	67 (87)	38 (83)	0.53
ISTC 9: Patient-centered approach to treatment; includes DOTS for treatment administration	*Supported treatment via RNTCP, PPM, or PPM Community DOTS reported for PTB*	92 (40)	3 (8)	39 (36)	50 (62)	**<0.001**
ISTC 10: Assessment of patient response to therapy for pulmonary TB with sputum microscopy	*Performs treatment monitoring using smear, culture, or Xpert MTB/RIF*	76 (33)	27 (69)	23 (21)	26 (32)	0.77
ISTC 11: Drug-resistance testing using molecular tests and/or bacterial culture based on patient history and risk factors	*Assesses MDR based on appropriate risk factors*	43 (19)	29 (74)	8 (7)	6 (7)	**<0.001**
Addressing HIV Infection and other Co-morbid Conditions						
ISTC 14: HIV testing and counseling recommended to all patients with suspected TB	*Performs HIV testing done Always or Often for TB patients*	87 (38)	25 (64)	34 (32)	28 (35)	0.41
Standards for Public Health						
ISTC 21: All providers must report TB cases and treatment outcomes to public health authorities.	*Reports notifying TB cases to RNTCP in the past year*	49 (22)	16 (41)	16 (15)	17 (21)	0.89
Mean ISTC score, mean(SD)Ŧ**	*Sum out of 10 standards evaluated*	4.5 (1.9)	6.5 (2.0)	4.0 (1.5)	4.1 (1.8)	**0.03**

Table 3.3. Footnotes:

*Abbreviations used: Smear= sputum smear microscopy, PTB= pulmonary TB, EP-TB= extrapulmonary TB, FNAC=fine needle aspiration cytology, DOTS= directly observed therapy short course. H=isoniazid, R=rifampicin, Z=pyrazinamide, and E=ethambutol, irrespective of whether the regimen was daily or intermittent.

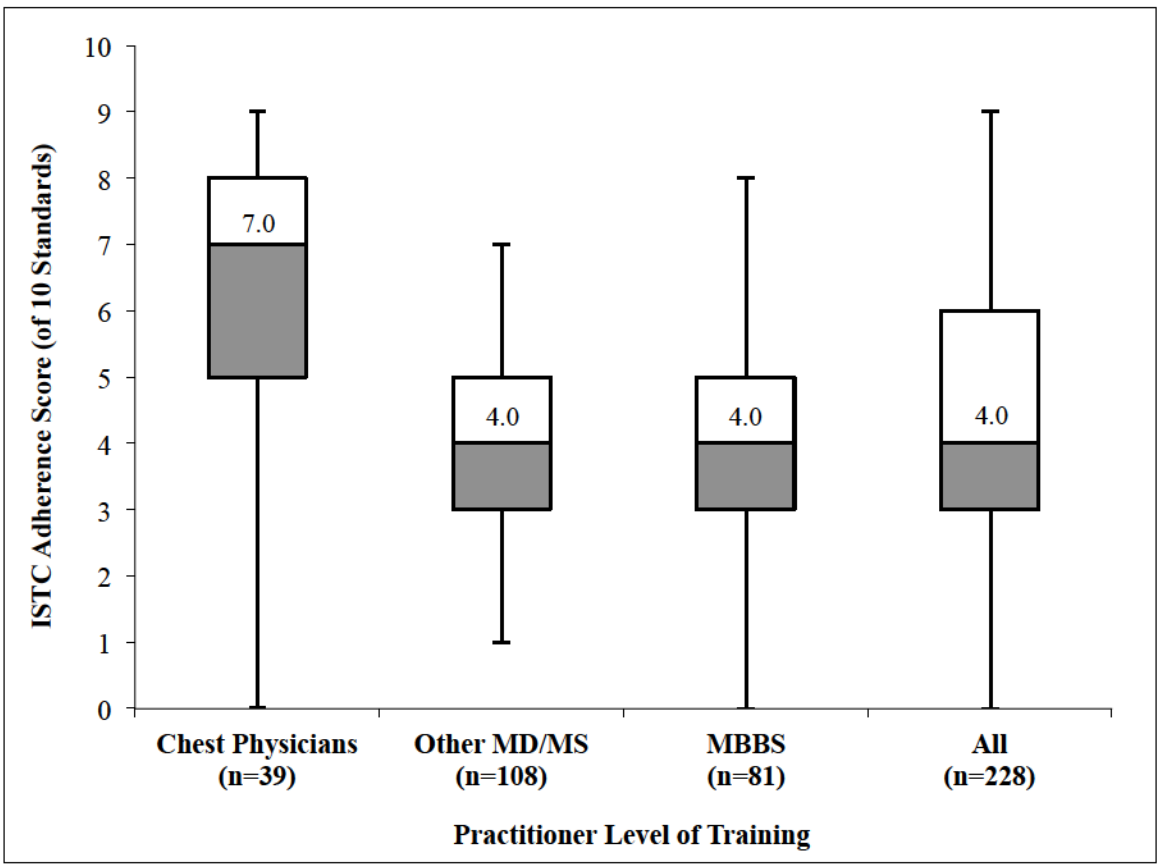
**Pearson's chi-squared (or Fisher's exact) test for categorical variables comparing chest physicians plus other MD/MS practitioners versus MBBS practitioners in the private sector; mean ISTC score assessed using linear regression.

†Data for 50 private practitioners who did not report seeing any patients with prolonged cough were excluded from evaluation for ISTC1 and considered non-adherent for calculation of the ISTC score.

‡Data for 68 private practitioners who refer all patients with TB for treatment were excluded from evaluation for ISTC8. This standard was excluded from calculation of the ISTC score.

Figure 3.2. Distribution of aggregate practitioner-reported adherence scores to ten of the International Standards for TB Care by practitioner training in the private sector in Chennai.

Legend: Practitioner-reported practices were evaluated against 10 of the International Standards for TB Care (ISTC) for which comparative data were collected, and an ISTC score was calculated by summing the total number of standards for which reported practices agreed with ISTC recommendations. For example, a score of seven means the corresponding practitioner reported practices in accordance with seven of the 10 standards that we evaluated. Of 10 standards evaluated, the overall median ISTC adherence score was 4.0 (IQR 3.0-6.0). Chest physicians reported greater adherence than other MD/MS practitioners with higher levels of training (median 7.0 vs. 4.0, P<0.001), or MBBS practitioners (7.0 vs. 4.0, P<0.001). Box plots depict the median (central line), interquartile range (box), and range (whiskers).



Transition to Chapter IV

The previous two chapters illustrate the dichotomy of the patient-provider relationship in TB diagnosis and treatment in India. While patient delay in seeking healthcare for TB-related symptoms plays a role in delaying TB diagnosis and thus total delay, the varied and inadequate TB management practices employed by practitioners in the Indian private sector contribute to prolonged health systems delay and total symptomatic time. Practitioners who used sputum smear microscopy as the initial TB diagnostic test reported the shortest health systems delays in this study, highlighting the importance of TB-specific microbiological tests that can be performed at a low cost in lower levels of the healthcare system. However, overall practices for TB diagnosis, treatment, and notification among these private providers were suboptimal giving cause for concern. Stronger private sector engagement and regulation is crucial to improve diagnostic capacity of private providers. TB diagnostic tests that can be used at the point of care to deliver same-day clinical are essential to decrease total delay, increase case detection, and reduce community TB transmission. The next chapter addresses private practitioners current usage of point-of-care tests and their attitudes and priorities for future TB diagnostic assays that may be used at the point-of-care.

Chapter IV: Usage of rapid, point-of-care assays by private practitioners in Chennai, India: Priorities for tuberculosis diagnostic testing

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This chapter has been submitted as a manuscript and is under peer review for publication with the journal PLOS ONE.

Abstract

Setting: Private practitioners are frequently the first point of healthcare contact for patients with tuberculosis (TB) in India, but their diagnostic practices and preferences are not well understood. As new molecular tests are developed for point-of-care (POC) diagnosis of TB, it is imperative to understand existing practices and preferences for POC testing in the Indian private sector.

Objective: To evaluate rapid testing practices and identify priorities for novel POC TB tests among private practitioners.

Design: We conducted a cross-sectional survey of 228 practitioners practicing in the private sector from January 2014 to February 2015 in Chennai city who saw at least one TB patient in the previous year. Practitioners were randomly selected from both the general community and a list of practitioners who referred patients to a public-private mix program for TB treatment. We used standardized questionnaires to collect data on current practices related to point-of-care diagnosis and interest in hypothetical POC tests.

Results: Among 228 private practitioners, about half (48%) utilized any rapid testing in their current practice. The most commonly used POC tests were glucose (43%), pregnancy (21%), and malaria (5%). Providers using POC tests were more likely to work in hospitals (56% vs. 43%, $P=0.05$) and less likely to be chest specialists (21% vs. 54%, $P<0.001$). Only half (51%) of providers would use a hypothetical POC test for TB that was accurate, equipment-free, and took 20 minutes to complete. Chest specialists were half as likely to express interest in performing the hypothetical POC TB test in-house as other practitioners (aPR 0.5, 95%CI: 0.2-0.9).

Conclusion: Interest in POC testing for TB was surprisingly low among practitioners in India's urban private sector, particularly among chest specialty physicians. As novel POC tests for TB are developed and scaled up, attention must be paid to integrating these diagnostics into healthcare providers' routine practice.

Introduction

Despite efforts to increase case detection, 3 million new tuberculosis (TB) cases are not notified to national TB programs each year; over one-quarter (27%) of these "missed cases" are estimated to occur in India.[1,31] Improvements in case detection through increased diagnostic capabilities could substantially reduce the gap between notified cases and estimated incidence.[1] In particular, a rapid, low cost, accurate diagnostic assay for TB that can be used at the point of care to make rapid treatment decisions would be a major advance in efforts to reach these individuals.[40] Target product profiles for such POC tests have been developed and published.[81]

The Government of India's Revised National TB Control Program (RNTCP) provides free TB healthcare services; however, up to 85% of patients experiencing TB-related symptoms in urban Indian settings first seek healthcare in the private sector.[4,5,78] Thus, any efforts to implement novel TB diagnostic tests in India (and other similar countries) would need to engage private practitioners. As TB control programs worldwide begin to prioritize molecular diagnostics that are more sensitive than smear microscopy[58], it is imperative to consider the implementation of tests for TB that could be deployed at the point-of-care.[53,59]

A critical element of implementing any novel diagnostic test is to evaluate existing capacity for, and acceptability of, the test among those healthcare providers who would be responsible for using it.[39,53] For example, if primary care providers are already using rapid tests for diseases such as malaria and HIV, then they may be more likely to adopt a novel POC TB test in future. In this context, we sought to evaluate point-of-care (POC) testing practices and to identify priorities for novel POC tests for TB among private practitioners in Chennai, India.

Methods

Setting

Chennai is the sixth largest city in India with a population of 4.6 million.[71] We collaborated with the Resource Group for Education and Advocacy for Community Health (REACH) to perform cross-sectional interviews with urban private medical practitioners (PPs) in Chennai. As a non-governmental public-private mix (PPM) organization, REACH collaborates with Corporation of Chennai to involve PPs in the RNTCP.[24] Through advocacy and outreach efforts, REACH networks with PPs in Chennai that refer patients with TB to REACH's four PPM Centers located in private hospitals. Patients referred to REACH receive free TB treatment with supervision by REACH staff or community supporters.

Sample selection and data collection

From January 2014 through February 2015, we recruited and enrolled qualified, allopathic medical practitioners of all specialties working in the private sector in Chennai. REACH study staff used a structured movement algorithm to recruit a maximum of five PPs per health facility and minimum of five PPs in each of Chennai's ten 2011 census tract zones. We also randomly recruited PPs from REACH's database of PPM-referring PPs. All consenting, qualified PPs with formal medical training who diagnosed at least one patient with pulmonary TB (PTB) in the year prior to recruitment were eligible for interview. Up to three attempts were made to complete the interview after a PP agreed to participate. The structured interviews, performed privately in the PPs' offices by trained study staff, lasted 15 to 20 minutes and included PP socio-demographic information (with the exception of age, which was deemed to be potentially identifiable during ethical review), self-reported education (medical doctor/MD, master of surgery/MS, or bachelor of medicine and surgery/MBBS degrees), patient volume, clinical specialty, TB disease knowledge, and diagnostic and treatment practices including POC testing practices. Interviewers asked practitioners about POC testing practices for pregnancy, glucose, HIV, TB antibody, malaria, syphilis, hepatitis, dengue, and typhoid using reference cards listing the tests.

Priorities for a novel point-of-care test

As part of the interview, PPs were asked about a hypothetical POC test for TB "*that could be used to replace the tests that [they] currently use. This test could potentially be done rapidly in [their] clinic, like a pregnancy test or blood glucose test,*" and was described as accurate, taking 20 minutes to perform, and requiring no equipment. PPs were asked if they would perform this test in their clinic (versus sending patients out to a lab or not performing it), and about the maximum amount they would be willing to pay to use this POC test for most patients with symptoms of TB.

Statistical analysis

We assessed univariate differences in proportion using Pearson's (or Fisher's exact) test. We evaluated differences in medians for continuous variables using the non-parametric Wilcoxon test. To estimate univariate and multivariable associations with self-reported preference to use a new POC test for TB in-house, we used Poisson regression models with robust standard errors to calculate prevalence ratios, as the outcome was not rare and log-binomial models failed to converge.[72] We examined collinearity using variance inflation factors, which were below 1.5 for all covariates included in the model.

Results

Description of population and point-of-care testing practices

Among 249 eligible PPs recruited, 228 (92%) completed the interview. Of these, 161 (71%) were randomly selected within Chennai city and 67 (29%) were randomly selected from REACH's PPM database. More than half (56%) of PPs worked in private standalone clinics, and 17% were chest specialist physicians (Table 1). The median number of TB patients seen per year was 12 [IQR 4-28]: 65 [IQR 20-125] among chest specialists versus 8 [IQR 4-20] among other practitioners (P<0.001). Just under half (110/228, 48%) of all PPs utilized any POC tests in their clinics; these included glucose (43%), pregnancy (21%), malaria (5%), hepatitis (4%), dengue (4%), typhoid (4%), and HIV (2%) POC tests. Providers who used POC tests were more likely to be women, work in a private hospital, have fewer years of practice experience, and be general medicine practitioners or other specialists (Table 1). Among practitioners who used point-of-care testing, the median volume was 38 POC tests [IQR 15-100] per month, median turnaround time was 5 minutes [IQR 3-5], and median cost to patients was 50 INR [IQR 50-88] per test (approximately US$0.79) (Table 2). Support staff or nurses performed 55% (60/110) of POC tests, while practitioners interpreted the majority (98/110, 89%) of test results. Only one-quarter (27/110, 24%) of PPs kept records of the POC test results.

Barriers for use of hypothetical point-of-care tests

When asked about major barriers to performing any POC tests in their clinics, chest physicians cited time constraints as their primary barrier (69%, versus 40% of other practitioners, P<0.001), whereas other practitioners also cited the availability of nearby lab services (56%, versus 21% of chest specialists, P<0.001) and the lack of an attached lab (24%, versus 8% of chest specialists, P=0.03) (Figure 1). There were no significant differences in the PP-reported challenges to using POC tests by patient volume or current POC test usage. Those PPs working in hospitals were substantially less likely to express concern about lack of lab services compared to those in private standalone clinics (39% vs. 57%, P=0.01), though they also reported greater time management challenges (57% vs. 35%, P<0.01).

Interest in a point-of-care test for TB

Approximately one-tenth (24/228, 11%) of PPs were not interested in any POC testing for TB even for a novel test requiring no equipment that could be completed in 20 minutes, while 38% (87/228) would only order a test for TB from a private lab and 51% (117/228) would perform the novel POC test in-house. Practitioner specialty was independently associated with interest in POC testing in adjusted analyses; chest specialists were half as likely to express interest in performing a novel TB POC test in-house as were other practitioners (aPR 0.5, 95% CI: 0.2-0.9) (Table 3). Practitioners practicing in private hospitals and PPs who did any POC testing were also more likely to opt to use the novel test in-house (aPR 1.3, 95%CI: 1.1-1.7; and aPR 1.8, 95%CI: 1.4-2.4; respectively).

Key priorities for use of a point-of-care test for TB

When asked to provide the three most important characteristics of a hypothetical new POC test for TB, 96% (195/204) listed accuracy and reliability as one of the top three priorities (Figure 2). Low cost was named by 52% (106/204), and 39% (79/204) wanted a test that utilized blood samples. PPs were willing to pay a maximum of 200 INR [IQR 100-500] (approximately US$3.15) to use the novel test for most patients with suspicion of TB.

Discussion

If future POC tests are to make an important impact in the fight against TB in high-burden settings like India, they must be implemented in a way that is consistent with current providers' practices and preferences. This cross-sectional survey of 228 private providers in Chennai provides important insight in this regard. Specifically, only half of practitioners surveyed utilized any POC tests as part of their current diagnostic practices, and utilization was particularly low among chest physicians – who also saw the largest number of TB patients, were most likely to use private labs, and had the least enthusiasm for using a hypothetical new POC test for TB in their clinical practice. These findings suggest that chest physicians, the private lab network, and practitioners who do not currently use POC tests may need to be further engaged in India before any novel POC test for TB could have maximum impact.

Our results also suggest the types of POC tests for TB that are likely to be most favorably received and utilized by qualified Indian PPs. Overwhelmingly, the characteristic voted most important to a new POC test was accuracy and reliability, suggesting that providers may intrinsically not trust POC tests for TB to be accurate. As in other studies[80], we also found a strong preference for blood rather than sputum as the main sample for TB testing. Rapid test usage was higher among our urban sample of qualified, private practitioners, though still under 50%, than in a study of predominantly rural Indian primary health care providers where only one-quarter used POC tests.[82] These results highlight differences in POC testing practices in different sectors of India's healthcare system, though willingness to use POC tests for TB was similar in both studies.[82] These findings are consistent with those from rapid diagnostic tests (RDTs) for malaria where provider uptake of these POC tests varied despite widespread availability.[70] Provider reliance on clinical symptoms and lack of confidence in RDT results versus perceived advantages of more familiar tests (i.e., microscopy) posed barriers to clinical usage[83–85] and more than half of providers continue to prescribe antimalarial medications despite a negative RDT result.[85,86] Building on these findings, to be successful, novel POC diagnostic tests for TB must first show demonstrated accuracy and also be usable in a variety of settings.

Key challenges to performing POC testing for TB in this study included time constraints, easy access to local private labs and lack of an attached lab facility, such that – when asked about a hypothetical, novel point-of-care test for TB that was accurate, rapid, and equipment-free – only about half of all providers, and less than one-quarter of chest physicians, were interested in using the novel test in-house. These barriers and recent qualitative research in India[52] reinforce the importance of understanding existing infrastructure challenges to POC testing and suggest the ideal placement for future POC tests in such community labs to ensure completion of the test and treat loop for patients with TB.

Although Xpert MTB/RIF has been demonstrated as a feasible point-of-care test in African settings[65], and as a decentralized test in various Indian settings[62,87], it remains a high cost test that requires sophisticated equipment.[64] Low-cost POC tests for HIV and malaria have transformed the management of these diseases, yet the need for POC tests for active pulmonary TB remains unmet contributing to delayed diagnoses that fuel the epidemic in high burden countries like India.[21,59,64] The urine lipoarabinomannan (LAM) lateral flow assay represents a simple, low cost diagnostic test that can be used at the point of care, but its niche use is limited to screening for HIV-associated pulmonary TB in patients with advanced immunodeficiency, which likely represents a small number of patients in the context of the Indian TB epidemic.[39,66] As future POC TB diagnostic tests become available that can be integrated more broadly into outpatient practice, studies such as this one and others[52,82], will be helpful in guiding implementation.

Several important limitations must be considered in this cross-sectional study. Our sample included only formally trained, qualified practitioners who had diagnosed a case of TB in the past year and also sampled from providers referring to a public-private mix organization in Chennai. This enabled us to attain a high response rate with less recall bias; however, our results may not be representative of all urban private practitioners providing TB care (including unqualified providers) in India. We also used structured questionnaires for data collection to allow us to collect a larger volume of data in the short times available to interview PPs; however, vignette-based questions may be preferred for describing actual practices and identifying priorities for future diagnostics.[41] Additionally, our survey captured practitioner-reported practices and preferences for a hypothetical new TB diagnostic test, but not actual practices (as no such TB test currently exists) or qualitative information on diagnostic priorities. A recent study from India using standardized patients to evaluate PP practices has reported a wide gap between what providers know and what they do in real practice[74], which indicates the need for ongoing empiric data collection on practice patterns to better gauge actual POC test usage.

Our findings underscore several important implications for point-of-care testing for TB in urban Indian settings. The low usage and limited interest in POC tests reported by chest physicians represents a potential obstacle to implementation among the providers who see the most patients with TB. Furthermore, the majority of chest physicians and nearly half of all PPs preferred to order a test from a private lab even when it could be performed as a POC test on-site, suggesting that a shift in culture will be required before POC testing for TB will be widely adopted in the Indian private sector. Additionally, it will be important to engage small, local laboratories at the community level in India, and take advantage of the strong existing relationships between private doctors and their local laboratories and pharmacies.

Conclusion

In conclusion, our study demonstrates variable use and interest in point-of-care testing for TB among qualified private practitioners in urban India. To ensure successful uptake of future POC tests for TB in urban India, such tests may need to be integrated into the private lab system, and chest physicians and providers who do not currently use POC tests may need to be specifically engaged. Accuracy, low physician time demand, low cost, and use of blood samples would all help increase the acceptability of such tests. Ultimately, if we are to use POC diagnostics to improve case detection and halt TB transmission in India, the practices and preferences of private providers with regard to POC testing must continue to be addressed and better understood to ensure test results can be translated into clinical plans for action.

Acknowledgements

We express our deepest gratitude to the entire staff at REACH for their collaboration and assistance in conducting this study. We are also thankful to the practitioners who agreed to be interviewed for this research study. This study was supported by a grant by the Bill & Melinda Gates Foundation (grant OPP1061487). Madhukar Pai is a recipient of a Tier 1 Canada Research Chair from the Canadian Institutes of Health Research. David Dowdy is supported in part by the B. Frank and Kathleen Polk Assistant Professorship in Epidemiology at the Johns Hopkins Bloomberg School of Public Health.

Tables and Figures

Table 4.1. Study population characteristics among private practitioners comparing point-of-care (POC) testing practices in Chennai, India (n=228).

Characteristic	Total (n=228) n(%)	Point-of-Care Testing Practices: Any POC Testing* (n=110) n(%)	No POC Testing (n=118) n(%)	P**
Gender				
Male	160 (70)	68 (62)	92 (78)	**<0.01**
Female	68 (30)	42 (38)	26 (22)	
Education level				
MBBS	81 (36)	38 (35)	43 (36)	0.96
MS	10 (4)	5 (4)	5 (4)	
MD	137 (60)	67 (61)	70 (59)	
Type of facility				
Government with private practice in evening	22 (10)	8 (7)	14 (12)	**0.02**
Private standalone clinic or polyclinic	129 (56)	55 (50)	74 (63)	
Private hospital or nursing home	77 (34)	47 (43)	30 (25)	
Years practicing				
Median [IQR]	20 [15-30]	20 [14-28]	25 [15-30]	**0.02**
Practitioner specialty				
General medicine	153 (67)	77 (70)	76 (65)	**<0.001**
Pulmonary specialist	39 (17)	8 (7)	31 (26)	
Other‡	36 (16)	25 (23)	11 (9)	
Number of patients diagnosed with TB annually				
≤12 patients with TB	110 (48)	53 (48)	57 (48)	0.99
>12 patients with TB	118 (52)	57 (52)	61 (52)	
Action for pulmonary TB diagnosis				
Refer to RNTCP or PPM DOTS center	97 (42)	48 (44)	49 (42)	0.75
Treatment in private sector	131 (58)	62 (56)	69 (59)	
Usage of sputum smear microscopy for TB				
Orders at first patient visit for TB diagnosis	115 (50)	54 (49)	61 (52)	0.69
Not ordered at first patient visit	113 (50)	56 (51)	57 (48)	
Knowledge of serological antibody test ban				
Yes	126 (55)	60 (55)	66 (56)	0.83
No	102 (45)	50 (46)	52 (44)	
Source of information on TB†				
No sources/non-chest specialty	39 (17)	14 (13)	25 (21)	0.09
Journals, books, newspaper, newsletters	82 (36)	42 (38)	40 (34)	0.50
Internet	71 (31)	38 (35)	33 (28)	0.28
CME or workshop	99 (43)	46 (42)	53 (45)	0.64
Medical representative or colleague	25 (11)	11 (10)	14 (12)	0.65

*POC tests utilized included glucose (n=97), pregnancy (n=48), malaria (n=12), hepatitis (n=9), dengue (n=9), typhoid (n=9), and HIV (n=4).
**Pearson's chi-squared (or Fisher's exact) test for categorical variables comparing practitioners that perform point-of-care (POC) diagnostic tests in-house versus ordering from a private lab; Wilcoxon test for continuous variables.
‡Other MD and MS practitioner specialties included Obstetrics and gynecology (n=15), Pediatrician (n=5), Surgeon (General/Orthopedic/Ophthalmologic) (n=4), Diabetes Specialist (n=6), Ear nose and throat (n=2), Oncologist (n=1), and Radiologist (n=1).
†Categories are not mutually exclusive.

Table 4.2. Point-of-care testing practices and preferences among private practitioners current using any POCTs by patient volume in Chennai.

	Total (n=110) n(%)	Point-of-Care Testing Preferences ≤12 Patients (n=53) n(%)	>12 Patients (n=57) n(%)	P*
Practitioner level of training				
MBBS/MS/MD (Non-chest specialty)	102 (93)	52 (98)	50 (88)	0.06
MD (Chest/Pulmonary specialty)	8 (7)	1 (2)	7 (12)	
Type of facility				
Private hospital or nursing home	55 (50)	20 (38)	35 (61)	**0.02**
Private standalone clinic or polyclinic*	55 (50)	33 (62)	22 (39)	
Number of tests per month				
Median [IQR]	38 [15-100]	20 [15-55]	75 [30-120]	**<0.001**
Time to get test results (minutes)				
Median [IQR]	5 [3-5]	5 [4-5]	5 [3-5]	0.30
Staff performing test				
Practitioner/Doctor	50 (45)	29 (55)	21 (37)	0.06
Support Staff/Nurse	60 (55)	24 (45)	36 (63)	
Staff interpreting test results				
Practitioner/Doctor	98 (89)	45 (85)	53 (93)	0.23
Support Staff/Nurse	12 (11)	8 (15)	4 (7)	
Cost to patients per test (INR)				
Median [IQR]	50 [50-88]	50 [50-100]	50 [50-75]	0.12
Keeps record of test results				
Yes	27 (25)	31 (58)	52 (91)	**<0.001**
No	83 (76)	22 (42)	5 (9)	
Reasons for performing POC tests**				
Results available immediately	96 (87)	42 (79)	54 (95)	0.14
Convenience for patients	70 (64)	30 (57)	40 (70)	0.46
Diagnosis and treatment in same visit	35 (32)	19 (36)	16 (28)	**0.02**
More affordable for patients	13 (12)	5 (10)	8 (14)	0.38
Interested in using novel POC TB test				
Perform in-house	78 (71)	39 (74)	39 (68)	0.55
Order from lab	32 (29)	14 (26)	18 (32)	

*Pearson's chi-squared (or Fisher's exact) test for categorical variables comparing practitioners who diagnosed 12 patients or less with TB to those who diagnosed more than 12 patients with TB in the past year; Wilcoxon test for continuous variables.

**Categories are not mutually exclusive.

Figure 4.1. Distribution of challenges in performing point-of-care tests in-house according to practitioners' level of training (n=228).

Practitioner-reported reasons for not performing rapid point-of-care tests in their health facility among 228 randomly selected private practitioners in Chennai. Practitioners gave multiple responses; thus, response categories are not mutually exclusive. Figures show the distribution of PP-reported challenges in performing POC tests in-house by practitioners' specialty and level of training. Statistically significant differences across specialty and level of training included: time constraints (listed by 69% of chest physicians versus 40% of non-chest specialists, $P<0.001$), general interest in POC tests (10% versus 3%, $P=0.03$), use of nearby lab services (21% versus 56%, $p<0.001$) and lack of an attached lab (8% versus 24%, $p=0.03$). Error bars represent 95% confidence intervals for each estimate.

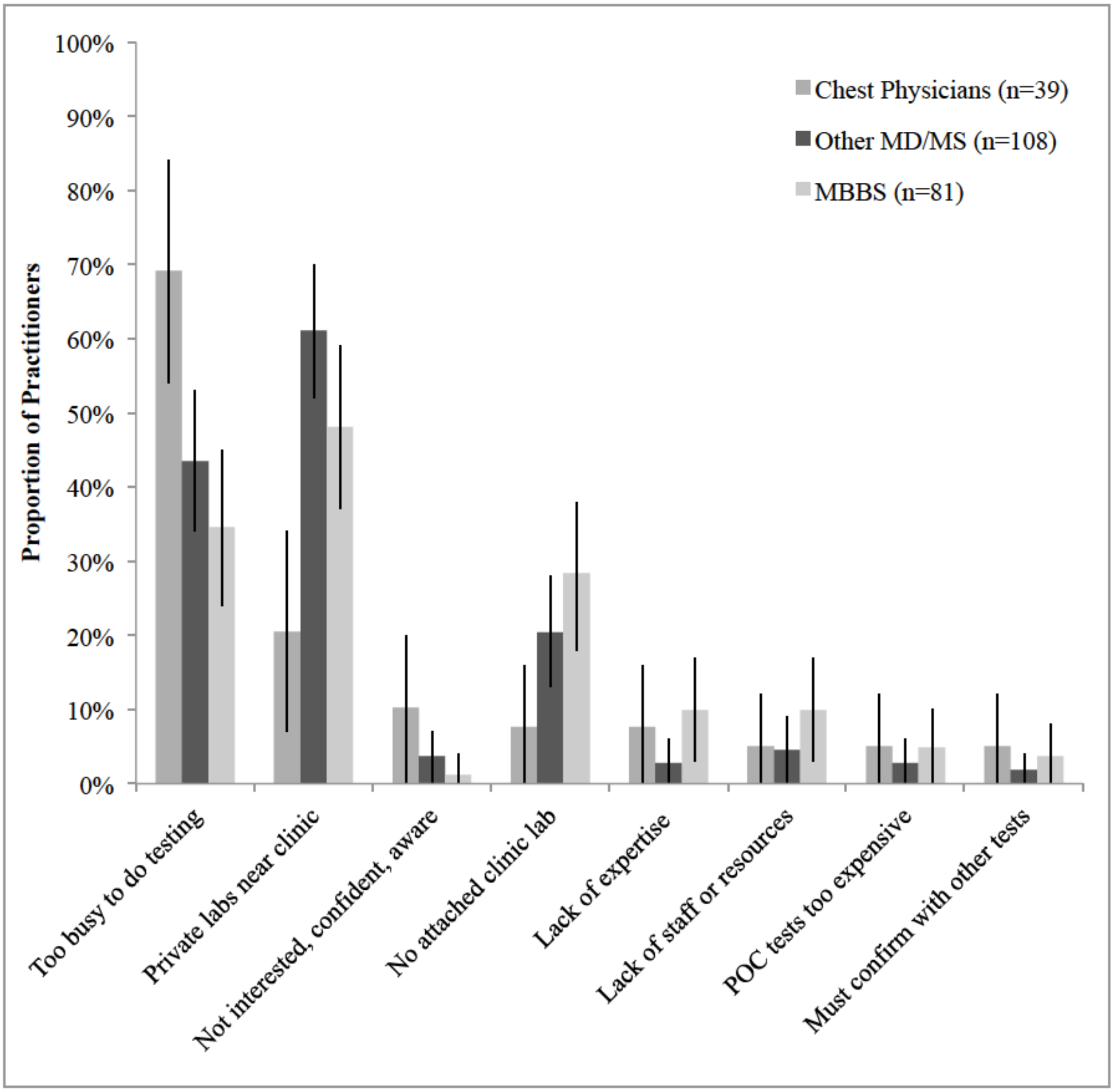


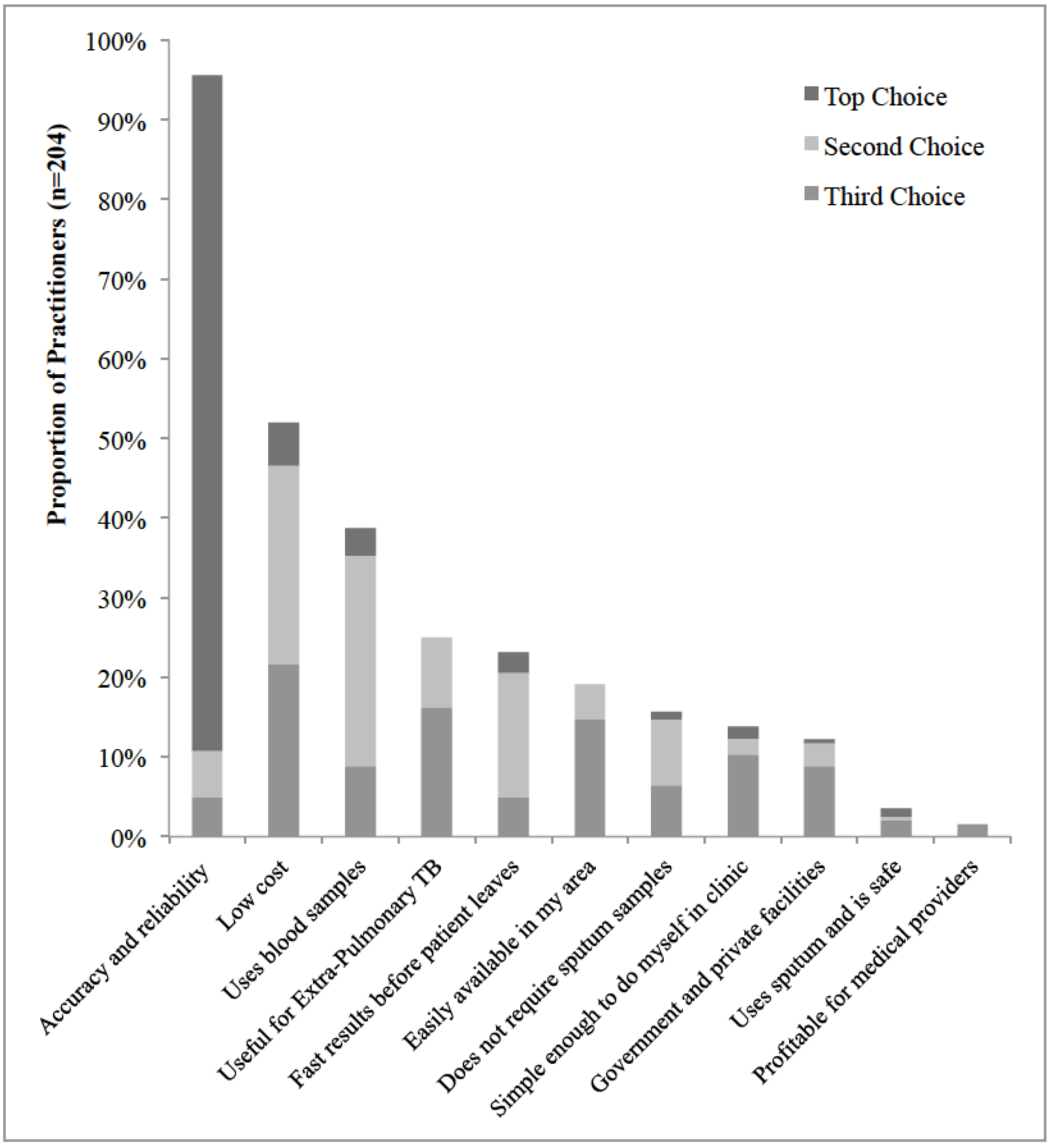
Table 4.3. Prevalence and factors associated with interest in performing point-of-care testing for TB in-house among private practitioners in Chennai.

Characteristic*	Interested in POC in-house (n=117/228) n/total (%)	Unadjusted PR (95% CI)	*P***	Adjusted PR (95% CI)*	*P***‡
Gender					
Male	75/160 (47)	**0.8 (0.6 - 0.9)**	**0.01**	0.9 (0.8 - 1.2)	0.61
Female	42/68 (62)	Ref		Ref	
Years practicing					
≤20 years	65/117 (56)	1.2 (0.9 - 1.6)	0.23	1.1 (0.9 - 1.4)	0.33
>20 years	52/111 (47)	Ref		Ref	
Practitioner level of training					
MD (Chest/Pulmonary specialty)	9/39 (23)	**0.4 (0.2 - 0.8)**	**<0.01**	**0.5 (0.2 - 0.9)**	**0.03**
MBBS/MS/MD (Non-chest specialty)	108/139 (57)	Ref		Ref	
Type of facility					
Private hospital or nursing home	61/99 (62)	**1.4 (1.1 - 1.8)**	**<0.01**	**1.3 (1.1 - 1.7)**	**0.01**
Private standalone clinic or polyclinic†	56/129 (43)	Ref		Ref	
Number of patients diagnosed with TB annually					
>12 patients	60/118 (51)	1.0 (0.8 - 1.3)	0.88	1.1 (0.8 - 1.4)	0.59
≤12 patients	57/110 (52)	Ref		Ref	
Point-of-care testing practices					
Any POC diagnostic testing	78/110 (71)	**2.1 (1.6 - 2.8)**	**<0.001**	**1.8 (1.4 - 2.4)**	**<0.001**
No POC testing	39/118 (33)	Ref		Ref	
Usage of sputum smear microscopy for TB					
Orders at first patient visit for TB diagnosis	54/115 (47)	0.8 (0.6 - 1.1)	0.23	0.9 (0.7 - 1.1)	0.35
Not ordered at first patient visit	63/113 (56)	Ref		Ref	
Knowledge of serological antibody test ban					
Yes	61/126 (48)	0.9 (0.7 - 1.2)	0.38	0.9 (0.7 - 1.2)	0.56
No	56/102 (55)	Ref		Ref	
Action for pulmonary TB diagnosis					
Refer to RNTCP or PPM DOTS center	70/131 (53)	1.1 (0.9 - 1.4)	0.46	1.2 (1.0 - 1.5)	0.11
Treatment in private sector	47/97 (49)	Ref		Ref	

*Abbreviations used include point-of-care testing (POC), prevalence ratio (PR), bachelor of medicine and surgery (MBBS), master of surgery (MS), medical doctor (MD), Revised National TB Program (RNTCP), public-private mix (PPM). ‡Adjusted for all other variables with data in this column. †Includes practitioners who practice in government facilities with private practice in the evening.

Figure 4.2. Top three characteristics ranked as priorities by private practitioners for a new point-of-care test for TB in Chennai, India.

Private practitioners were asked to rank their top three priorities for a hypothetical new rapid TB diagnostic test under development that could be used to replace the current TB tests and that could potentially be done rapidly in their clinic, like a pregnancy test or blood glucose test. Dark gray bars represent the characteristic ranked as the most important priority by practitioners, light gray presents the second most important characteristic, and medium gray the third most important characteristic. There were 24 practitioners that were not interested in performing POC testing who did not answer this question.



Chapter V: Conclusions

The previous chapters suggest a number of conclusions regarding private sector pathways to TB diagnosis in Chennai, India. First, the paths taken by patients to diagnosis and treatment of TB in urban Indian settings are diverse. However, the public-private mix organization operated by REACH in Chennai city is a model with the ability to link the majority patients diagnosed in the private sector to guideline-based care for TB. Nonetheless, mean delays to TB diagnosis exceeded two months, and were longer among those who first sought care from informal practitioners. Further engagement of informal and formal private practitioners is critical to improve their capacity to recognize and rapidly diagnose TB to reduce total symptomatic time and health system delays in particular to impact TB transmission. In this context, there was also considerable variability in the TB management practices utilized by practitioners in Chennai's private sector. These inconsistencies extended to a lack of adherence to the International Standards for TB Care, including among formal, qualified providers, high-volume providers, chest physicians, and those referring to a public-private mix organization. Broad-based approaches to engage private practitioners in TB control to ensure appropriate screening, TB-specific diagnostic testing, treatment monitoring, and prescription of first-line regimens for active pulmonary TB are necessary to impact TB incidence. Finally, the low levels of use and interest in point-of-care tests for TB diagnosis, particularly among chest specialists, represent potential barriers to implementation of novel diagnostic tests in India. The current private-sector practice of ordering diagnostic tests from private laboratories may necessitate an important shift in culture for point-of-care testing to be widely adopted. Innovative approaches to TB control must integrate future diagnostic tests more broadly into private outpatient practices, while also emphasizing their importance for improving case detection and halting TB transmission in India.

The results of this research present a number of future opportunities for investigation. While this study was among the first to characterize patients diagnosed with TB in Chennai's private sector, future endeavors may to address the challenges in accessing patients in the Indian private sector to gather more representative data from a broader patient population, use medical records to validate patient-reported pathways to diagnosis, and link patients being privately treated with their private practitioners. The private practitioners included in this study provided self-reported TB management practices and preferences for a hypothetical new TB diagnostic test, but not actual practices or qualitative information on diagnostic priorities. As such, our findings indicate the need for ongoing empiric data collection on practice patterns to better gauge actual test usage, priorities, and interest. Further, this research emphasizes the importance of ongoing efforts to develop accurate, rapid, low-cost TB diagnostic tests that will place minimum burden on busy private practitioners, as well as the need for an improved mechanism to engage and communicate with those practitioners managing patients outside of the RNTCP.

In summary, new diagnostics have the potential to improve case detection and halt TB transmission in India, but their application is limited by the pathways to care taken by the patients in need and by the practices and preferences of the private providers that they depend on to provide an accurate and timely diagnosis. Improvements to the private Indian health system are necessary for patients to gain more rapid care for TB-related symptoms, but also for the practitioners who remain dependent on these patients for their own livelihood thus driving at least in part their diagnostic practices; reforms to benefit both parties are essential in order to decrease TB transmission in the community and improve health outcomes. Ultimately, the intricacies of the Indian private sector must continue to be addressed and better understood if the individuals who access it are to have “universal access” to TB care, and if TB elimination is to be achieved in the foreseeable future in India.

References

1. World Health Organization. Global tuberculosis report 2014 [Internet]. WHO; 2014 [cited 2014 Oct 24]. Available from: http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf

2. Central Tuberculosis Division. Tuberculosis India 2011: Annual report of the Revised National Tuberculosis Control Programme, Ministry of Health and Family Welfare, Government of India [Internet]. 2011. Available from: http://www.tbcindia.nic.in/documents.html

3. World Health Organization. Global tuberculosis report 2013 [Internet]. WHO; 2013 [cited 2013 Dec 9]. Available from: http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf

4. Sreeramareddy CT, Qin ZZ, Satyanarayana S, Subbaraman R, Pai M. Delays in diagnosis and treatment of pulmonary tuberculosis in India: a systematic review. Int J Tuberc Lung Dis 2014;18(3):255–66.

5. Kapoor SK, Raman AV, Sachdeva KS, Satyanarayana S. How did the TB patients reach DOTS services in Delhi? A study of patient treatment seeking behavior. PloS One 2012;7(8):e42458.

6. Rao KD, Ramani S, Hazarika I, George S. When do vertical programmes strengthen health systems? A comparative assessment of disease-specific interventions in India. Health Policy Plan 2014;29(4):495–505.

7. Reddy KS, Patel V, Jha P, et al. Towards achievement of universal health care in India by 2020: a call to action. Lancet Lond Engl 2011;377(9767):760–8.

8. Dewan PK, Lal SS, Lonnroth K, et al. Improving tuberculosis control through public-private collaboration in India: literature review. BMJ 2006;332(7541):574–8.

9. Satyanarayana S, Nair SA, Chadha SS, et al. From where are tuberculosis patients accessing treatment in India? Results from a cross-sectional community based survey of 30 districts. PloS One 2011;6(9):e24160.

10. Udwadia ZF, Pinto LM, Uplekar MW. Tuberculosis management by private practitioners in Mumbai, India: has anything changed in two decades? PloS One 2010;5(8):e12023.

11. Charles N, Thomas B, Watson B, Sakthivel MR, Chandrasekeran V, Wares F. Care seeking behavior of chest symptomatics: a community based study done in South India after the implementation of the RNTCP. PloS One 2010;5(9):10.1371/journal.pone.0012379.

12. Sudha G, Nirupa C, Rajasakthivel M, et al. Factors influencing the care-seeking behaviour of chest symptomatics: a community-based study involving rural and urban population in Tamil Nadu, South India. Trop Med Int Health TM IH 2003;8(4):336–41.

13. Rao M, Rao KD, Kumar AKS, Chatterjee M, Sundararaman T. Human resources for health in India. Lancet 2011;377(9765):587–98.

14. M. Uplekar, S. Juvekar, S. Morankar, S. Rangan, P. Nunn. Tuberculosis patients and practitioners in private clinics in India. Int J Tuberc Lung Dis 1998;2(4):324–9.

15. Nagaraja SB, Achanta S, Kumar AMV, Satyanarayana S. Extending tuberculosis notification to the private sector in India: programmatic challenges? Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis 2014;18(11):1353–6.

16. Sachdeva KS, Kumar A, Dewan P, Kumar A, Satyanarayana S. New vision for Revised National Tuberculosis Control Programme (RNTCP): Universal access - "reaching the un-reached." Indian J Med Res 2012;135(5):690–4.

17. Pai M, Das J. Management of tuberculosis in India: time for a deeper dive into quality. Natl Med J India 2013;26(2):65–8.

18. Central TB Division, Directorate General of Health Services. TB India 2014: Revised National TB Control Programme, Annual Status Report [Internet]. New Delhi, India: Central TB Division, Directorate General of Health Services, Ministry of Health and Family Welfare; 2014. Available from: http://www.tbcindia.nic.in/pdfs/TB%20INDIA%202014.pdf

19. Pantoja A, Floyd K, Unnikrishnan KP, et al. Economic evaluation of public-private mix for tuberculosis care and control, India. Part I. Socio-economic profile and costs

among tuberculosis patients. Int J Tuberc Lung Dis 2009;13(6):698–704.

20. Selvam JM, Wares F, Perumal M, et al. Health-seeking behaviour of new smear-positive TB patients under a DOTS programme in Tamil Nadu, India, 2003. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis 2007;11(2):161–7.

21. Salje H, Andrews JR, Deo S, et al. The Importance of Implementation Strategy in Scaling Up Xpert MTB/RIF for Diagnosis of Tuberculosis in the Indian Health-Care System: A Transmission Model. PLoS Med 2014;11(7):e1001674.

22. M. Uplekar, S. Juvekar, S. Morankar, S. Rangan, P. Nunn. Tuberculosis patients and practitioners in private clinics in India. Int J Tuberc Lung Dis 1998;2(4):324–9.

23. Rajeswari R, Chandrasekaran V, Suhadev M, Sivasubramaniam S, Sudha G, Renu G. Factors associated with patient and health system delays in the diagnosis of tuberculosis in South India. Int J Tuberc Lung Dis 2002;6(9):789–95.

24. Krishnan N, Ananthakrishnan R, Augustine S, et al. Impact of advocacy on the tuberculosis management practices of private practitioners in Chennai City, India. Int J Tuberc Lung Dis 2009;13(1):112–8.

25. Small PM, Pai M. Tuberculosis diagnosis–time for a game change. N Engl J Med 2010;363(11):1070–1.

26. Small PM. Strengthening laboratory services for today and tomorrow. Plenary Lecture given during the 38th Union World Lung Conference on Lung Health, Cape Town, South Africa, 8-12 November 2007. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis 2008;12(10):1105–9.

27. Perkins MD, Small PM. Partnering for better microbial diagnostics. Nat Biotechnol 2006;24(8):919–21.

28. Ghosh A. Health Ministry set to ban commonly used TB test [Internet]. Indian Express. 2012 [cited 2013 Mar 27];Available from: http://www.indianexpress.com/news/health-ministry-set-to-ban-commonlyused-tb-test/925754/

29. Dowdy DW, Steingart KR, Pai M. Serological Testing Versus Other Strategies for Diagnosis of Active Tuberculosis in India: A Cost-Effectiveness Analysis. PLoS Med 2011;8(8):e1001074.

30. Serological tests for TB in India [Internet]. TB Factsorg. 2012 [cited 2013 Mar 27];Available from: http://www.tbfacts.org/serological-test-tb.html

31. WHO | WHO warns against the use of inaccurate blood tests for active tuberculosis [Internet]. WHO. [cited 2013 Mar 27];Available from: http://www.who.int/mediacentre/news/releases/2011/tb_20110720/en/

32. Steingart KR, Ramsay A, Dowdy DW, Pai M. Serological tests for the diagnosis of active tuberculosis: relevance for India. Indian J Med Res 2012;135(5):695–702.

33. Pai M. Tuberculosis Control in India: Time to get dangerously ambitious? Natl Med J India 2011;24(2):65–8.

34. Pai M, Menzies D. Interferon-γ Release Assays: What Is Their Role in the Diagnosis of Active Tuberculosis? Clin Infect Dis 2007;44(1):74–7.

35. Ling DI, Pai M, Davids V, et al. Are interferon-γ release assays useful for diagnosing active tuberculosis in a high-burden setting? Eur Respir J 2011;38(3):649–56.

36. Pai M. Accurate TB tests needed in the private sector [Internet]. Sunday Guard. 2013 [cited 2013 Mar 27];Available from: http://www.sunday-guardian.com/investigation/accurate-tb-tests-needed-in-the-private-sector

37. Pai M, Dewan P. Testing and Treating the Missing Millions with Tuberculosis. PLoS Med 2015;12(3):e1001805.

38. World Health Organization,, Central TB Division, Ministry of Health & Family Welfare, Government of India. Standards for TB Care in India [Internet]. India: 2014. Available from: http://tbevidence.org/wp-content/uploads/2014/04/STCI-2014.pdf

39. Lawn SD, Mwaba P, Bates M, et al. Advances in tuberculosis diagnostics: the Xpert MTB/RIF assay and future prospects for a point-of-care test. Lancet Infect Dis

2013;13(4):349–61.

40. Central TB Division, Directorate General of Health Services. TB India 2012 Revised National TB Control Programme Annual Status Report [Internet]. New Dehli: Government of India; 2012 [cited 2014 Feb 11]. Available from: http://www.tbcindia.nic.in/perfor.html

41. Satyanarayana S, Subbaraman R, Shete P, et al. Quality of tuberculosis care in India: a systematic review. Int Union Tuberc Lung Dis 2015;

42. Thomas A, Joseph P, Nair D, et al. Extensively drug-resistant tuberculosis: experience at the Tuberculosis Research Centre, Chennai, India. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis 2011;15(10):1323–5.

43. Paramasivan CN, Rehman F, Wares F, et al. First- and second-line drug resistance patterns among previously treated tuberculosis patients in India [Short communication]. Int J Tuberc Lung Dis 2010;14(2):243–6.

44. Dalal A, Pawaskar A, Das M, et al. Resistance Patterns among Multidrug-Resistant Tuberculosis Patients in Greater Metropolitan Mumbai: Trends over Time. PLoS ONE 2015;10(1):e0116798.

45. Achanta S, Jaju J, Kumar AMV, et al. Tuberculosis Management Practices by Private Practitioners in Andhra Pradesh, India. PLoS ONE 2013;8(8):e71119.

46. World Health Orgranization. Standards for TB Care in India. INdia: 2014.

47. TB CARE I,. International Standards for Tuberculosis Care, Edition 3 [Internet]. The Hague: 2014 [cited 2015 Apr 9]. Available from: http://www.who.int/tb/publications/ISTC_3rdEd.pdf

48. Chaisson LH, Katamba A, Haguma P, et al. Theory-Informed Interventions to Improve the Quality of Tuberculosis Evaluation at Ugandan Health Centers: A Quasi-Experimental Study. PLoS ONE 2015;10(7):e0132573.

49. Ahmad R, Matthys F, Dwihardiani B, et al. Diagnostic work-up and loss of tuberculosis suspects in Jogjakarta, Indonesia. BMC Public Health 2012;12(1):132.

50. Bharaswadkar S, Kanchar A, Thakur N, et al. Tuberculosis Management Practices of Private Practitioners in Pune Municipal Corporation, India. PLoS ONE 2014;9(6):e97993.

51. Paul D, Busireddy A, Nagaraja SB, et al. Factors associated with delays in treatment initiation after tuberculosis diagnosis in two districts of India. PloS One 2012;7(7):e39040.

52. Engel N, Ganesh G, Patil M, et al. Barriers to Point-of-Care Testing in India: Results from Qualitative Research across Different Settings, Users and Major Diseases. PLoS ONE 2015;10(8):e0135112.

53. Pai NP, Vadnais C, Denkinger C, Engel N, Pai M. Point-of-Care Testing for Infectious Diseases: Diversity, Complexity, and Barriers in Low- And Middle-Income Countries. PLoS Med 2012;9(9):e1001306.

54. Pai M, Dewan P. Testing and Treating the Missing Millions with Tuberculosis. PLoS Med 2015;12(3):e1001805.

55. Stop TB Partnership, World Health Organization. Global Plan to Stop TB 2011–2015 [Internet]. 2011. Available from: http://www.stoptb.org/assets/documents/global/plan/TB_GlobalPlanToStopTB2011-2015.pdf

56. Dye C, Williams BG. The Population Dynamics and Control of Tuberculosis. Science 2010;328(5980):856–61.

57. Scott SE, Walter FM, Webster A, Sutton S, Emery J. The Model of Pathways to Treatment: Conceptualization and integration with existing theory. Br J Health Psychol 2013;18(1):45–65.

58. Qin ZZ, Pai M, Van Gemert W, Sahu S, Ghiasi M, Creswell J. How is Xpert MTB/RIF being implemented in 22 high tuberculosis burden countries? Eur Respir J 2015;45(2):549–54.

59. Lin H-H, Dowdy D, Dye C, Murray M, Cohen T. The impact of new tuberculosis diagnostics on transmission: why context matters. Bull World Health Organ 2012;90(10):739–47A.

60. Lin H-H, Langley I, Mwenda R, et al. A modelling framework to support the selection and implementation of new tuberculosis diagnostic tools [State of the art series. Operational research. Number 8 in the series]. Int J Tuberc Lung Dis 2011;15(8):996–1004.

61. Cobelens F, van den Hof S, Pai M, Squire SB, Ramsay A, Kimerling ME. Which New Diagnostics for Tuberculosis, and When? J Infect Dis 2012;205(suppl 2):S191–8.

62. Sachdeva KS, Raizada N, Sreenivas A, et al. Use of Xpert MTB/RIF in Decentralized Public Health Settings and Its Effect on Pulmonary TB and DR-TB Case Finding in India. PLoS ONE 2015;10(5):e0126065.

63. Sun AY, Pai M, Salje H, Satyanarayana S, Deo S, Dowdy DW. Modeling the Impact of Alternative Strategies for Rapid Molecular Diagnosis of Tuberculosis in Southeast Asia. Am J Epidemiol 2013;178(12):1740–9.

64. Denkinger CM, Pai M. Point-of-care tuberculosis diagnosis: are we there yet? Lancet Infect Dis 2012;12(3):169–70.

65. Theron G, Zijenah L, Chanda D, et al. Feasibility, accuracy, and clinical effect of point-of-care Xpert MTB/RIF testing for tuberculosis in primary-care settings in Africa: a multicentre, randomised, controlled trial. The Lancet 2014;383(9915):424–35.

66. Lawn SD, Kerkhoff AD, Vogt M, Wood R. Diagnostic accuracy of a low-cost, urine antigen, point-of-care screening assay for HIV-associated pulmonary tuberculosis before antiretroviral therapy: a descriptive study. Lancet Infect Dis 2012;12(3):201–9.

67. Dorman S. Advances in the diagnosis of tuberculosis: current status and future prospects. Int J Tuberc Lung Dis 2015;19(5):504–16.

68. Nikam C, Jagannath M, Narayanan MM, et al. Rapid Diagnosis of Mycobacterium tuberculosis with Truenat MTB: A Near-Care Approach. PLoS ONE 2013;8(1):e51121.

69. Pai M, Yadav P, Anupindi R. Tuberculosis control needs a complete and patient-centric solution. Lancet Glob Health 2014;2(4):e189–90.

70. Jani IV, Peter TF. How point-of-care testing could drive innovation in global health. N Engl J Med 2013;368(24):2319–24.

71. Government of India Ministry of Home Affairs Office of the Registrar General and Census Commissioner. Primary Census Abstract: Chennai District, Tamil Nadu State, India [Internet]. 2011 [cited 2014 Feb 11]. Available from: http://www.censusindia.gov.in/pca

72. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. Am J Epidemiol 2005;162(3):199–200.

73. Ananthakrishnan R, Muniyandi M, Jeyaraj A, Palani G, Sathiyasekaran BWC. Expenditure Pattern for TB Treatment among Patients Registered in an Urban Government DOTS Program in Chennai City, South India. Tuberc Res Treat [Internet] 2012 [cited 2014 Feb 12];2012. Available from: http://www.hindawi.com/journals/trt/2012/747924/abs/

74. Das J, Kwan A, Daniels B, et al. First use and validation of the standardized patient methodology to assess quality of tuberculosis care: a pilot, cross-sectional study. Lancet Infect Dis 2015;

75. Bronner Murrison L, Ananthakrishnan R, Sukumar S, Krishnan N, Pai M, Dowdy DW. How do urban Indian private practitioners diagnose and treat tuberculosis? A cross-sectional study in Chennai. 2015;

76. Lal SS, Sahu S, Wares F, Lönnroth K, Chauhan LS, Uplekar M. Intensified scale-up of public-private mix: a systems approach to tuberculosis care and control in India. Int J Tuberc Lung Dis 2011;15(1):97–104.

77. Kumar MKA, Dewan PK, Nair PKJ, et al. Improved tuberculosis case detection through public-private partnership and laboratory-based surveillance, Kannur District, Kerala, India, 2001–2002. Int J Tuberc Lung Dis 2005;9(8):870–6.

78. Bronner Murrison L, Ananthakrishnan R, Swaminathan A, Krishnan N, Pai M, Dowdy DW. How do patients access the private sector in Chennai, India? An

evaluation of delays in tuberculosis diagnosis. 2015;

79. Miller R, Parkhurst JO, Peckham S, Singh RB. A qualitative study of HIV testing and referral practices of private hospital doctors treating patients with TB in Chennai, India. Int J Health Plann Manage 2012;27(2):180–91.

80. Jarosławski S, Pai M. Why are inaccurate tuberculosis serological tests widely used in the Indian private healthcare sector? A root-cause analysis. J Epidemiol Glob Health 2012;2(1):39–50.

81. WHO | High-priority target product profiles for new tuberculosis diagnostics [Internet]. WHO. [cited 2015 Aug 17];Available from: http://www.who.int/tb/publications/tpp_report/en/

82. Satyanarayana S, Sagili K, Chadha SS, Pai M. Use of rapid point-of-care tests by primary health care providers in India: findings from a community-based survey. Public Health Action 2014;4(4):249–51.

83. Reyburn H, Mbakilwa H, Mwangi R, et al. Rapid diagnostic tests compared with malaria microscopy for guiding outpatient treatment of febrile illness in Tanzania: randomised trial. BMJ 2007;334(7590):403.

84. Williams HA, Causer L, Metta E, et al. Dispensary level pilot implementation of rapid diagnostic tests: an evaluation of RDT acceptance and usage by providers and patients – Tanzania, 2005. Malar J 2008;7(1):239.

85. Yeung S, Patouillard E, Allen H, Socheat D. Socially-marketed rapid diagnostic tests and ACT in the private sector: ten years of experience in Cambodia. Malar J 2011;10(1):243.

86. Diggle E, Asgary R, Gore-Langton G, et al. Perceptions of malaria and acceptance of rapid diagnostic tests and related treatment practises among community members and health care providers in Greater Garissa, North Eastern Province, Kenya. Malar J 2014;13(1):502.

87. Raizada N, Sachdeva KS, Sreenivas A, et al. Feasibility of Decentralised Deployment of Xpert MTB/RIF Test at Lower Level of Health System in India. PLoS ONE 2014;9(2):e89301.

Curriculum Vitae

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PROFESSIONAL EXPERIENCE

4/2013-9/2015	Research Assistant Johns Hopkins Bloomberg School of Public Health, Baltimore, MD PI: Dr. David W. Dowdy
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5/2010-6/2013	Senior Research Associate Centers for Disease Control, Division of TB Elimination, Atlanta, GA South African Medical Research Council, Durban, South Africa
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8/2008-6/2010	Laboratory Assistant Emory Vaccine Center, HIV Immunology and Virology Lab, Atlanta, GA PI: Dr. Eric Hunter

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PROFESSIONAL ACTIVITIES

2012-present Johns Hopkins Tuberculosis (TB) Modeling Group, *Member*
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EDITORIAL ACTIVITIES

Peer Review Activities
Journal of the International AIDS Society
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HONORS & AWARDS

2012-present Johns Hopkins Bloomberg School of Public Health Doctoral Student Tuition Award
2013 Johns Hopkins Center for Global Health Field Research Award
2009 Emory University Rollins School of Public Health O.C. Hubert Charitable Foundation Award
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PUBLICATIONS

**Manuscripts prior to April 2015 are included as Liza E. Bronner and thereafter as Liza Bronner Murrison.*

Journal Articles

1. **Bronner Murrison L**, Ananthakrishnan R, Krishnan N, Dowdy DW, Pai M. Usage of point-of-care assays by private practitioners in Chennai, India: Priorities for tuberculosis diagnosis. (*Under review,* PLOS ONE 2015).

2. **Bronner Murrison L**, Ananthakrishnan R, Sukumar S, Krishnan N, Pai M, Dowdy DW. How do urban Indian private practitioners diagnose and treat tuberculosis? A cross-sectional study in Chennai. (*Revisions requested*, PLOS ONE 2015).

3. **Bronner Murrison L**, Ananthakrishnan R, Swaminathan A, Augustine S, Krishnan N, Pai M, Dowdy DW. How do patients access the private sector in Chennai, India? An evaluation of delays in tuberculosis diagnosis. (*Accepted*, IJTLD 2015).

4. **Bronner Murrison L**, Martinson NA, Moloney RM, Msandiwa R, Mashabela F, Samet JM, Golub JE. Tobacco smoking and tuberculosis among HIV-infected men in Johannesburg, South Africa: A case-control study. (*Under review*, IJTLD 2015).

5. Podewils LJ, **Bronner LE**, Bristow CC, Bantubani N, Mametja LD. The Other Side of Surveillance: Monitoring, Application, and Integration of Tuberculosis (TB) Data to Guide and Evaluate Program Activities in South Africa (*Under review*, SAMJ 2015).

6. Podewils LJ, Bantubani N, Bristow C, **Bronner LE**, Peters A, Pym A, et al. Completeness and Reliability of the Republic of South Africa National Tuberculosis (TB) Surveillance System. BMC Public Health. 2015 Aug 11;15(1):765.

7. Ershova, J., Podewils, L., **Bronner, L.,** Stockwell, H., Dlamini, S., Mametja, L. Evaluation of adherence to national treatment guidelines among tuberculosis patients in three provinces of South Africa. *South African Medical Journal, 104*(5), 362-368. doi:10.7196/samj.7655. March 2014. PMID: 25212205.

8. Bristow CC, Podewils LJ, **Bronner LE**, Bantubani N, Van der Walt M, Peters A, Mametja LD. TB Tracer Teams in South Africa: Knowledge, Practices and Challenges of Tracing TB Patients to Improve Adherence. BMC Public Health. 4 September 2013; 13:801. PMID: 24007294.

9. **Bronner LE,** Podewils LJ, Peters A, Somnath P, Nshuti L, van der Walt M, Mametja LD. Impact of Community Tracer Teams on Treatment Outcomes among Tuberculosis Patients in South Africa. BMC Public Health. 7 Aug 2012; 12:621. PMID: 22871071.

Reports and Other Documents

10. Podewils LJ and **Bronner LE**. Report on impact of community tracer teams on treatment outcomes among Tuberculosis patients in South Africa. [*Part I: Impact Assessment using ETR Data. Report to the Republic of South Africa National Department of Health*]. February 2012.

11. Podewils LJ and **Bronner LE**. Assessment of the Republic of South Africa National Tuberculosis Control Program Surveillance System and Electronic Tuberculosis Register. [*Part 2: Impact Assessment using ETR Data. Report to the Republic of South Africa National Department of Health*]. February 2012.

TEACHING

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PH.340.612 Epidemiologic Basis for TB Control, Winter 3rd Term 2014
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PRESENTATIONS

2015 An Evaluation of Private Sector Pathways to Diagnosis of Tuberculosis in Chennai, India. *University of Cincinnati Department of Environmental Health Sciences Wednesday Seminar.* Cincinnati, OH. (Invited Guest Presentation).

2015 How do urban Indian private practitioners diagnose and treat tuberculosis? A cross-sectional study in Chennai. Johns Hopkins Center for TB Research 2015 Annual Meeting. Baltimore, MD. (Presentation)

2015 How Do Patients Access the Private Sector in Chennai, India? Johns Hopkins Center for TB Research: TB Clinical and Epidemiology Meeting. Baltimore, MD. (Presentation, http://tbcenter.jhu.edu/events/how-do-patients-access-the-private-sector-in-chennai-india/).

2015 FlexDx-TB: Introducing a user-friendly model of impact and cost-effectiveness for TB diagnostic interventions. U.S. Centers for Disease Control and Prevention Division of TB Elimination Seminar Series. Atlanta, GA. (Invited Guest Presentation).

2014 Understanding patient pathways to care and practitioner diagnostic practices for TB in the private health sector in India. Johns Hopkins Center for Global Health Research Symposium. Baltimore, MD. (Poster).

2013 Evaluation of Diagnostic Practices for Tuberculosis in South Africa: Implications for New Technologies. Union World Conference on Lung Health. Paris, France. (Presentation).

2013 Diagnosis of Tuberculosis in South Africa: Diagnostic practices and implications for new technologies. Johns Hopkins Center for TB Research: TB Clinical and Epidemiology Meeting. Baltimore, MD. (Presentation).

2013 The other side of surveillance: Monitoring, application, and integration of tuberculosis data to guide and evaluate program activities in South Africa. South African National Department of Health Quarterly TB Meeting. Johannesburg, South Africa. (Presentation).

2012 Impact of community tracer teams on treatment outcomes among TB patients in

South Africa. South African National Department of Health Quarterly TB Meeting. Durban, South Africa. (Presentation).

2012	Diagnosis of TB in a high HIV prevalence setting - evaluation of programmatic practices and implications for new diagnostic technologies in South Africa. American Thoracic Society 2012 Conference. San Francisco, CA. (Presentation).
2011	Impact of community tracer teams on treatment outcomes among TB patients in South Africa. Union World Conference on Lung Health, Lille, France. (Poster).
2010	Predictors of false positive rapid HIV tests in couples from a clade A HIV endemic city. AIDS Vaccine 2010 Conference. Atlanta, GA. (Poster).

VOLUNTEER ACTIVITIES

9/2010-present	Team Captain and Member 2010-2015 Pancreatic Cancer Action Network
7/2008	Medical Volunteer and Member Bicol Clinic Foundation, Buena Vista, Sorsogon City, Philippine Islands