



TARGETING TB IN INDIA

Advancing diagnostic tools to improve patient outcomes



Because diagnosis matters

IMPACT OF FIND INDIA

Progress as of end 2013 through various projects implemented by FIND India

> Over **40,000** patients diagnosed with MDR-TB

> **90** rapid TB and MDR-TB diagnostic facilities established

> More than **2,000** lab workers trained

TUBERCULOSIS IN INDIA

A disease of poverty and a cause of greater poverty

Every year, more than two million people in India develop tuberculosis (TB). This accounts for nearly one quarter of TB cases worldwide, and places the country among those with the highest TB burden. The statistics tell a sobering story: nearly 750 people die each day from the disease – a rate of one person every two minutes. Every case of TB costs the Indian economy about 700,000 rupees, which rises to over 3.5 million rupees if the illness leads to mortality.

Treating TB is greatly compromised by a reduction in the effectiveness of available medicines: the disease is becoming increasingly resistant to first-line TB drugs, resulting in the appearance and spread of multidrug-resistant TB (MDR-TB). This form of TB represents around 2% of new TB cases and 15% of cases in people who have previously been treated. An estimated 64,000 cases of MDR-TB were diagnosed in India in 2012. The spread of MDR-TB could

become a threat of significant magnitude, which is why accurate and timely diagnosis is indispensable for ensuring prompt and appropriate treatment, as well as infection control.

FIND's aim is to make a decisive impact on patient outcomes and, ultimately, on these statistics. Since FIND was first launched in 2003, we have acted as a bridge between partners in the public and private sectors, bringing together diverse groups of experts to address the technical, financial, and logistical barriers to the development and deployment of cutting-edge diagnostic tests for the developing world.

Our goal is to shorten the period between diagnosis and start of treatment, thereby reducing transmission. Good diagnosis is an effective investment in the health of individuals, families, and communities, and is paramount to improving the health of the nation.

Estimated burden of TB in 2012 (Source WHO Global Tuberculosis Report 2013)	India	Globally
Number of new cases	2.2 Million	8.6 Million
Mortality	270,000	940,000
Estimated MDR-TB burden	India	Globally
% of new TB cases with MDR-TB	2.2%	3.6%
% of previously treated TB cases with MDR-TB	15%	20.2%
MDR-TB cases among notified pulmonary TB cases	64,000	300,000
TB diagnosis and laboratory services under RNTCP in India*		
Solid culture	37	
Liquid culture	25	
Liquid culture DST	12	
LPA	41	
Second-line DST	6	
Private sector / NGO labs involved in programme	7	

* <http://tbindia.nic.in/Pdfs/TB%20INDIA%202014.pdf>



> Training human resources is key to ensuring the appropriate use of newer TB diagnostic technologies, resulting in accurate patient diagnosis.

FIND IN INDIA

Supporting global and national policy change

Headquartered in Geneva, Switzerland, FIND opened its India office in 2007. On August 24 of the same year, we signed a memorandum of understanding with the Central TB Division (CTD), Ministry of Health and Family Welfare, to demonstrate and introduce new, rapid, and quality-assured tests for TB at affordable prices for the public health sector.

As a high-priority TB country, India has the conditions and infrastructure needed for large-scale studies and high-quality data. Our in-country activities initially focused on evaluation and demonstration studies

of the diagnostic tools we had co-developed with our partners. These included liquid culture and drug susceptibility testing (DST), rapid speciation, molecular line probe assay (LPA), LED-based fluorescence microscopy, and Xpert MTB/RIF. The data from these studies formed part of the body of evidence that enabled their endorsement by the World Health Organization (WHO). India's Revised National TB Control Programme (RNTCP) has also used this data to help formulate its guidelines for the detection and management of drug-resistant TB (DR-TB) across the country.

The four pillars of the FIND India model

- a) Participating in the successful demonstration and validation of new diagnostics for TB and DR-TB, leading to WHO endorsement and contributing to RNTCP efforts to scale up rapid diagnosis of TB and MDR-TB;
- b) Creating effective partnerships with RNTCP and states, in addition to donor and development agencies;
- c) Ensuring quality implementation of new diagnostic technologies through uniform national level standardized training at the International Centre of Excellence for Laboratory Training (ICELT) situated at the National Tuberculosis Institute in Bangalore, as well as onsite training sessions;
- d) Providing support for strong programme management and implementation through a multi-disciplinary team of programme managers, medical officers, microbiologists, and bio-medical engineers; and logistics, procurement, and finance teams.

Increasing access to improved diagnostics by building laboratory capacity

The challenge of responding to the number of MDR-TB cases with innovative diagnostics is compounded by the need to ensure that these new technologies are properly implemented and that laboratories are able to handle all of the associated requirements.

Expanding access to new diagnostics for patients at risk of MDR-TB

Funded by UNITAID, EXPAND-TB is a six-year project (2009 to 2014) whose goal is to improve the capacity to diagnose MDR-TB in upgraded laboratories in 27 high-endemic countries. The project is coordinated by the Global Laboratory Initiative hosted by the WHO in collaboration with FIND and the Stop TB Partnership's Global Drug Facility.

As the main implementing agency, FIND is responsible for project management, including support for procurement and logistics, in line with ISO 13485 and 9001 standards. As part of our efforts to transfer technology to countries, we provide training and share manuals, guidelines, and operating procedures to facilitate the introduction and proper use of new diagnostics. In India, the EXPAND-TB project aims to assist the introduction of LPA in 43 laboratories and to establish 37 liquid culture and drug susceptibility testing (DST) facilities with equipment and consumables, and to provide training and close follow-up.

Building laboratory capacity

In recent years, an unprecedented effort by multi-partner initiatives to establish and upgrade laboratories has led to improved quality of laboratory services and enabled implementation of recently developed diagnostic technologies for improved diagnosis of TB and MDR-TB. Since 2010, with funding from The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), FIND's interventions have contributed towards the development of a functional and efficient

laboratory network across the country, which can offer quality assured services, thus increasing the reach of new TB diagnostic testing.

Funding from the GFATM is complementing the EXPAND-TB project and providing additional support for all the established laboratories. This involves providing additional human resources, onsite technical support, specimen processing equipment, and consumables, which contribute to increasing the lab's capacity to process tests. This means more people are screened for TB, which leads to increased diagnosis of TB and MDR-TB. This also means more patients are put on appropriate treatment with minimum delay, which helps prevent the spread of the disease.

The project is being implemented in partnership with the Ministry of Health's CTD, with FIND as sub-recipient. The long-term goal of this project is to ensure a strong mentorship model that will support laboratory quality improvements for future years.

We also work closely with global agencies and implementing partners such as PATH, the International Union Against Tuberculosis and Lung Disease (The Union), the US Centers for Disease Control and Prevention (CDC), USAID, and the President's Emergency Plan for AIDS Relief (PEPFAR).

Establishing a state-of-the-art training facility

In early 2011, we opened the International Centre for Excellence in Laboratory Training (ICELT) at the National TB Institute in Bangalore to further support the scaling up of laboratory capacity in India. ICELT provides hands-on training courses on the diagnosis and monitoring of TB, and on biosafety and infection control measures. ICELT also trains master trainers to ensure sustainability of the initiative and help build quality assurance expertise in India.

IN SIGHT OF THE TARGET

We have shown that a significant improvement in TB and MDR-TB detection in India is possible. The number of cases identified as a result of these efforts has increased enormously, allowing for the correct treatment of patients and contributing to halt disease progression. However, the vast majority of people suffering from TB and MDR-TB still fail to be diagnosed. Recent assessments have shown that more new tools are needed to fill the remaining diagnostic gaps and that access to these tools needs to be expanded to reach the missing cases.

Beyond 2014, FIND will continue to maintain its close collaboration with RNTCP and to support its

objective of providing universal access to TB and MDR-TB diagnosis and treatment by 2017. This will require further expansion and strengthening of the existing laboratory network, which will include training of laboratory personnel, upgrading of infrastructure, accreditation, and quality assessment. Building laboratory capacity – our primary focus – is one of our key strengths, and will remain a priority. We plan to expand the scope of our activities in this domain by developing strong links to the private health care sector and by enhancing our monitoring and evaluation capabilities, which are key components in achieving the Indian government's targets.

> Working within the framework of the Government of India's RNTCP we are extending the reach of new diagnostic tools through upgrading and strengthening of laboratories.

ACHIEVEMENTS

> 2008

LED fluorescence microscopy demonstration study:

Data from large LED-based fluorescence microscopy (LED FM) demonstration studies in India were used to support the 2009 WHO recommendation that LED FM be phased in to replace conventional light microscopy, the traditional mainstay of TB diagnostics in most high-burden countries. LED FM is more sensitive and faster, thus shortening diagnostic delays. The findings also led to the implementation by the International Union Against Tuberculosis and Lung Disease of LED FM in 200 medical colleges in India. As a result, more TB cases were diagnosed, and LED FM was included in the training of technicians.

Line probe assay (LPA) demonstration project:

India was identified as one of the reference settings for the demonstration studies that indicated that LPA is highly accurate and cost-effective for detection of MDR-TB. Early demonstration studies in India covered seven sites and involved close to 1,500 patients. As a result, LPA was targeted to be implemented in 46 identified sites in the country through various projects by FIND. 36,830 MDR-TB cases had been identified using LPA by the end of 2013.

Liquid culture lab preparedness study:

Carried out at three regional laboratories, the study demonstrated the importance of strong infrastructural support and appropriate training. This led RNTCP to entrust FIND to support implementation of liquid culture technology in 40 targeted labs to ensure management and treatment monitoring of MDR-TB patients.

> 2009

Xpert MTB/RIF global demonstration project:

India was selected as one of the sites for the multi-centric Xpert MTB/RIF demonstration study to assess implementation of this technology and the feasibility of its decentralized use to improve TB and MDR-TB control. Carried out at Christian Medical College (Vellore) and Hinduja Hospital (Mumbai) in the fourth quarter of 2009, the study led to WHO endorsement of Xpert MTB/RIF. As of March 2014, over six million cartridges have been procured worldwide in 104 of 145 eligible countries.

> 2010

EXPAND-TB project:

This project was initiated in India to accelerate the introduction and scaling up of newer technologies in 40 institutions. Three more sites were subsequently identified to receive support.

ICELT training facility:

A proposal to establish a specialized training facility was submitted by FIND India and the EXPAND-TB team to the Ministry of Health. As a result, the International Centre of Excellence for Laboratory Training (ICELT) was set up at the National TB Institute in Bangalore, one of India's National Reference Laboratories. Trained manpower is crucial for the introduction of newer TB diagnostics; today, ICELT ensures the country has the capacity to conduct national training.

Global Fund project:

FIND became a sub-recipient of The Global Fund to Fight AIDS, Tuberculosis and Malaria under RNTCP of India to augment the diagnosis of TB and MDR-TB.

Xpert MTB/RIF feasibility and impact assessment study:

This was a two-year project (2011 to 2013) implemented across 18 sites to assess the feasibility of decentralized deployment of Xpert at lower levels of health systems in India. Over 100,000 presumptive pulmonary TB cases were tested for TB and DR-TB. The study concluded that Xpert MTB/RIF meets robust requirements for rapid scale-up – more people will have access to TB testing in the coming years, which is crucial to halting transmission.

EXPAND-TB Xpert project:

14 Xpert labs were established across the country in 2012 and 2013. 31,296 Xpert tests were conducted at these sites; 4,114 Rifampicin-resistant cases were diagnosed.

Additional sites identified for integration of new tests:

Three additional sites were identified for integration of LPA, and six for liquid culture and DST with EXPAND-TB backing. This brings the total number of sites to be supported under EXPAND-TB to 43 and 37 for LPA and LC, respectively. Two additional sites – one for LC and one for LPA – were identified for upgrading with support from the GFATM. In total, 55 institutions are identified by CTD for the establishment of 46 LPA, 40 LC, and 14 Xpert facilities, with FIND acting as implementing partner.

Pilot project tests multidrug-resistant TB in children:

A short-term pilot study aiming to accelerate access to TB diagnosis for children was launched by RNTCP, the National Institute for Research in Tuberculosis, and other agencies in April. Funded by USAID and implemented with technical support from FIND, the study was conducted at four laboratories in Hyderabad, Chennai, Kolkata and New Delhi. More than 6,000 children between 0 - 14 years have been tested using Xpert MTB/RIF, including 50% non-sputum specimens. Overall positivity was 7.6%, compared to 2.4% positivity on smear.

2011 <

2012 <

2013 <

2014 <



IMPACT OF FIND INDIA

Over 40,000 patients diagnosed

As of the end of 2013, over 40,000 patients in India were diagnosed with MDR-TB and were subsequently identified to receive appropriate treatment with second-line drugs. We expect that a total of 62,000 cases of MDR-TB will be detected by the end of 2014.

Over 280,000 tests performed

This figure includes all of the technologies implemented under FIND India projects for the same period.

90 rapid TB and MDR-TB diagnostic facilities established

- Line probe assay: 35
- Liquid culture: 23
- Xpert MTB/RIF: 32

More than 2,000 health care workers trained

Above 200 master trainers were trained to support the rapid scale-up of new tools at the ICELT facility, where 34 national training sessions were held. In addition, the competencies of about 1,800 microbiologists, technical officers, and laboratory technicians from across the country were strengthened through 141 on-site training sessions. Upgraded infrastructure and well-trained people translate into correct use of tests, improved accuracy, and speed. Patients benefit because they have access to reliable diagnosis, which leads to timely initiation of treatment and prevention of transmission.

Improved case detection and treatment initiation

As a result of combined efforts and initiatives, the detection rate of multidrug-resistant TB in India has been progressing significantly since 2010 and the country has been able to diagnose a greater number of patients than ever before. FIND India's laboratory strengthening activities have made a major contribution to achieve this result.

Noteworthy is the exponential increase in the number of multidrug-resistant TB cases detected. Based on

data from the latest WHO Global Tuberculosis report, 90% of all multidrug-resistant TB cases reported in 2012 in India were diagnosed in laboratories supported by EXPAND-TB.

Since the beginning of FIND's activities in laboratory strengthening, 41,860 multidrug-resistant TB patients were put on treatment. Detection and rapid access to treatment is the only way to improve patient outcomes and to reduce transmission of the disease.

PATIENT STORIES

Paving a path back to health



Dini

You don't need magic to make miracles happen

Dini Khillo had been coughing and feverish for over a month before she decided to go and see a local Tantrik for Jhaad-Phoonk, or a 'magic cure'. His prayers and a fee of Rs 1,000 failed to prove effective to any degree, and merely delayed proper diagnosis and treatment. Dini – aged 28 and with three children to care for – then visited a local government hospital, where a gynaecologist gave her antibiotics for a couple of months: another waste of precious time and money. By now, Dini and her husband, a railway worker, had spent Rs 5,000 on inappropriate medication, all to no effect.

Some six months later, she visited the Railway Hospital and was referred to the Government Hospital in

Koraput for an Xpert test. That same day, she was found to be positive for TB and sensitive to Rifampicin. The medical officer identified a DOTS (directly observed treatment short course) provider living close to her and, under supervision, she was immediately able to start on first-line anti-TB medication.

Although she continued to cough and be short of breath, her symptoms soon subsided and she gained 10 Kg over the next three months. Dini was grateful to the medical staff who came through for her, ensuring she received quality diagnosis and treatment. She said she had learned – the hard way – that nothing but prompt diagnosis and appropriate medication can cure an illness.

> Detection and rapid access to treatment is the only way to improve patient outcomes and to reduce transmission of the disease.



Easing work of laboratories and patient follow-up



Dr. Pranav Patel, Intermediate Reference Laboratory, Ahmedabad
Thanks to LPA, patients are diagnosed in 48 hours

The Intermediate Reference Laboratory in Ahmedabad, Gujarat started using line probe assay (LPA), a novel molecular diagnostic test for MDR-TB, in 2009. "Prior to that," reports Dr. Pranav Patel, "the lab was using a Löwenstein-Jensen solid media test for the diagnosis and follow up of MDR-TB cases – a time-consuming procedure that resulted in patients being prevented from starting treatment as early as they should. All this has changed, thanks to the speed with which the lab was able to achieve results using the new test."

The LPA test was validated and compared with solid culture and DST, and the results were found to be accurate and comparable. Consequently, RNTCP opted to use it as a first method for diagnosis of

MDR-TB. It's now possible to diagnose patients in two days.

Not surprisingly, there has been a high demand from the national programme for early diagnosis using the LPA test. As of December 2013, more than 22,000 LPA tests were performed at the Ahmedabad laboratory, resulting in the diagnosis of more than 3,000 MDR-TB cases.

"We are happy to be one of the first few labs to roll out new TB diagnostics in the context of the Revised National TB Control Programme of India," writes Dr. Patel, "and to have made history with the support of the Central TB Division, Government of India and FIND India."

"Thanks to the speed with which we are now able to deliver results using new tests, patients are not lost for follow-up and can start early treatment."



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