FIND
Because diagnosis matters

Centre international de TB McGill

McGill International TB Centre

McGill GLOBAL HEALTH PROGRAMS

Evaluation of new TB diagnostics:

A capacity building workshop for public sector institutions in India

Goals and key considerations

Grant support from:

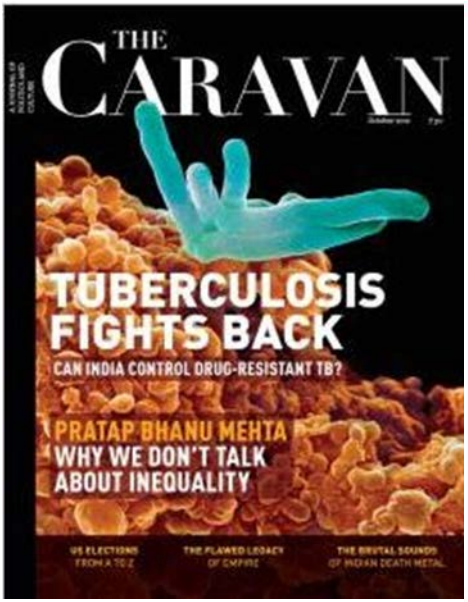
CapitalforGood

Our previous course in Chennai in Dec 2010

Goal

- To contribute to improved policy development in India, by strengthening TB diagnostics validation capacity and collaboration among the key Institutions involved in TB research (including ICMR institutes, medical colleges and National TB institutes under the Ministry of Health) and policy (RNTCP).

TB in India remains a major public health challenge



THE WALL STREET JOURNAL.

India in Race to Contain Untreatable Tuberculosis

By Geeta Anand

MUMBAI—India's slow response to years of medical warnings now threatens to turn the country into an incubator for a mutant strain of tuberculosis that is proving resistant to all known treatments, raising alarms of a new global health hazard.

"We finally have ended up with a virtually untreatable strain" of tuberculosis in India, said Dr. Zarir Udwadia, one of the country's leading TB authorities.

In December, Dr. Udwadia reported in a medical journal that he had four tuberculosis patients resistant to all treatment. By January, he had a dozen cases, then 15.

A government backlash began immediately. Anonymous health-ministry officials denied the reports through media outlets. They accused Dr. Udwadia and his colleagues of starting a panic. A Mumbai city health official seized patient samples for verification in government labs.

In April, the government quietly confirmed the strain, according to internal Indian health-ministry documents reviewed by The Wall Street Journal.

Spread of the strain could return tuberculosis to the fatal plague that killed two-thirds of people afflicted, before modern treatments were developed in the 1940s, said Mario Raviglione, director of the Stop TB Department of the World Health Organization. The WHO is now assisting India to combat the strain.

The number of known cases in India is small but geographically dispersed. Dr. Udwadia's patients are in Mumbai, at the P.D. Hinduja National Hospital & Medical Research Center. In the high-tech hub of Bangalore, St. John's National Academy of Health Sciences has seen six cases. And in New Delhi, the All India Institute of Medical Sciences has confirmed another two, said officials at the institutions.

"While this handful of cases is worrying, it's just the tip of the iceberg," said Dr. Soumya Swaminathan, of India's National Institute for Research in Tuberculosis. For treatments, Dr. Udwadia said, "We've got nothing."

Ashok Kumar, head of India's tuberculosis-con-

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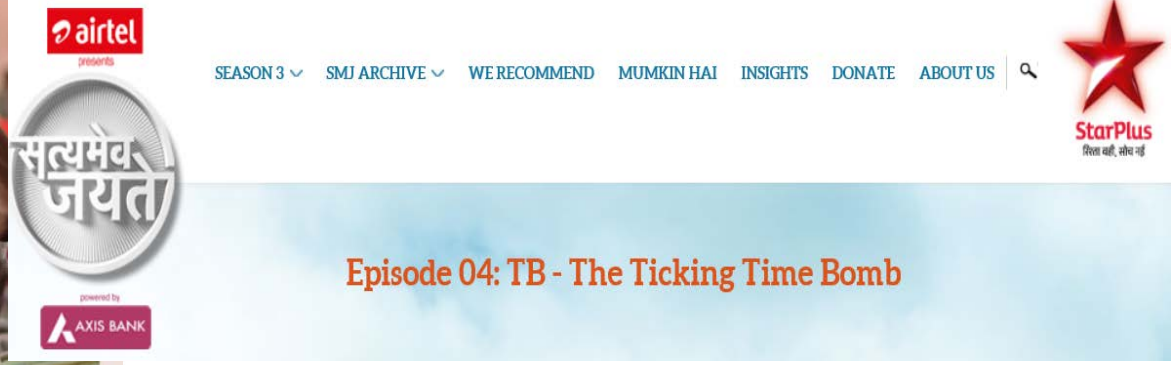
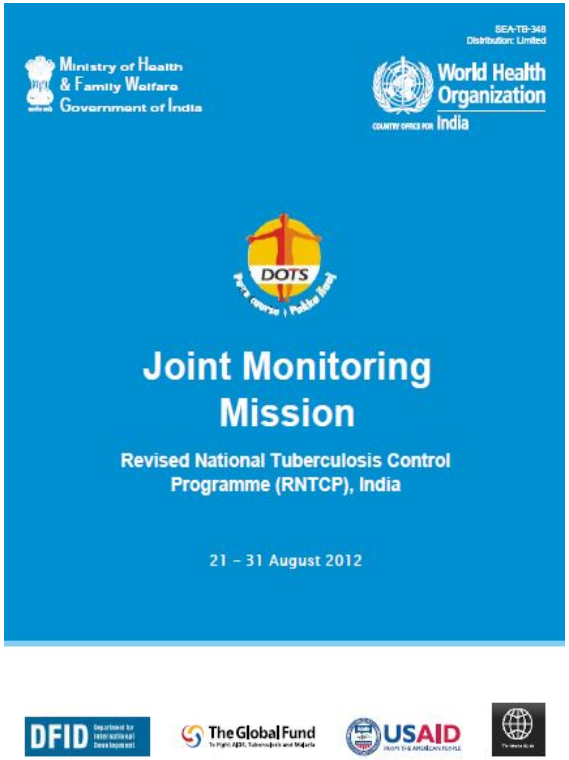
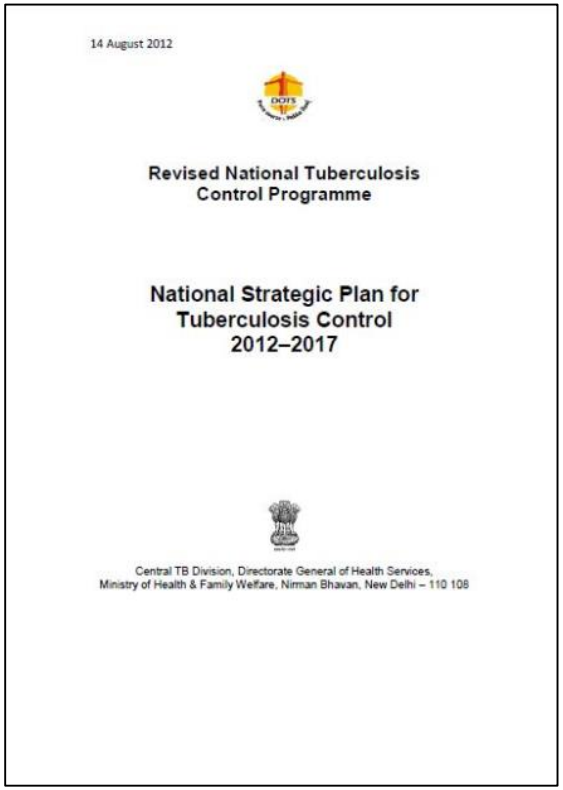


The problem has been analyzed and reported

JMM Report , RNTCP, India, 2012



National Strategic Plan for TB Control (2012-2017)



VHAI Health For Millions

What can explain the high incidence, missing cases and MDR problem?

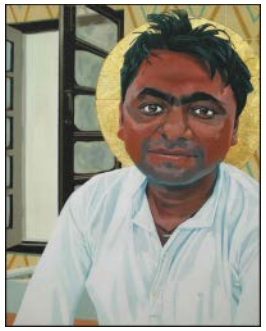
- Underlying social determinants are hardly addressed
- There is considerable diagnostic delay and thus ongoing transmission
- Even if diagnosis is made, treatment and monitoring are suboptimal
- We are still working with outdated tools and antiquated systems

Average TB patient in India continues to struggle to find a diagnosis

Public sector

?

Private sector



- Diagnosis by smear
- Free treatment, but not convenient
- Can now get MDR Dx/Rx, but poor access

- High OOP expenditure
- Mismanaged diagnosis
- Sub-standard treatment
- Unaffordable MDR Rx

India has articulated high ambitions to transform TB control

National Strategic Plan ('12-17) committed:

- **<u>Universal Access</u>:**

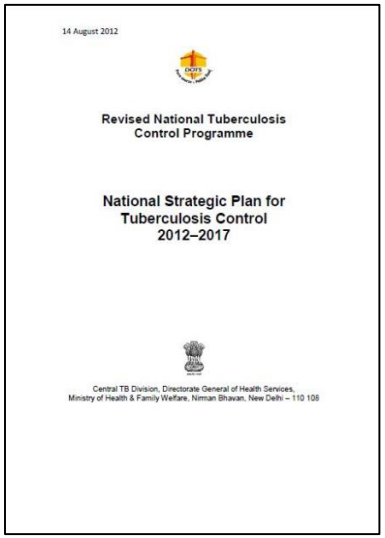
  90% of estimated incident TB cases diagnosed & treated as per nationally-accepted protocols

- **<u>Reduction in TB deaths</u>**

  ≥30% TB mortality reduction compared to 2010

- **<u>Real-time ICT surveillance</u>**:

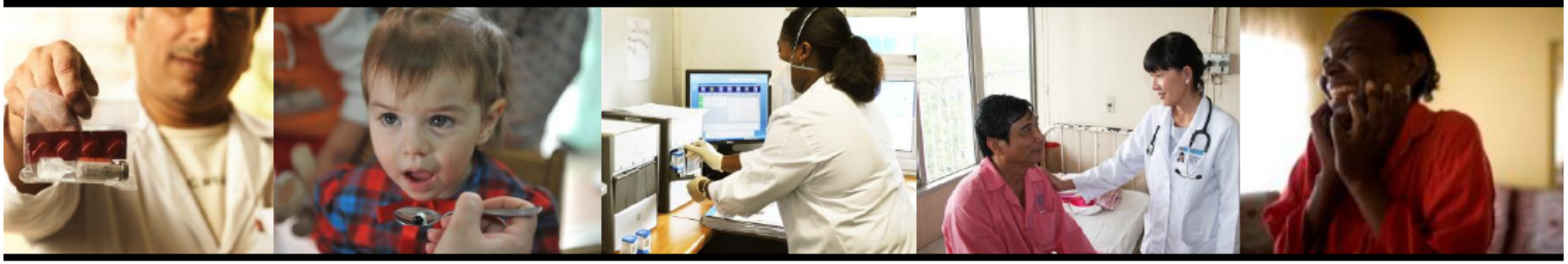
  100% of districts with RNTCP integrated into health blocks, with full ICT system implementation



THE END TB STRATEGY

World Health Organization

Global strategy and targets for tuberculosis prevention, care and control after 2015



VISION	**A world free of tuberculosis** – zero deaths, disease and suffering due to tuberculosis
GOAL	**End the global tuberculosis epidemic**
MILESTONES FOR 2025	– 75% reduction in tuberculosis deaths (compared with 2015); – 50% reduction in tuberculosis incidence rate (compared with 2015) (less than 55 tuberculosis cases per 100 000 population) – No affected families facing catastrophic costs due to tuberculosis
TARGETS FOR 2035	– 95% reduction in tuberculosis deaths (compared with 2015) – 90% reduction in tuberculosis incidence rate (compared with 2015) (less than 10 tuberculosis cases per 100 000 population) – No affected families facing catastrophic costs due to tuberculosis

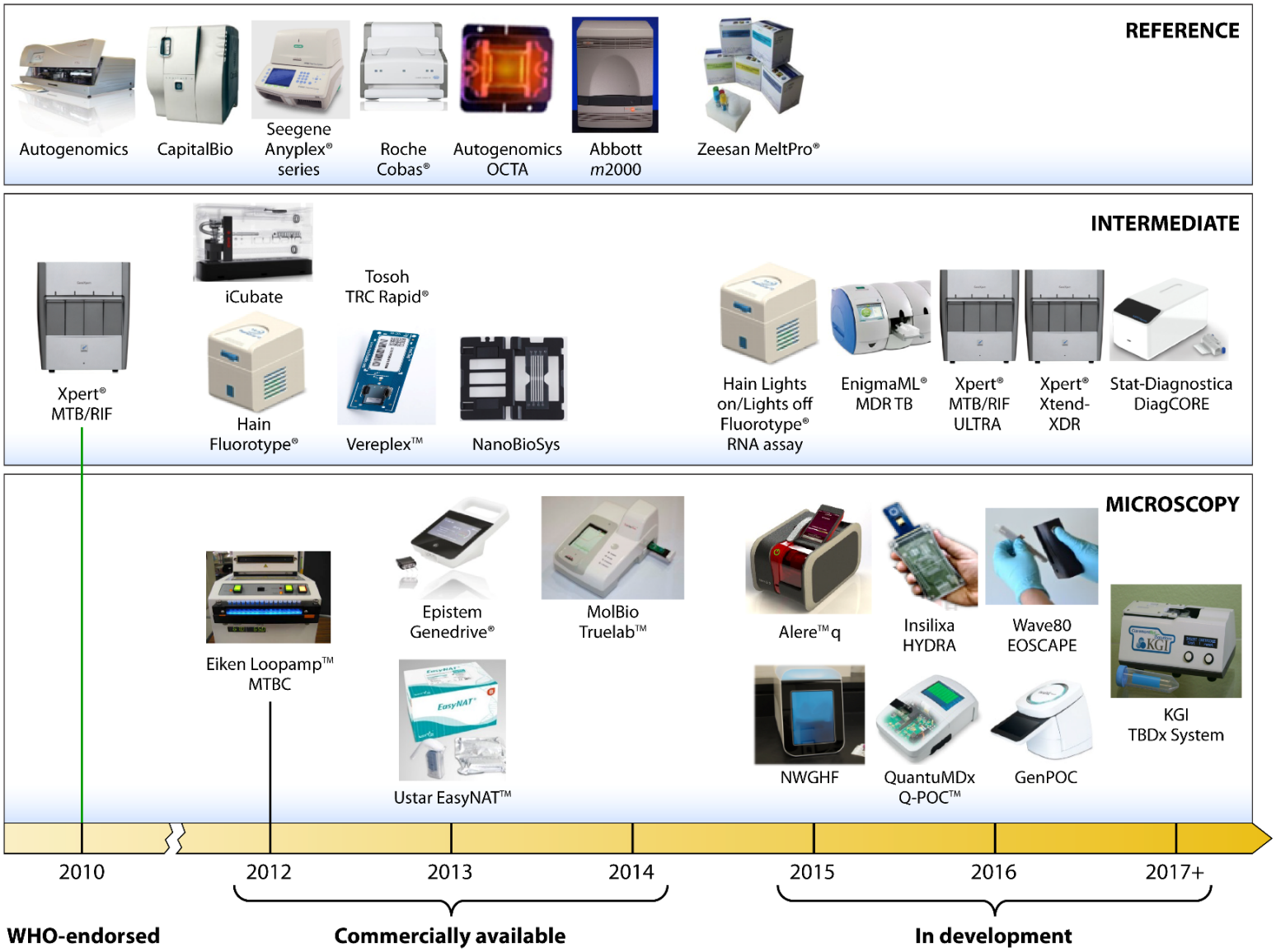
We will not reach these targets without modernizing DOTS

Key elements	Current/Past	Future
Political commitment with increased and sustained financing	Poor funding for TB	Funding to match the goal of universal access and National Strategic Plan; universal health care
Case detection through quality-assured bacteriology	Mostly direct ZN microscopy	Rapid molecular testing with upfront DST
Standardized treatment, with supervision and patient support	HRZE, 6 months DOT	PaMZ or other shorter regimens (4 months); Multifaceted approach, including electronically observed therapy
An effective drug supply and management system	Erratic supply and stockouts	Improved supply chain management
Recording and reporting system	Paper-based	Fully digital/ICT

We have always wanted new tools, and they are here!

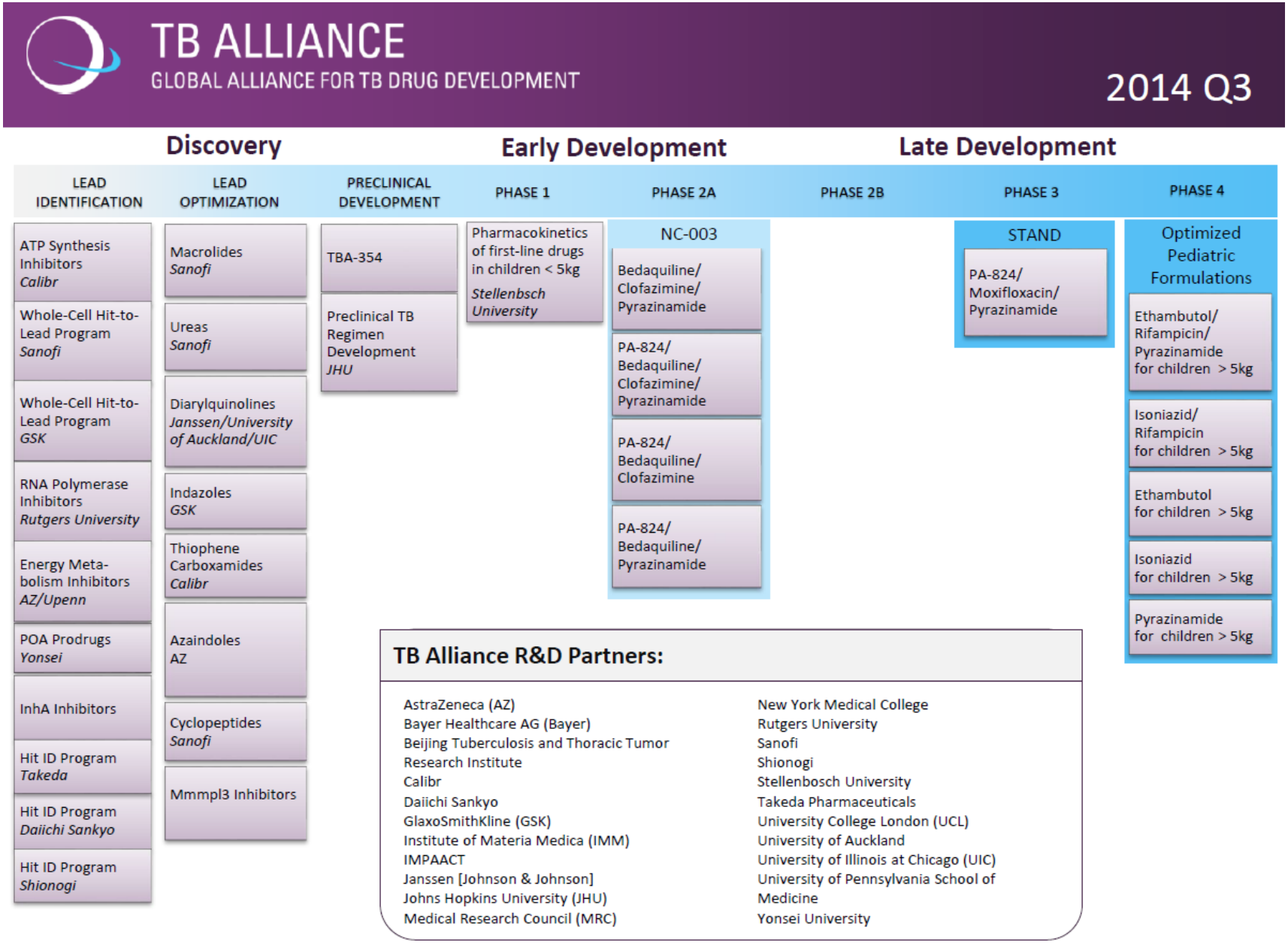
- New diagnostics
- New TB drugs and regimens
- ICT for adherence monitoring, notification, etc.

New molecular diagnostics

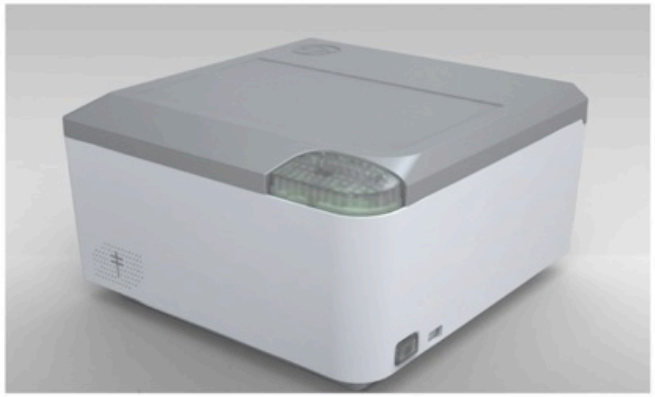


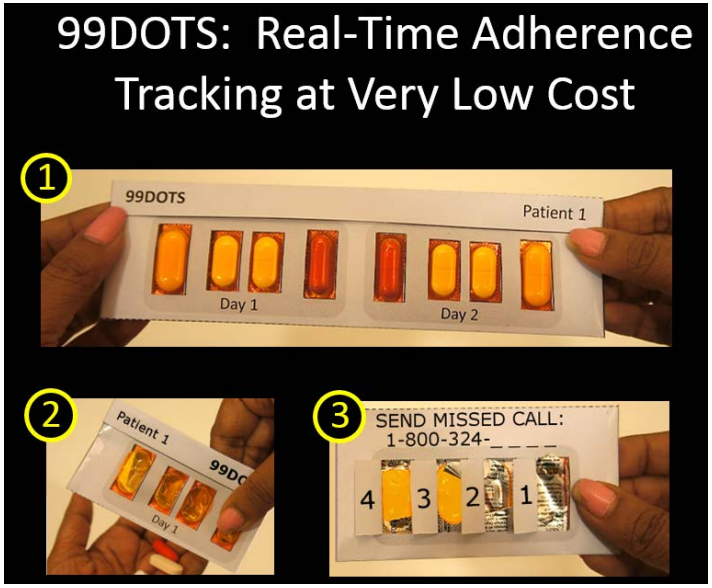
Source: UNITAID 2014

New TB drugs and regimens



New adherence monitoring tools

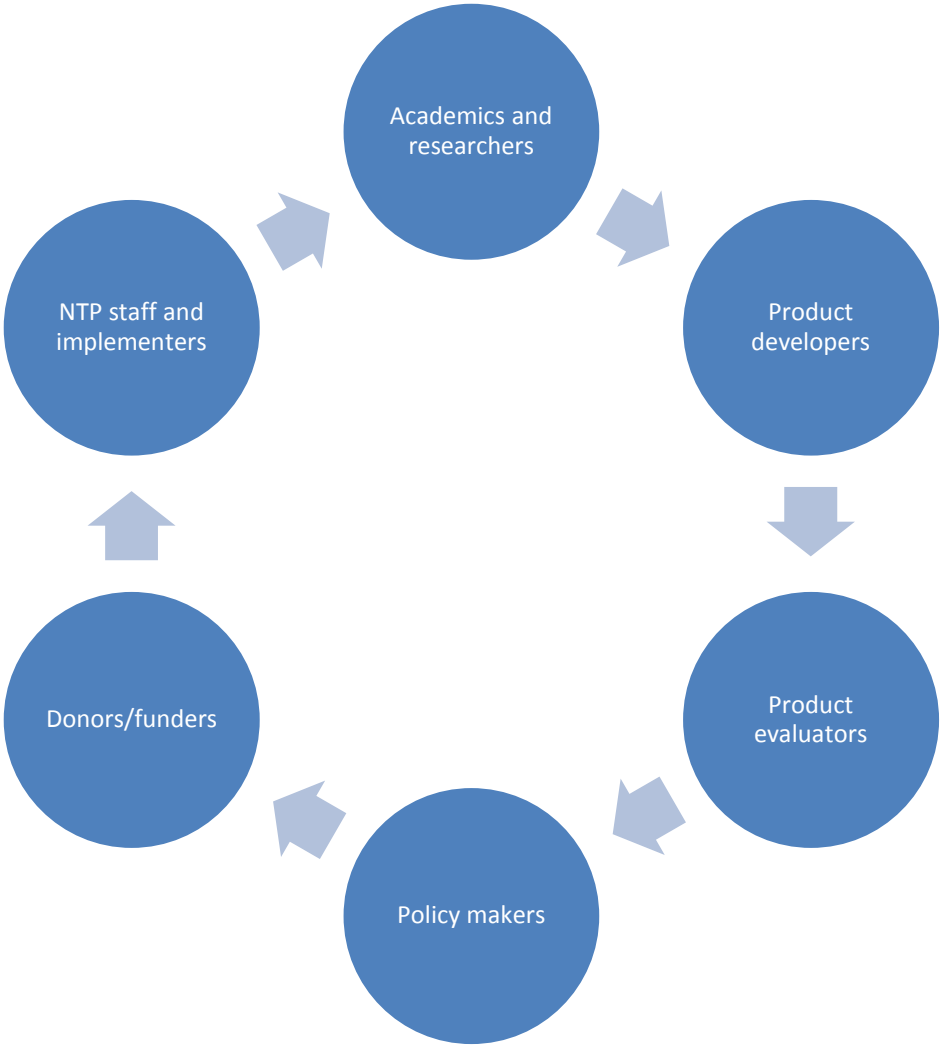




Urgent need

A clear, coordinated strategy to evaluate new tools and technologies, and to decide on their policy and scale-up

To scale up new tools, we need key stakeholders to work together



Evaluation of new diagnostics

- Public sector
  - Revised National TB Control Program
  - National TB Institutes: NIRT, NTI, NITRD, JALMA
  - Other public sector research institutes and medical colleges
  - Supported by FIND, WHO, BMGF, USAID, and other partners

- Private sector
  - Private medical colleges and hospitals (e.g. Hinduja, CMC, St John's)
  - IPAQT (83 private labs engaged), coordinated by Clinton Health Access Initiative

What we really care about

- New tools get developed
- They undergo adequate evaluation
- Evidence-based policies get formulated
- Products and policies get implemented in countries
- Impact is seen on disease burden

This could be a single long value chain…

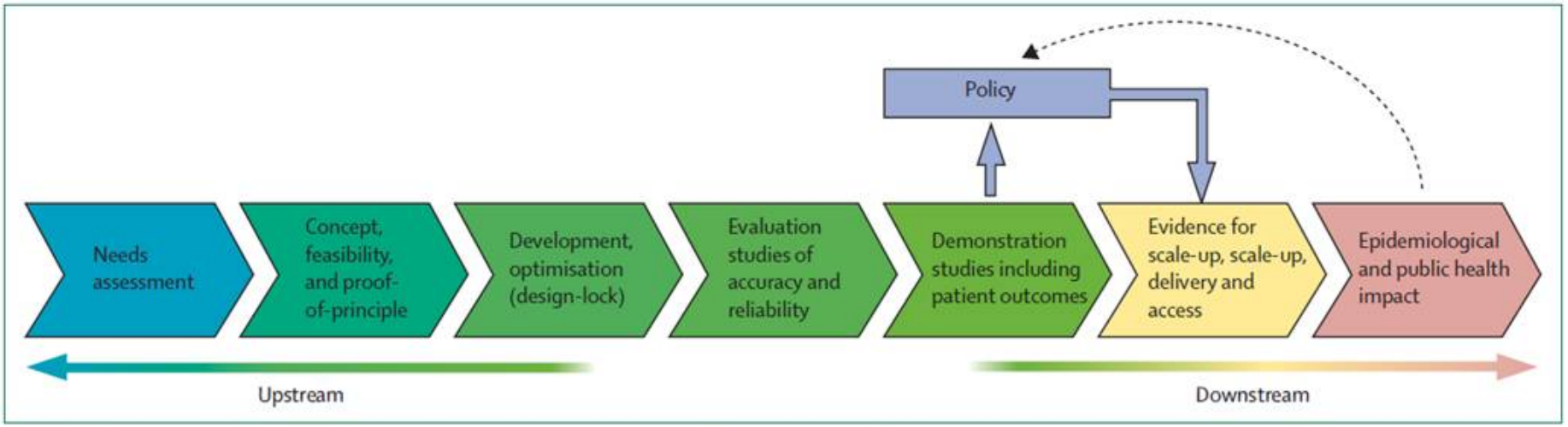


Figure 4: **Schematic showing the pathway to tuberculosis diagnostics, from concept to delivery**

Source: Stop TB Partnership's New Diagnostics Working Group. Pathways to better diagnostics for tuberculosis: a blueprint for the development of TB diagnostics (2009),[180] and reproduced with permission from author and publisher.

Value chain for Xpert MTB/RIF


The NEW ENGLAND JOURNAL of MEDICINE

Rapid Molecular Detection of Tuberculosis and Rifampin Resistance

Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicentre implementation study

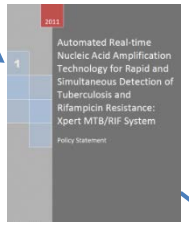
WHO Expert Group meeting on Xpert Sept 1 & 2, 2010

World Health Organization

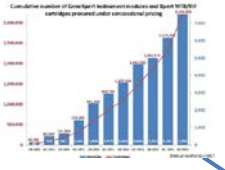
Implementation and scale-up of the Xpert MTB/RIF system for rapid diagnosis of tuberculosis and multidrug-resistance

GLOBAL CONSULTATION

Date and time: 30 November - 2 December 2010
Venue: Centre International de Conférences de Genève (CICG)
17, Rue de Varembé, Geneva, Switzerland


Automated Real-time Nucleic Acid Amplification Technology for Rapid and Simultaneous Detection of Tuberculosis and Rifampicin Resistance: Xpert MTB/RIF System

Policy Statement



Looks linear, but is not

Scale-up at the country level & impact (future)

In reality, several intersecting* value chains…

- Product development value chain
- Product evaluation value chain (diagnostic research and evidence)
- Policy value chain (global and country-specific)
- Implementation value chain (scale up)
- Impact assessment value chain

*often, these value chains do not intersect and that is a problem!

Weak links in this value chain

- Global value chain is envisioned in a linear way
- The global and local value chains are not well aligned
- WHO approval not mandatory, but might help for country adoption

- Even if WHO approved, local studies are often needed

  - On feasibility, cost-effectiveness, fit with algorithms, HR and lab implications, delivery models, willingness to pay, price point analysis, etc.
  - There is a need for a coordinated mechanism to collect in-country evidence quickly to support local scale-up decisions

Proposed revised value chain for new TB diagnostics

Which New Diagnostics for Tuberculosis, and When?

Frank Cobelens,[1] Susan van den Hof,[1,2] Madhukar Pai,[3] S. Bertel Squire,[4] Andrew Ramsay,[5] and Michael E. Kimerling[6] on behalf of the Evidence for Scale-up Group

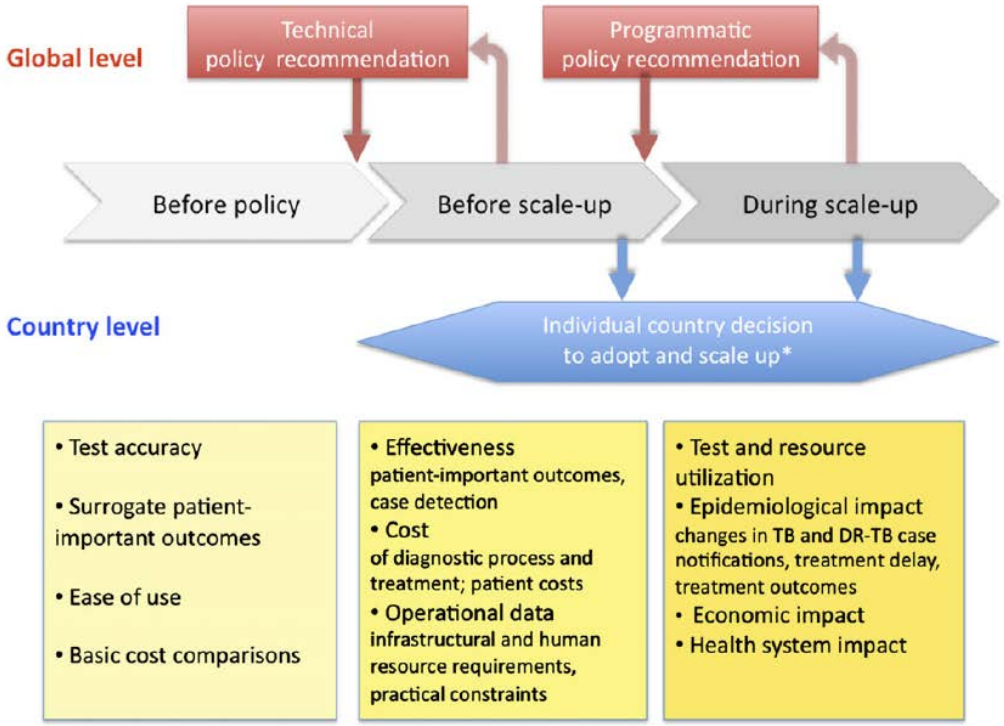


Figure 3. Proposal for a revised pathway focused on the postaccuracy phase of tuberculosis diagnostics, showing the proposed value chain for new diagnostic tests for tuberculosis. The grey arrows in the middle represent the stages in the evaluation pathway, and the colored boxes represent policy decisions at the global level (red) and the country level (blue). Countries would adopt implementation at different points and should provide feedback about their experiences (* in the blue box). In the stages before scale-up and during and after scale-up, evaluation data would be collected on diagnostic algorithms incorporating the new test.

Journal of Infect Dis 2012

Product evaluation is the focus of this workshop, and protocol development is a key outcome

- We will hear about new diagnostics and innovations
- We will learn how to design high-quality evaluation studies
- We will work in 5 small groups to develop protocols for their evaluation
  - Team Koch (Mayank Ghedia and Ranjani R)
  - Team Mullis (Neeraj Raizada)
  - Team Pasteur (Samuel Schumacher)
  - Team Buchner (Hojoon Sohn)
  - Team Rontgen (Srinath S)

Our hope

- You will go home excited about the potential of new tools
- You will consider taking on evaluation studies of new diagnostics
- You will join multi-centric evaluation studies
- Once policies are made, you will help implement new tools

Resources

- USB drive with lots of very good materials, including sample protocols
- PPT of all talks will be uploaded on www.teachepi.org

- Some important resources:

  - www.teachepi.org
  - www.tbevidence.org
  - www.tbfaqs.org
  - UNITAID landscape reports

teach epi

A website for learning and teaching epidemiology

Madhukar Pai, MD, PhD
Associate Professor
McGill University, Montreal, Canada

Evidence-Based Tuberculosis Diagnosis

A Comprehensive Resource For Evidence Syntheses, Policies, Guidelines And Research Agendas On TB Diagnostics

Home

Developed with the support of:

Stop TB Partnership's New Diagnostics Working Group (NDWG)
World Health Organization (WHO)
Foundation for Innovative New Diagnostics (FIND)
Special Programme for Research and Training in Tropical Diseases (TDR)
Global Laboratory Initiative (GLI)
Public Health Agency of Canada (PHAC)
Curry International Tuberculosis Center, UCSF
McGill TB Research Group

tbfaqs.org

EVIDENCE-BASED TB DIAGNOSIS CREDITS RELATED LINKS CONTACT US

TB Diagnostics: Top 10 FAQs By Test Developers

RESOURCES POSTED

Useful resources for each question are now available on our website.

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Tuberculosis diagnostics: test developers' FAQs

Diagnostics for tuberculosis: what test developers want to know

A new resource for TB diagnostics developers


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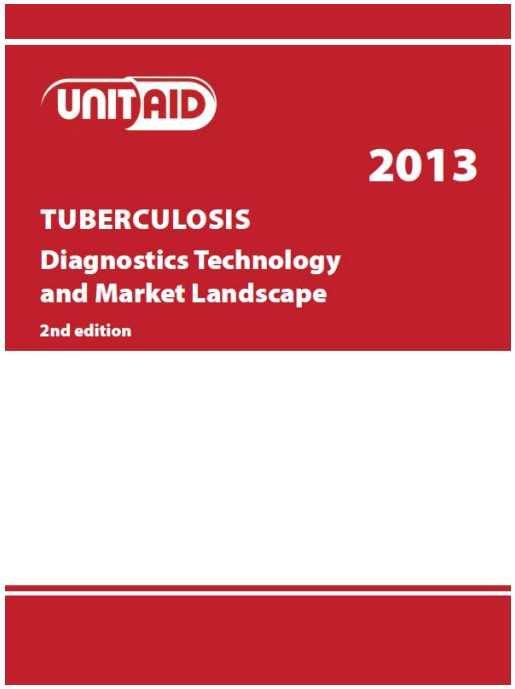
Diagnostic Technology Landscape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2nd edition


UNITAID
2014
TUBERCULOSIS
Diagnostics Technology
and Market Landscape
3RD EDITION

Thank you

- Everyone, for your interest & participation
- Soumya Swaminathan, NIRT
- NIRT Team: Dina Nair, S Balaji, Banu Rekha, Senthil Murugan
- Speakers, panelists, and small group facilitators
- FIND: Catharina Boehme, Neeraj Raizada, Claudia Denkinger
- Kate Volpicelli, Geneva Global and Capital for Good
- McGill team: Samuel Schumacher, Hojoon Sohn, Srinath S, Caroline Vadnais
- Industry colleagues