FIND and NDWG symposium
Panel Discussion

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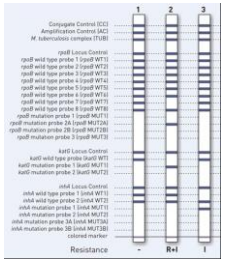
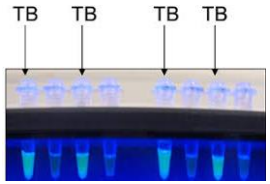
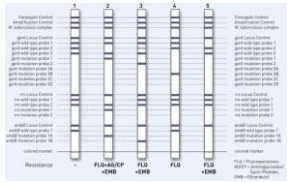
48° Union World Conference, Guadalajara October 11th 2017

Molecular tests for diagnosis of TB and drug resistance







2008 Dec 2010 2016 2017

THE END TB STRATEGY

KEY DIAGNOSTIC OBJECTIVES:

- Early diagnosis of TB
- Universal drug-susceptibility testing*
  *all bacteriologically confirmed TB patients should recive DST at least for RIF; all patients with RR-TB should receive DST at least for FQs and SLIDs
- Systematic screening of contacts and high-risk groups

An overview on TB diagnostics uptake

- 52% (15/29) countries recommend Xpert as initial test for all
- 97% (28/29) of countries recommend Xpert as initial test for high risk groups. Only 54% (15/28) of them have implemented it widely

25-30% avg. global
Xpert utilization rate (2016 est)

- 56% (15/27) of countries have guidelines that require line probe assays (LPAs) for second-line drug-resistance as the initial test for people with confirmed RR- and MDR-TB

COUNTRY	Xpert MTB/RIF is the initial TB diagnostic test for adults and children being investigated for TB	TB-LAM is used to diagnose TB in PLWHA with CD4 ≤ 100 µL or seriously ill	First-line DST (rifampicin and isoniazid) is done for all RR-TB cases or for people at risk of DR-TB	Second-line DST (fluoro-quinolones and second-line injectable agents) is done for at least all RR-TB cases
Afghanistan	No	No	Yes	Yes
Armenia	Yes [a]	No	Yes	Yes
Bangladesh	No	No	No	No
Belarus	Yes [b]	No	Yes	Yes
Brazil	Yes	No	Yes	Yes
Cambodia	No	No	Yes	No [c]
CAR	No	Unknown	Yes, but not widely	Unknown
China	No	No	Yes	Yes
DRC	No	No	Yes	No [c]
Ethiopia	No	No	No	Yes, but not widely
Georgia	Yes	No	Yes	Yes
India	No	No	Yes, but not widely	Yes, but not widely
Indonesia	Yes, but not widely	No	Unknown	Yes, but not widely
Kazakhstan	No	No	Yes	Yes
Kenya	Yes, but not widely	No	Yes	Yes, but not widely
Kyrgyzstan	Yes, but not widely [d]	No	Yes, but not widely	Yes, but not widely
Mozambique	Yes, but not widely	No	Yes, but not widely	No [e]
Myanmar	No	No	Yes, but not widely [f]	No [f]
Nigeria	Yes, but not widely	No	Yes	No
Pakistan	No	No	Yes	Unknown
PNG	Yes, but not widely	No	Yes, but not widely	Yes, but not widely
Philippines	No	No	Yes, but not widely	Yes, but not widely
Russian Fed.	Yes, but not widely [g]	No	Yes	Yes, but not widely
South Africa	Yes	No	Yes	Yes
Swaziland	Yes	No	Yes	Yes
Tajikistan	Yes, but not widely	No	Yes, but not widely	Yes, but not widely
Ukraine	No	No	Yes	Yes
Viet Nam	No	No	No	Yes
Zimbabwe	Yes, but not widely	No	Yes	Yes

LEGEND
Is this policy in place at the national level? Yes / No / Unknown
If Yes, is the policy being implemented? Yes / Yes, but not widely / No / Unknown

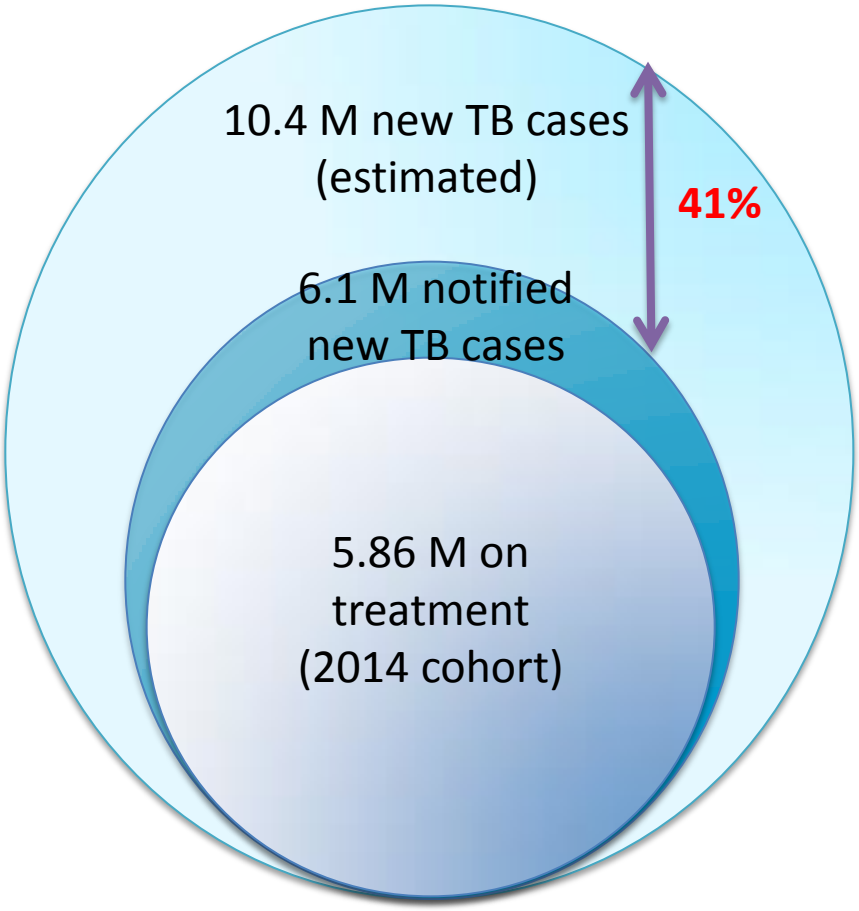
(a) The initial diagnostic test is microscopy, but regardless of microscopy result, every person to be evaluated for TB is tested with Xpert. **(b)** Part of an initial diagnostic package of tests. **(c)** Only select groups of patients are eligible. **(d)** At facilities that offer DR-TB regimens with BDQ or DLM. **(e)** No, but second-line DST is available at National Reference Lab. **(f)** Implementation of the 2017 guidelines is expected for the second half of 2017. **(g)** Xpert is part of a package of diagnostic tools; other diagnostic tests can be used, including other rapid molecular methods.

Available at: https://www.msfaccess.org/outofstep2017

Diagnostic gaps

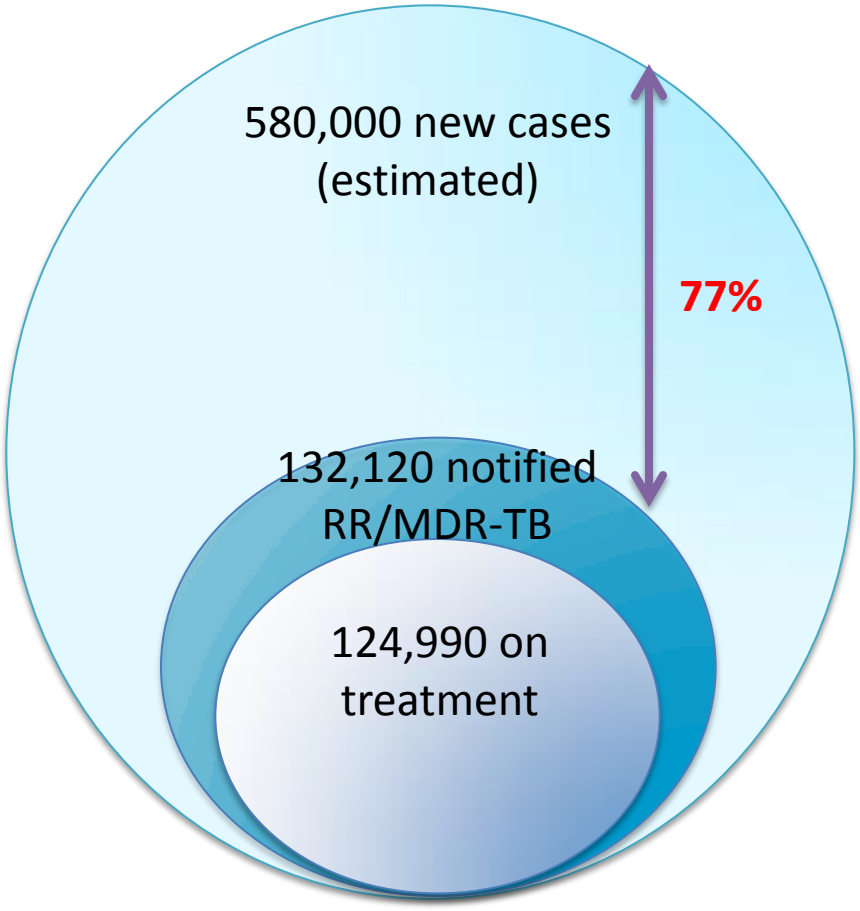
Case finding is the biggest gap in the TB and MDR TB cascades

Global TB burden (2015)



4.3 M new TB cases UNDETECTED or UNREPORTED

Global DR-TB burden (2015)



30% of bacteriologically confirmed cases and previously treated cases received RIF DST

Global Tuberculosis Report, WHO, 2016

Evolving DST needs: what role for molecular testing?

	Regimen acronym		
	PaMZ	BPaMZ	BPaOx
Components			
BDQ			
MFX			
Oxazolidinone			
PA-824			
PZA			
New chemical entities, *n*	1	2	3*
Target treatment duration, months†	4	3	3‡
Study acronym	STAND Phase 3	NC005	Nix-TB

Murray et al 2016 INT J TUBERC LUNG DIS 20(12):S38–S41

- BPaZ
- BPaML
- BCZ
- BCZPa

Testing Need	Current	Future
Isoniazide		?
Ethambutol		
Pyrazinamide		
?		
Bedaquiline		
Delamanid		
Pretomanid		
Sutezolid		

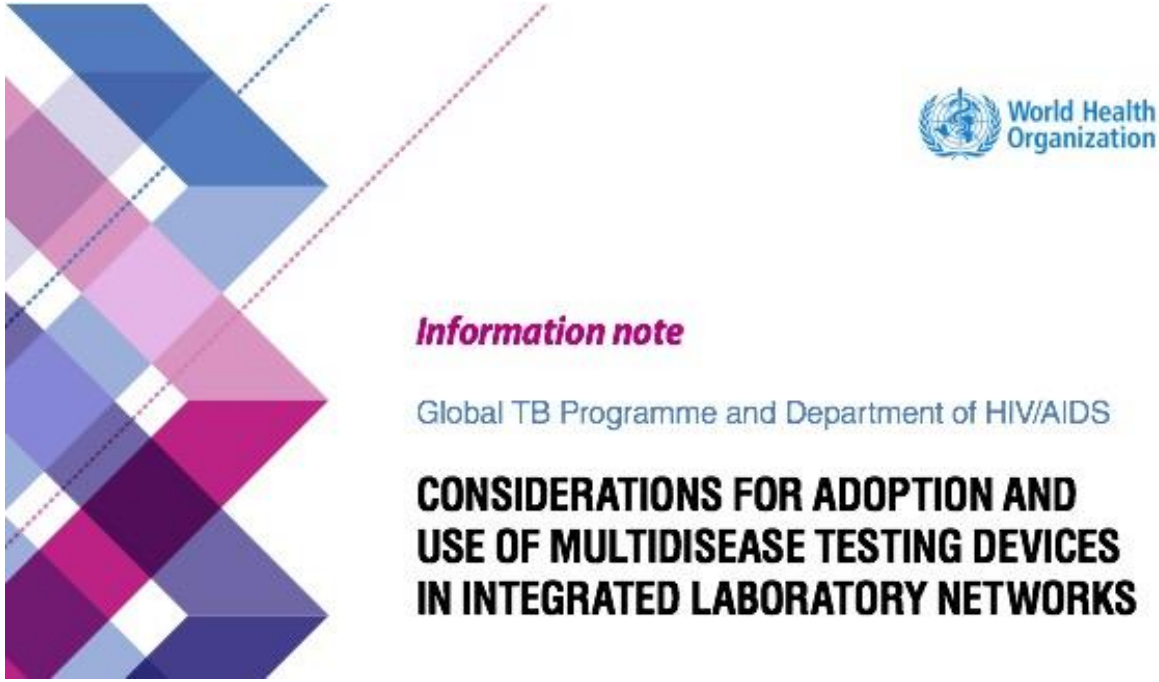
	High priority
	Medium priority
	Low priority

Adapted from slide courtesy of CHAI

➢ Priority DST needs must be updated (in the NDWG workplan)

➢ Which role for sequencing- based DST?

Molecular platforms and multi-disease testing capacity : need for collaboration across programs (eg. TB, HIV, HCV)



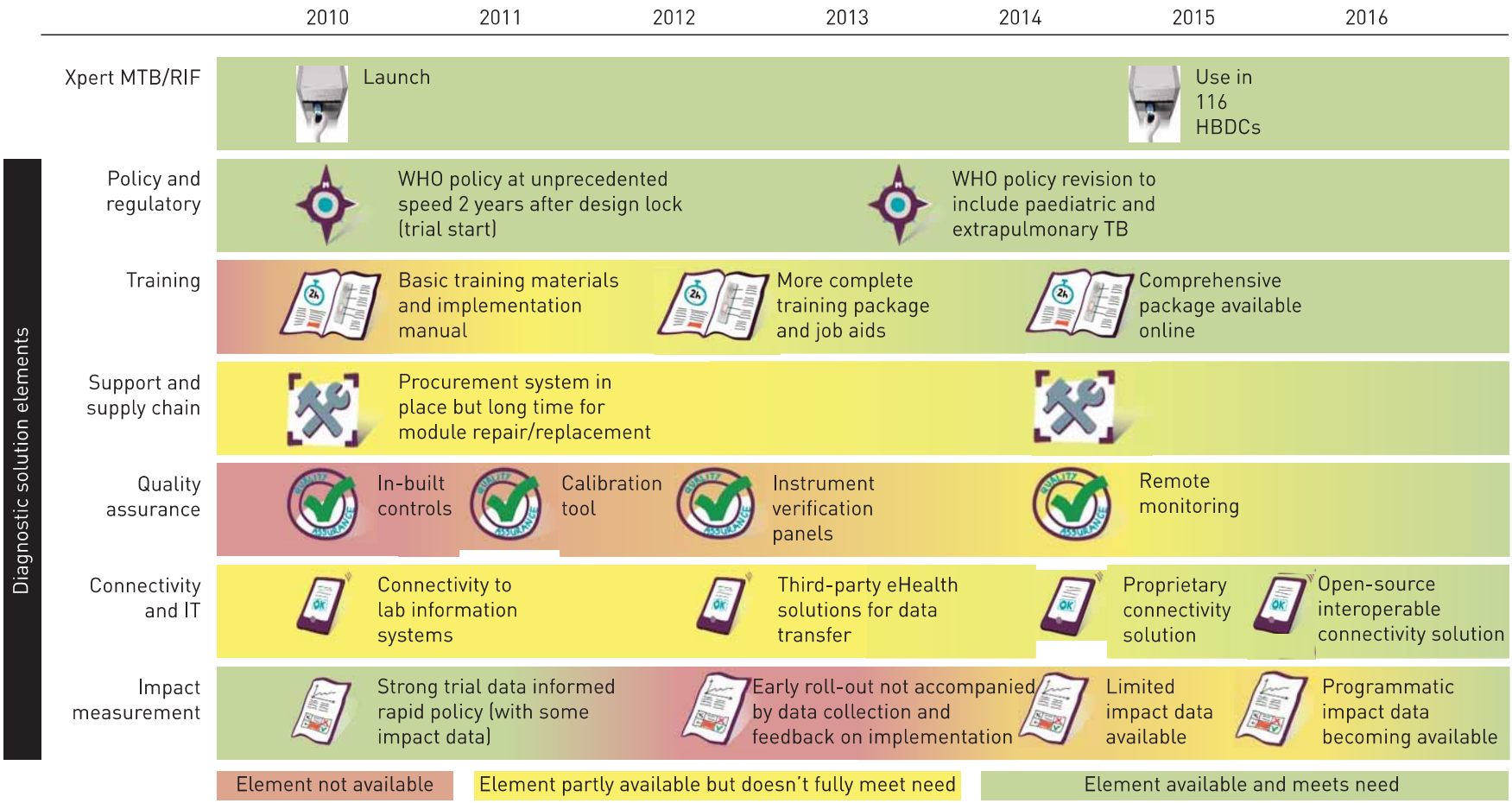
ADVANTAGES:

- An incentive for integration between programs
- Cost efficiencies (due to increase utilization of testing capacity)
- Increased negotiating power

- IS THIS FEATURE BEING CONSIDERED AND EXPLOIT?
- IF NOT, WHAT ARE THE KEY CHALLENGES THAT PREVENT USE OF PLATFORM FOR MULTIPLE DISEASES

Introducing new diagnostic tools requires a comprehensive strategy

Diagnostic solutions + « enabling contexts » = IMPACT



Albert H. et al (2016). Eur Respir J. Aug;48(2):516-25

Introducing new diagnostic tools requires a comprehensive strategy

Key elements towards establishement of « enabling contexts »

National Programs

- Patient Centered models of care and/or strategies that support continuum of care
- Timely development of training programs and PSM plans
- Key diagnostic elements included in NSP and national budgets

WHO and Platforms for Technical Guidance

- Timely guidance on use and implementation of new technologies
- Timely guidance on model algorithms
- Timely guidance on interpretation of results/reference standards for DST

Donors

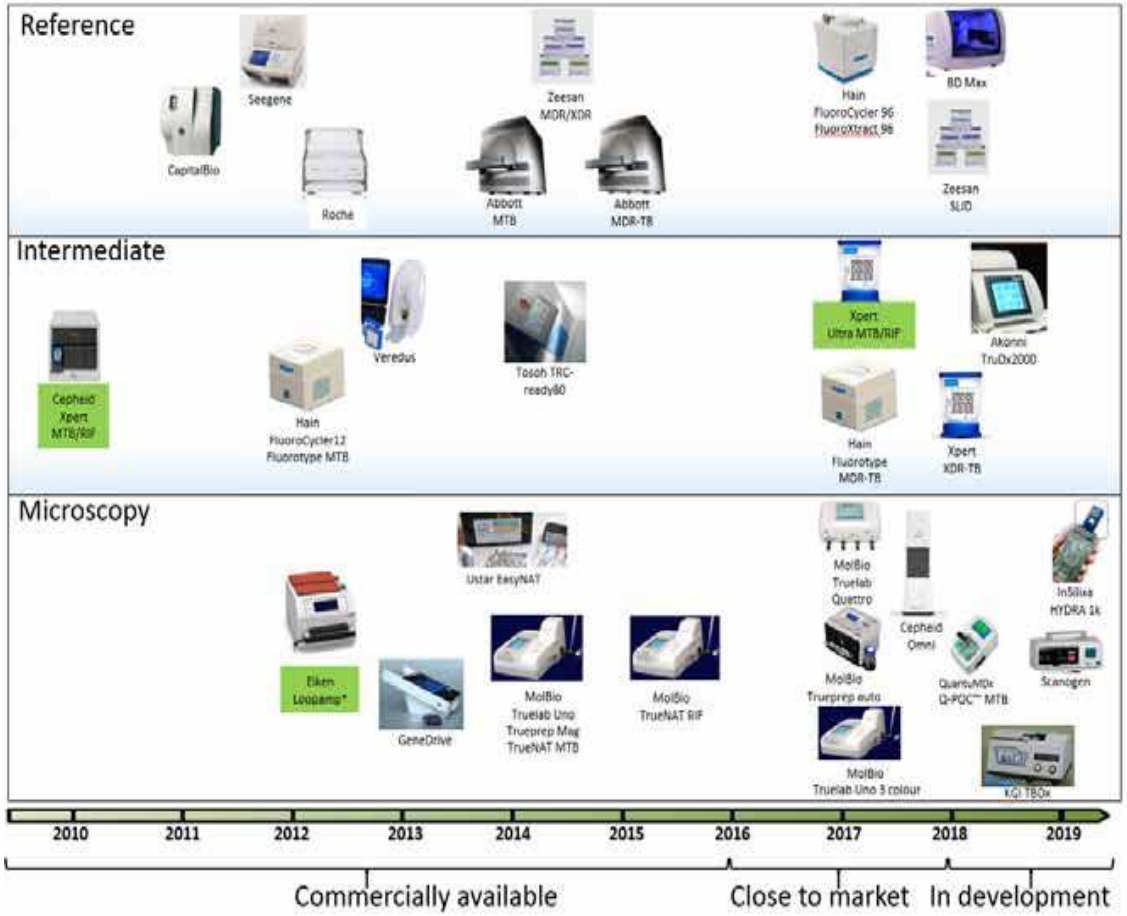
- Support roll-out of new technologies, including operational research
- Support improvement of laboratory capacity and sample referral systems
- support training programes

Panel discussion: Challenges in molecular testing roll-out and optimization at a programmatic level

- More technologies will become available

- How can we :
- keep improving patient access to existing rapid molecular tools?

- get adequately prepared for effective uptake of new tools?



Source: Tuberculosis diagnostics technology Landscape, UNITAID, May 2017)

Panel discussion

Challenges in molecular testing roll-out on a programmatic level

Panelists:

- Stephanie Denamps, CHAI
- Gunta Dravniece, KNCV
- Kathleen England, MSF Access Campaign
- Kaiser Shen, USAID

Panel discussion

1. Based on **lessons learnt through the Xpert and LPA roll-out**:
   a) What are the **top 3 challenges that have yet to be overcome** to boost uptake of existing technologies?
   b) What are the key aspects that you would improve in terms of **preparedness for timely and efficient uptake** of future ones?
   c) Molecular testing platforms provide **capacity for multi-disease testing**
      - Are you looking at exploiting this feature?
      - If yes, how are you approaching this and does this pose additional challenges for implementation?

2. Are we doing enough to ensure **generation of country-level evidence** that can inform roll-out and use of molecular testing ?

3. **Interpretation of results and discordance between phenotypic and genotypic DST** has emerged as one of the key challenges during roll-out of existing molecular tests:
   To help overcoming this challenge, what kind of support is needed from key stakeholders?

Panel discussion

4. **NGS has the potential to improve access to extended DST for additional drugs** included in treatment regimens and therefore support design of more effective therapy
   - Are countries aware of this opportunity? And **are countries planning to build NGS capacity at central level**?
   - What **alternative/interim strategies** should be considered while countries are working on building capacity for NGS?

5. **New technologies are on the horizon that have the potential to further improve rapid diagnosis of TB and drug resistance** (including sequencing based technologies)
   - What would be your **key recommendations to manufacturers** working on these technologies?
   - What **actions are required from manufacturers** to facilitate in-country uptake and roll-out?