



# Implementation and scale-up of the Xpert MTB/RIF system for rapid diagnosis of TB and MDR-TB

## Global Consultation

*Geneva, 30 November 2010*

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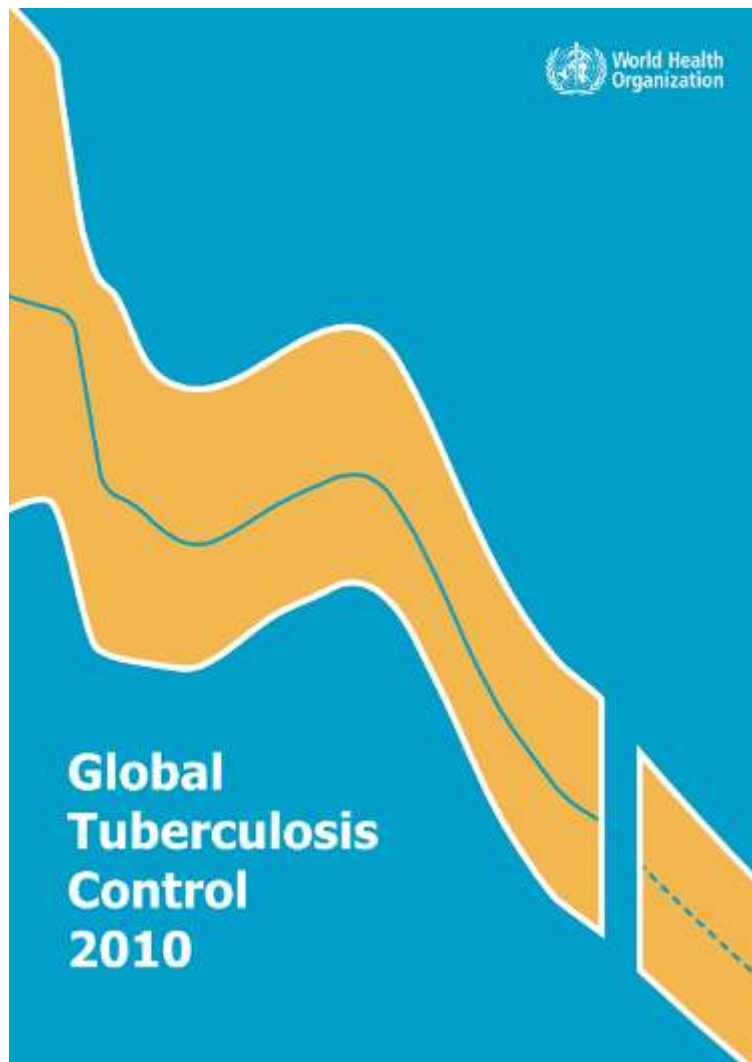


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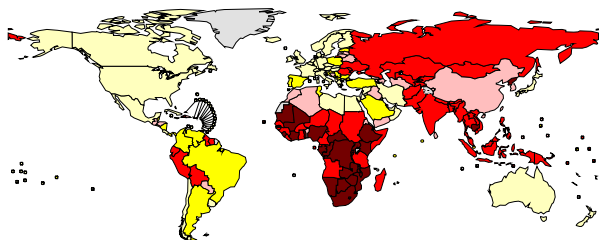
# Global Tuberculosis Control Report 2010



Launched in Berlin  
11 November 2010



# The Global Burden of TB - 2009



**Estimated  
number of cases**

**Estimated  
number of deaths**

**All forms of TB**

9.4 million  
(range: 8.9–9.9 million)

1.3 million\*  
(range: 1.2–1.5 million)

**HIV-associated TB**

1.1 million (12%)  
(range: 1.0–1.2 million)

380,000  
(range: 320,000–450,000)

**Multidrug-resistant  
TB (MDR-TB)**

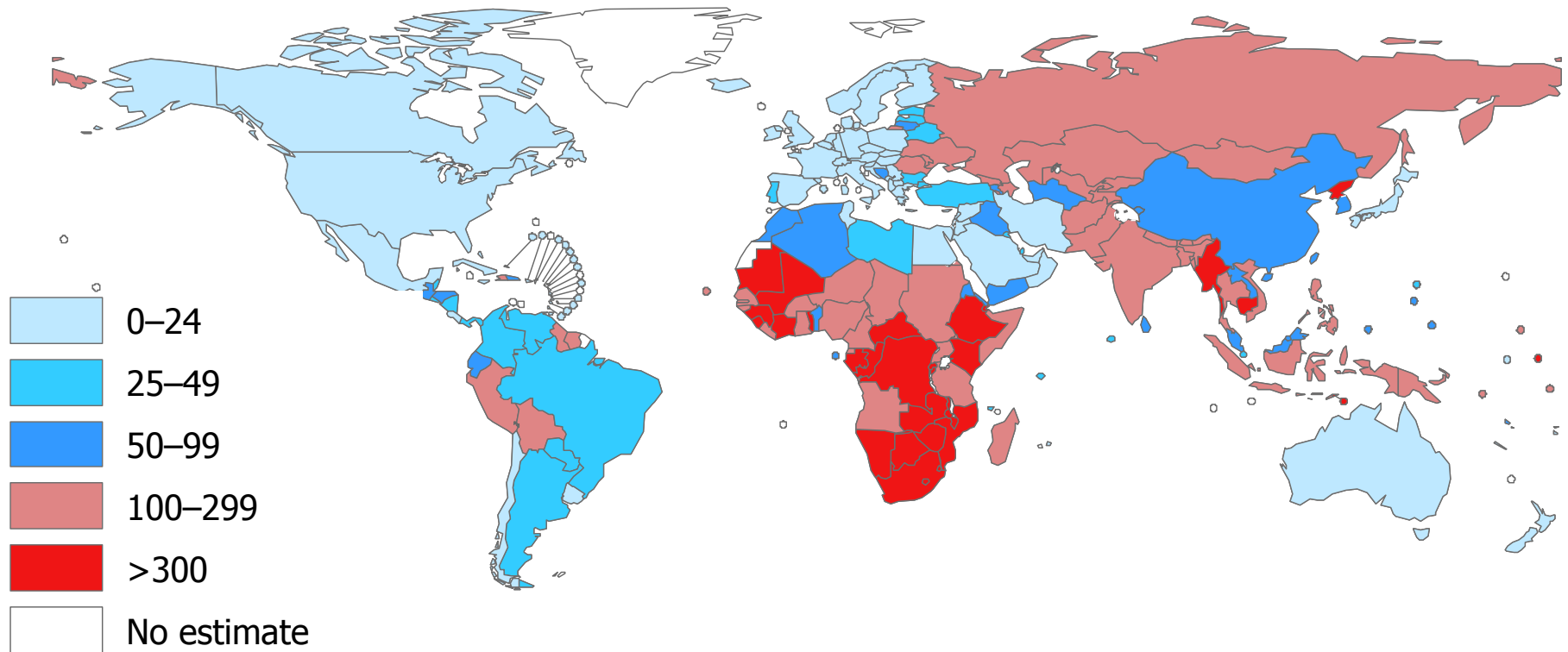
440,000  
(range: 390,000–510,000)

about 150,000

\*excluding deaths among PLHIV



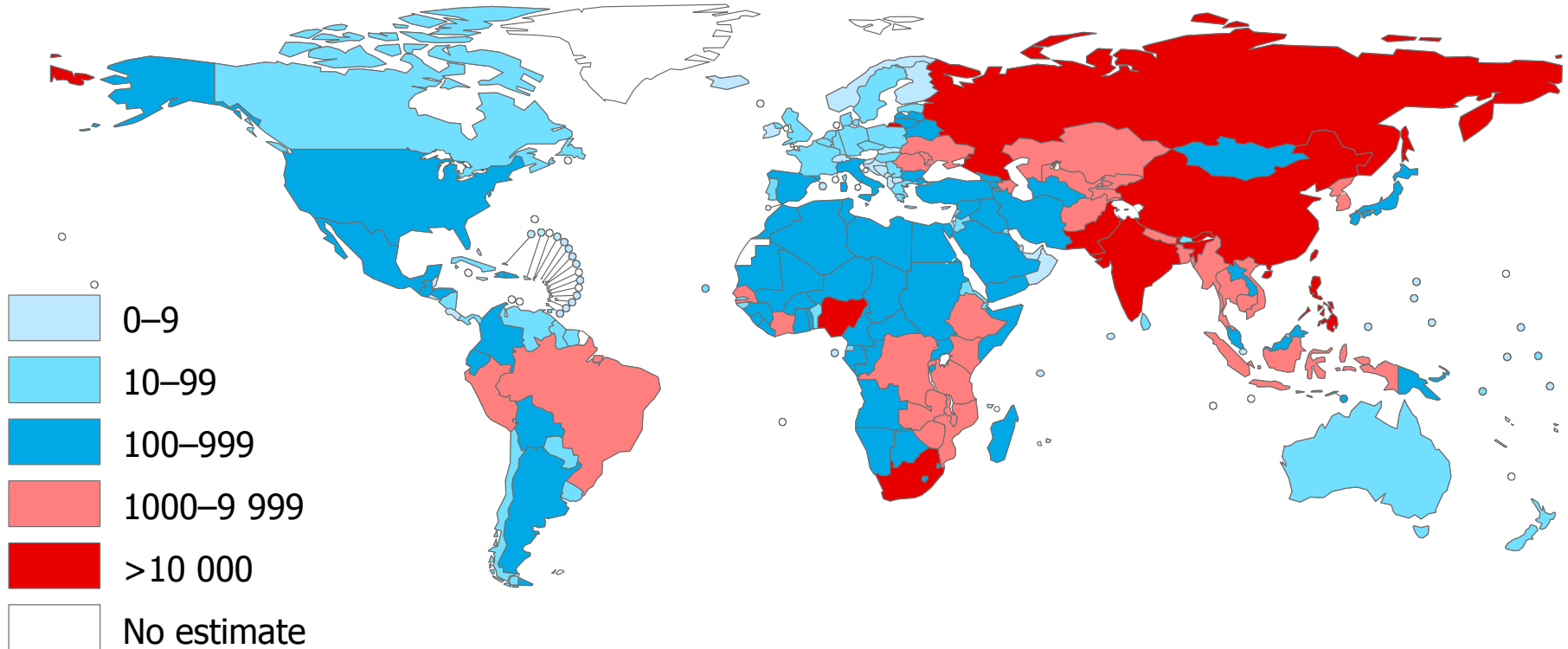
# TB Incidence Rates - 2009



**Per 100 000 population**

- Highest burden in Asia (55% of 9.4 million cases)
- Highest rates in Africa, due to high HIV infection rate  
~80% of HIV+ TB cases in Africa

# Absolute Number of MDR-TB Cases 2009



~ 45% of cases in China + India

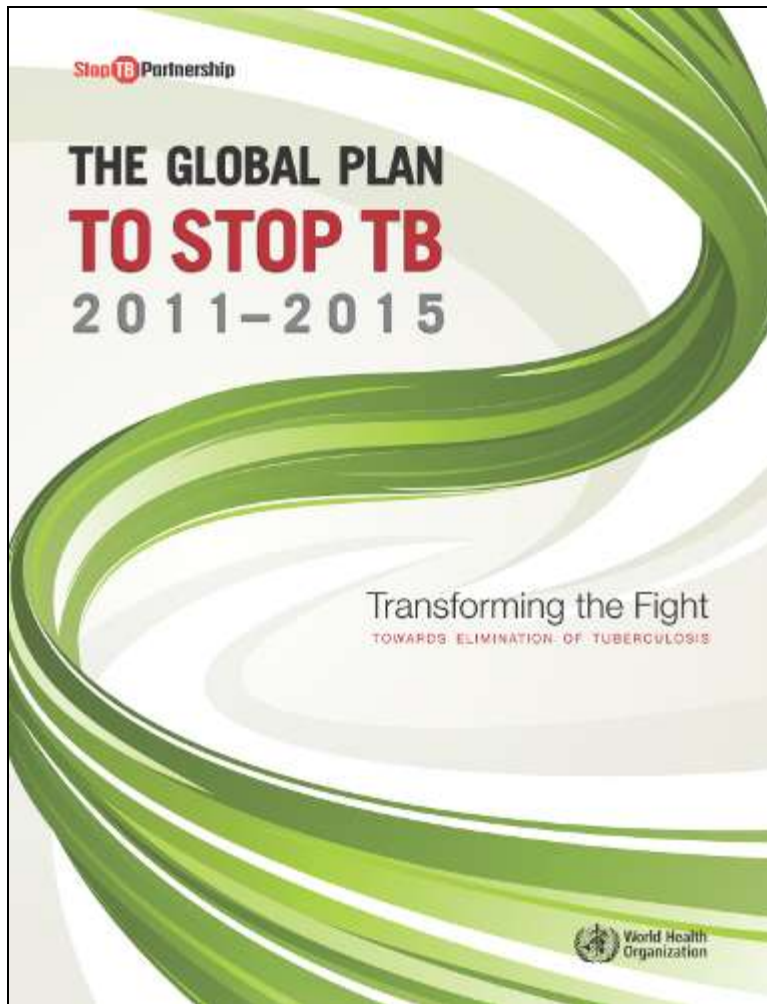
~ 55% in China + India + Russian Federation

# Global Plan to Stop TB 2011-2015



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DEPARTMENT

Launched in Johannesburg  
13 October 2010





# 10 major targets for 2015

## DOTS/lab strengthening

INDICATOR	TARGET
Number of countries with $\geq 1$ smear microscopy lab per 100 000 population	<b>149</b> (All countries in plan)
Patients notified + treated	6.9 million
Treatment success rate	90%

## TB/HIV

INDICATOR	TARGET
TB patients tested for HIV	<b>100%</b>
HIV+ TB patients on CPT	<b>100%</b>
HIV+ TB patients enrolled on ART	<b>100%</b>

*\*CPT, cotrimoxazole preventive therapy  
ART, antiretroviral therapy*

## MDR-TB/lab strengthening

INDICATOR	TARGET
Number of 22 HBCs and 27 MDR-TB HBCs with $\geq 1$ Cx & DST lab to cover 5M population	<b>36/36</b>
Previously treated cases tested for MDR	<b>100%</b>
New cases tested for MDR	<b>20%, all at high-risk</b>
MDR-TB patients treated following WHO guidelines	<b>100%, or ~ 270k</b>



# Urgent need for new rapid diagnostics

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- To face the burden of TB, TB/HIV and especially MDR-TB, we need a rapid test for TB and drug susceptibility
- To achieve the Global Plan targets new diagnostics rapidly implemented in the field are a "must"
- In the past 4 years, WHO has worked intensively with FIND, UNITAID, USAID and other partners to pursue new TB diagnostics and rapid uptake at country level



# WHO TB diagnostics policy formulation process





# Xpert MTB/RIF System



# Expert Committee: GRADE summary

Xpert MTB/RIF	Absolute difference per 1000 persons				Quality of evidence
	TP	TN	FP	FN	
Pre-test prevalence 10%					
TB detection	92	891	9	8	
R detection	95	891	9	5	
Overall quality of evidence					Moderate
Desirable vs undesirable effects					Highly favourable
Patient values and preferences					No data
Cost and requirements					Moderate cost
Added value to conventional methods					Significant

# Expert Committee Recommendations

- 1. Xpert MTB/RIF should be used as the initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB (**strong recommendation**)**
- 2. Xpert MTB/RIF may be used as a follow-on test to microscopy where MDR and/or HIV is of lesser concern, especially in smear-negative specimens (**conditional recommendation**, recognising major resource implications)**

# Expert Committee Remarks

- **Recommendations also apply to children**
- **Access to conventional microscopy, culture and DST is still needed**
- **Recommendations apply to the use of Xpert MTB/RIF in sputum specimens**
- **Recommendations support the use of one sputum specimen**

# Strategic and Technical Advisory Group for TB (STAG-TB)



- Meets once a year
- 22 members –on rotation- from various constituencies: epidemiology, control, research, public health, surveillance, laboratory, community etc
- Reviews policies and strategies prepared by WHO or expert groups
- Provides recommendations for WHO to make policies, strategies and standards
- Preparatory for WHA resolutions
- Today, also a global endorsement mechanism for new tools

# Changing TB control dynamics

- **Changes in diagnostic and screening algorithms**
- **Increased capacity needed to treat TB and MDR-TB**
- **Need to re-define case and outcome definitions**
- **Monitoring of impact on case detection and cure**
- **Resource awareness by donors/funders**
- **Use in non-traditional TB settings (HIV, private sector)**
- **Innovative new partnerships needed**

**Global Consultation: 30 Nov - 2 Dec 2010**



# Moving forward quickly...

## WHO endorsement 2010



- **Global Consultation**
- **WHO Policy Guidance**
- **Roadmap for implementation**

## Phased implementation 2011



- **Through EXPAND-TB, TBREACH, TBCARE, PEPFAR, ?GF R10, ?UNITAID**
- **Selected countries, different health service levels**

## Scale up 2012



- **EXPAND-TB, Global Fund R11, TBREACH, TBCARE, PEPFAR, country budgets, etc**

# Expectations from the Global Consultation

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- 1. Diagnostic algorithms for risk groups**
- 2. Programmatic implementation: tiered lab services**
- 3. Pricing considerations and market dynamics**
- 4. Cost-effectiveness and cost-benefit considerations**
- 5. Global framework for rapid uptake in countries**





*Global Consultation: Geneva, 30 November 2010  
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# **Responding to change: rapid policy development by WHO**

**K Weyer  
Stop TB Department**



**THE  
STOP TB  
DEPARTMENT**



**World Health  
Organization**

- **Expert Group assessment: 1 Sep 2010**
- **STAG-TB evaluation: 27 Sep 2010**
- **Global Consultation: 30 Nov-2 Dec 2010**
- **WHO Policy announcement: 7 Dec 2010**

# Expert Group: Findings

- **Test accuracy high**, single test detecting 91% of culture-confirmed TB patients (99% smear-pos and 80% smear-neg), unaffected by HIV. R resistance detected with 95% sensitivity and 98% specificity;
- **Time to detection <1day**, compared to 17 days (liquid culture); >30 days (solid culture); >75 days (phenotypic DST). Smear-negative TB patients started Rx after 4 days vs 58 days when Xpert not used;
- **TB and MDR-TB case detection significantly increased**, cost-comparison favourable to phenotypic culture and DST; cost-effectiveness highest when used as add-on to microscopy, but impact highest when used as initial diagnostic test in high-risk groups;
- **Operational findings confirmed robustness, safety, minimal training needs, high user satisfaction**. Uninterrupted and stable power supply, security against theft, annual validation, adequate storage capacity and waste disposal management required.

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# Expert Group: Recommendations

1. Xpert MTB/RIF should be used as the initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB (**strong recommendation**)
2. Xpert MTB/RIF may be used as a follow-on test to microscopy where MDR and/or HIV is of lesser concern, especially in smear-negative specimens (**conditional recommendation**, recognising major resource implications)

# Expert Group Remarks

- **Recommendations also apply to children**, based on generalisation of data from adults and acknowledging the limitations of microbiological diagnosis of TB (including MDR-TB) in children;
- **Access to conventional microscopy, culture and DST is still needed** for monitoring of therapy, for recovering isolates for drug susceptibility testing other than rifampicin (including second-line anti-TB drugs); and for prevalence surveys and/ or surveillance;
- **Recommendations apply to the use of Xpert MTB/RIF in sputum specimens** (including pellets from decontaminated specimens), as data on the utility of Xpert MTB/RIF in extra-pulmonary specimens are still limited;
- **Recommendations support the use of one sputum specimen** for diagnostic testing, acknowledging that multiple specimens increase the sensitivity of Xpert MTB/RIF but have major resource implications.

# Expert Group: Research needs

While not preventing or delaying implementation, **operational research** should include:

- **Evaluation of different diagnostic algorithms**
- **Cost-effectiveness and impact in different settings**
- **Feasibility of decentralised use (rural, point-of-care)**
- **Cartridge & device stability in adverse conditions**
- **Evaluation in extra-pulmonary & paediatric TB**
- **Assay for fluoroquinolones and aminoglycosides**

- **Endorsed EG findings and recommendations**
- **Recommended phased implementation within national TB and MDR-TB strategic plans**
- **Requested WHO to:**
  - **Proceed with policy guidance**
  - **Develop a global strategy for rapid uptake**
  - **Organise a Global Consultation on implementation**
  - **Assist countries with uptake**

# Draft WHO Policy Guidance

- **Positioning at district or sub-district level**
- **Risk analysis (country-specific epidemiology, available resources, cost-effectiveness)**
- **Stand-alone diagnostic test\***
- **Rx response monitored by conventional tests**
- **Operational issues**
- **Rapid communication of results and access to appropriate treatment imperative**

\* Supported by conventional DST in low MDR settings to identify possible FPs