

# **The Challenges of MDR-TB Control in the Next Decade**

**NAR-IUATLD  
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**Marcos Espinal  
Executive Secretary  
Stop TB Partnership**

# Background

1994 WHO / IUATLD Global Drug Resistance Surveillance

*New Eng J Med (1998 and 2001), Lancet (2006)*

1999 Working Group on MDR-TB

*Guidelines for the management of MDR-TB*

*Concessional prices of 2<sup>nd</sup> line drugs by the industry*

2000 Green Light Committee to increase access to 2<sup>nd</sup> line drugs

*MSF, CDC, Estonia NTP, PIH, WHO*

2000-05 Feasibility and cost-effectiveness studies

*Estonia, Latvia, Peru, Philippines, Russia*

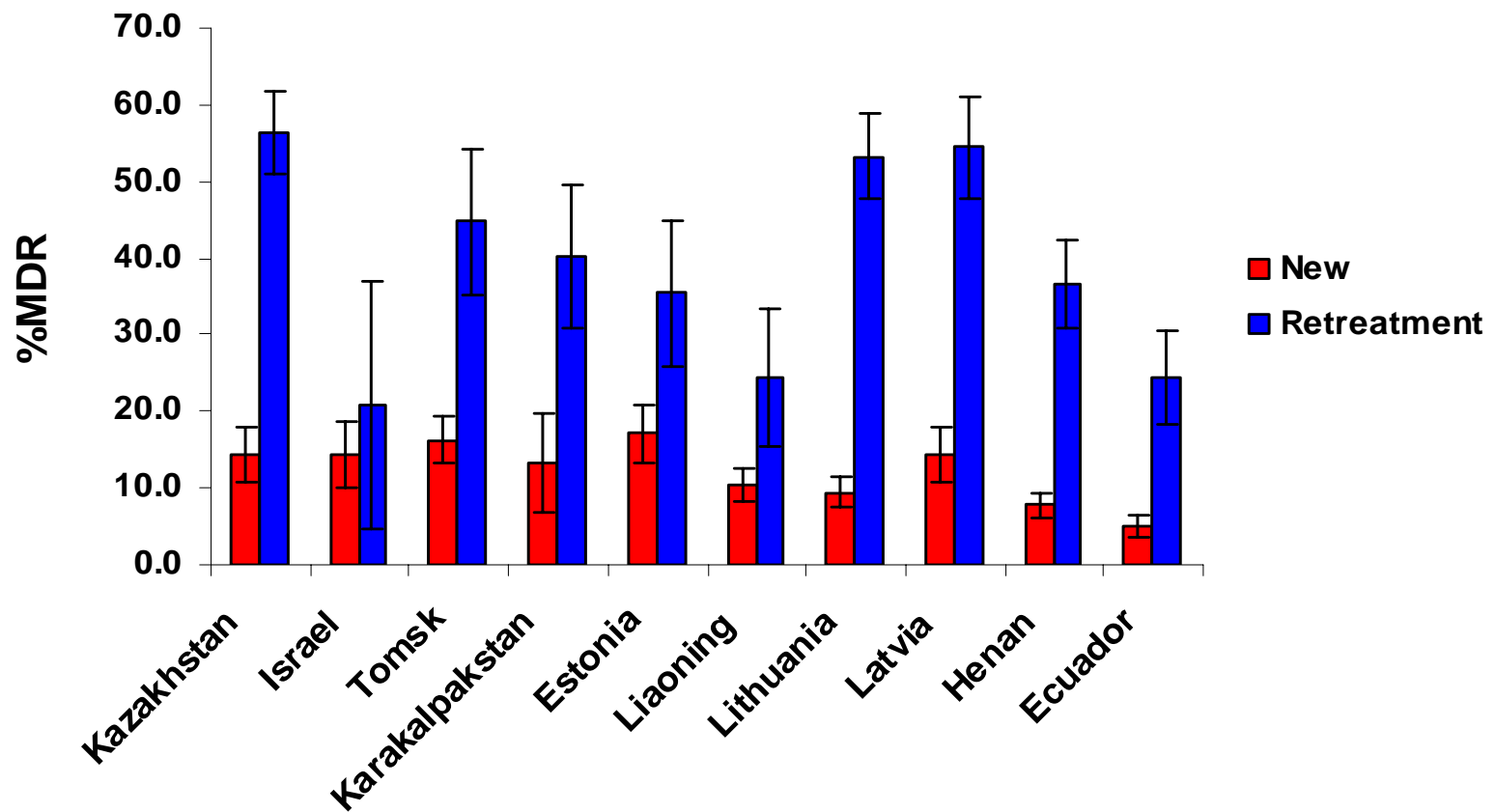
2003 Eli Lilly technology transfer of 2<sup>nd</sup> line drugs

2006 Global Plan to Stop TB 2006-15,

*Management of MDR-TB – scale up*

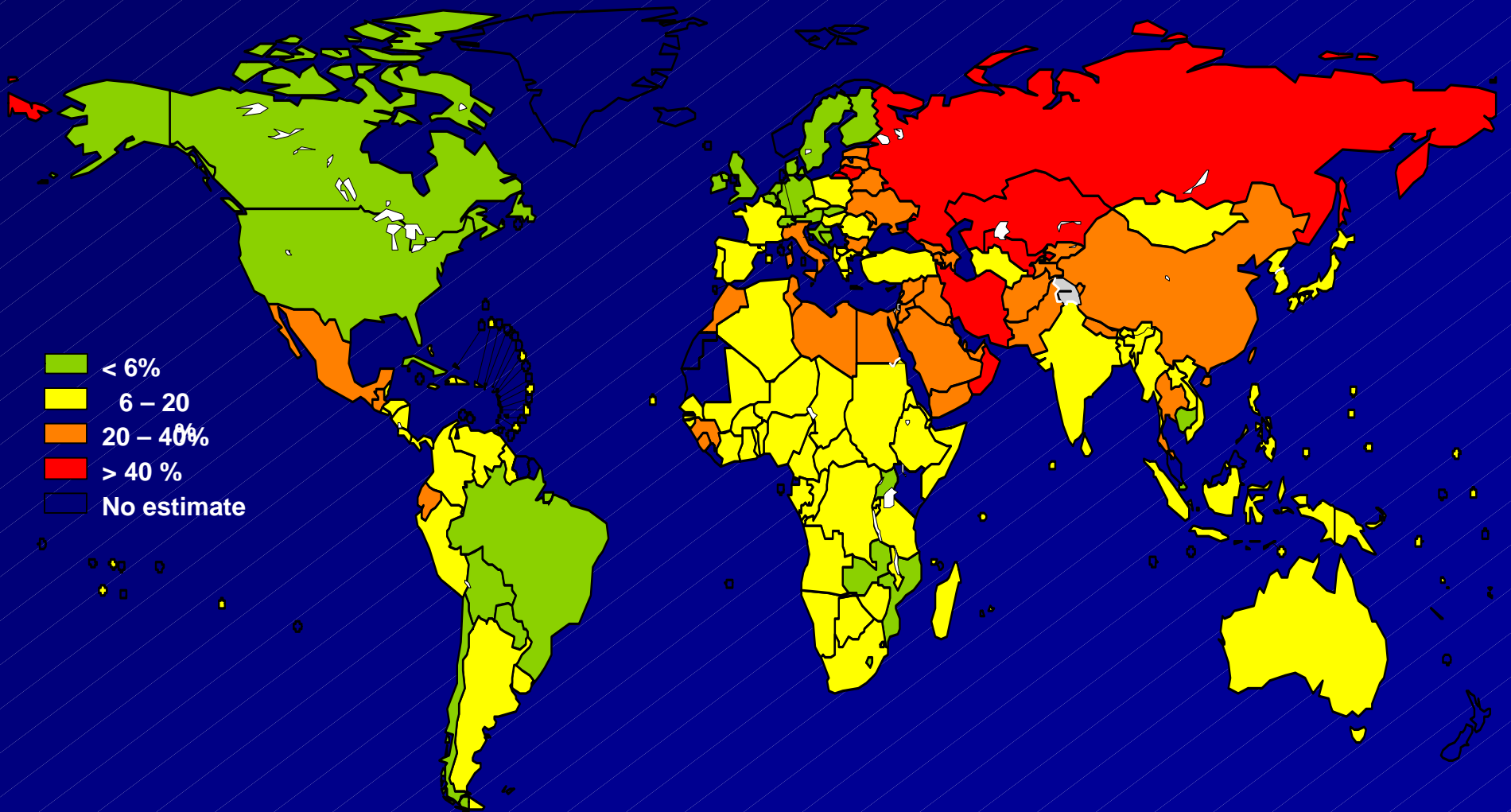
*XDR-TB*

# Prevalence of MDR by treatment status



# VERY HIGH RATES OF DRUG-RESISTANT TB IN EASTERN EUROPE

MDR-TB among previously treated TB patients (%)



# Emergence of XDR-TB

## March 2006



### World TB Day — March 24, 2006

World TB Day is March 24. This annual event commemorates the date in 1882 when Robert Koch announced his discovery of *Mycobacterium tuberculosis*, the bacterium that causes tuberculosis (TB). Worldwide, TB remains one of the leading causes of death from infectious disease. An estimated 2 billion persons (i.e., one third of the world's population) are infected with *M. tuberculosis*. Each year, approximately 9 million persons become ill from TB, and approximately 2 million die as a result. World TB Day provides an opportunity for TB programs, nongovernmental organizations, and other partners to describe TB-related problems and solutions and to support TB control worldwide.

During 1985–1992, after more than 30 years of decline, the number of TB cases reported in the United States increased by 20%. This resurgence generated a renewed emphasis on TB control and prevention during the 1990s, which reversed the trend. Although the 2005 TB rate was the lowest recorded in the United States since national reporting began in 1953, the average annual decline has slowed during the past 3 years, multidrug-resistant TB remains a threat, and disparate rates of TB persist among certain racial, ethnic, and foreign-born populations.

Many states are offering educational programs organized by local TB coalitions in recognition of World TB Day. For example, the Georgia Department of Human Resources, Division of Public Health, Tuberculosis Program is hosting an observance recognizing the activities of a coalition working to reduce disparities in TB among blacks in the Atlanta area. Additional information about World TB Day and CDC TB-elimination activities is available at <http://www.cdc.gov/nchstp/tb/worldtbd/2006/activities.htm>.

### Emergence of *Mycobacterium tuberculosis* with Extensive Resistance to Second-Line Drugs — Worldwide, 2000–2004

During the 1990s, multidrug-resistant (MDR) tuberculosis (TB), defined as resistance to at least isoniazid and rifampin, emerged as a threat to TB control, both in the United States (1) and worldwide (2). MDR TB treatment requires the use of second-line drugs (SLDs) that are less effective, more toxic, and costlier than first-line isoniazid- and rifampin-based regimens (3). In 2000, the Stop TB Partnership's Green Light Committee was created to increase access to SLDs worldwide while ensuring their proper use to prevent increased drug resistance. While assisting MDR TB treatment programs worldwide, the committee encountered reports of multiple cases of TB with resistance to virtually all SLDs. To assess the frequency and distribution of extensively drug-resistant (XDR) TB cases,\* CDC and the World Health Organization (WHO) surveyed an international network of TB laboratories. This report summarizes the results of that survey, which determined that, during 2000–2004, of 17,690 TB isolates, 20% were MDR and 2% were XDR. In addition, population-based data

\* Defined as cases in persons with TB whose isolates were resistant to isoniazid and rifampin and at least three of the six main classes of SLDs (aminoglycosides, polypeptides, fluoroquinolones, thioamides, cycloserine, and para-aminosalicylic acid).

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DEPARTMENT OF HEALTH AND HUMAN SERVICES  
CENTERS FOR DISEASE CONTROL AND PREVENTION

XDR = Multidrug-resistant TB (MDR-TB) plus resistance to (i) any *fluoroquinolone*, and (ii) at least 1 of 3 injectable second-line drugs *capreomycin*, *kanamycin*, *amikacin* (new definition agreed October 2006)

MDR-TB = resistance to at least *isoniazid* and *rifampicin*, the two most powerful first-line anti-TB drugs

Of 17,690 isolates from 49 countries during 2000–2004, 20% were MDR-TB and 2% were XDR-TB

XDR-TB found in:  
USA: 4% of MDR-TB  
Latvia: 19% of MDR-TB  
S Korea: 15% of MDR-TB

# XDR-TB in South Africa

## August 2006

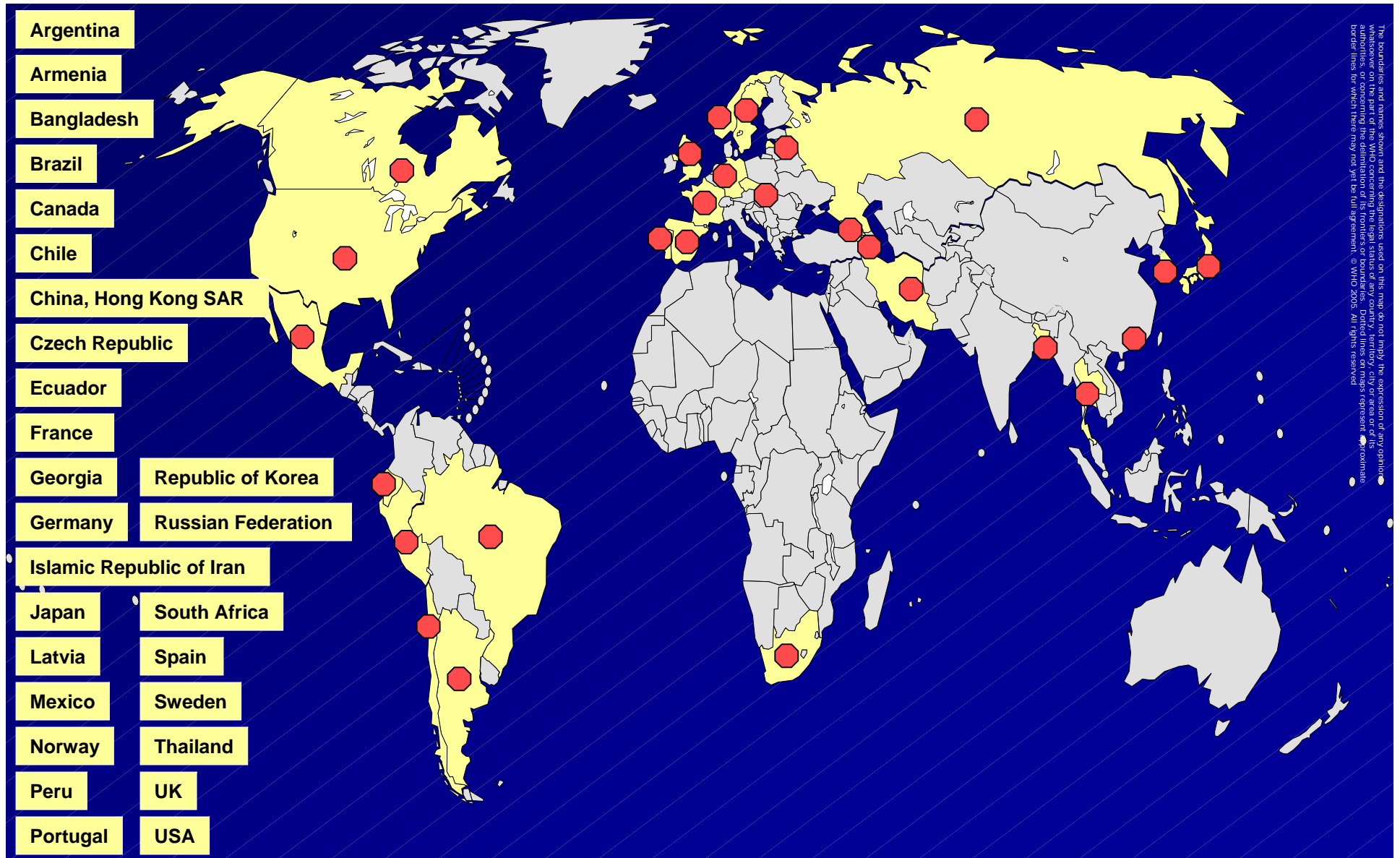
Church of Scotland Hospital, Tugela Ferry,  
KwaZulu-Natal Province, South Africa

- 53 of 544 patients defined as XDR-TB cases
- 52 of the 53 patients died on average within 25 days, including those on antiretroviral therapy
- Further investigations being carried out
- XDR-TB likely in bordering African countries



Given the underlying HIV epidemic in Africa,  
drug-resistant TB could have a major impact on mortality  
and requires urgent action on care and prevention

# Countries with XDR-TB Confirmed cases to date



*Evidence from the pilot projects shows that  
management of MDR-TB is feasible and  
cost-effective*

*(Lancet 2002, Lancet 2005, NEJM 2005, Em Inf Dis 2005, PLoS 2006)*

*The data also show there are challenges to  
be addressed...*



*Scaling up access to quality  
second-line anti-TB drugs*

## Fact

*By the end of 2005 > 2% of the estimated  
425 000 MDR-TB patients were being  
treated with 2nd line drugs*

*Global Plan to Stop TB 2006-15*



*Strengthening and expanding  
laboratory capabilities*

## Fact

*To address the needs of the 22 high burden countries for tuberculosis, 250 laboratories should be in place by 2010*

*Sub-Group on Laboratory Strengthening*



*Enhancing human capacity  
to act efficiently*

## Fact

*WHO estimates that 57 countries are currently experiencing critical shortages of health professionals (doctors, nurses, midwives) of which 36 are in sub Saharan Africa*

*WHO Global Alliance on Health Workforce*



*Making available rapid  
diagnostic testing*

## Fact

*Because the United Nations Secretary General  
Special Envoy to Stop TB could not find the bug  
in this 100 years old microscope*



*Enhancing infection control and  
protecting health care workers*



*Development of affordable new drugs, diagnostics and vaccines*

# **Global Plan activities on MDR-TB 2006-15**

- 1. Scale up drug sensitivity testing for new and re-treatment TB cases**
- 2. Scale up treatment for new and re-treatment cases with MDR-TB**
- 3. Expansion of drug resistance surveillance**
- 4. Strengthen human capacity**
- 5. Creation of a healthy and competitive market for quality-assured second-line drugs**
- 6. Enhancement of advocacy efforts**
- 7. Provision of technical assistance**
- 8. Development and introduction of new diagnostics, drugs, and vaccines**
- 9. Reform of the Green Light Committee mechanism**

**Implementation of the Global Plan activities will result in  
1.3 m MDR-TB cases detected and 0.78 m treated**

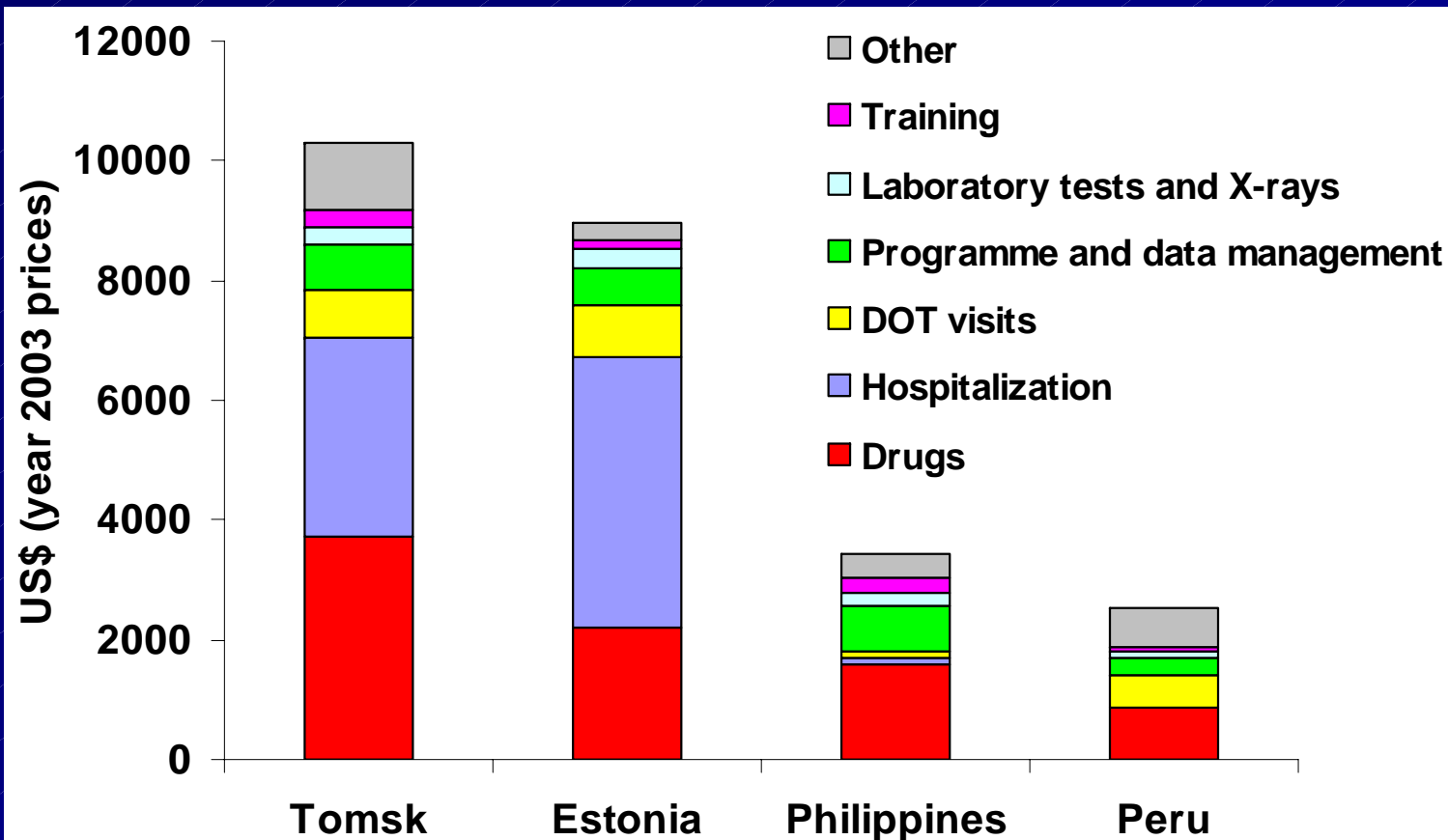
# MDR-TB targets - Global Plan 2006-15

During the 10-year period

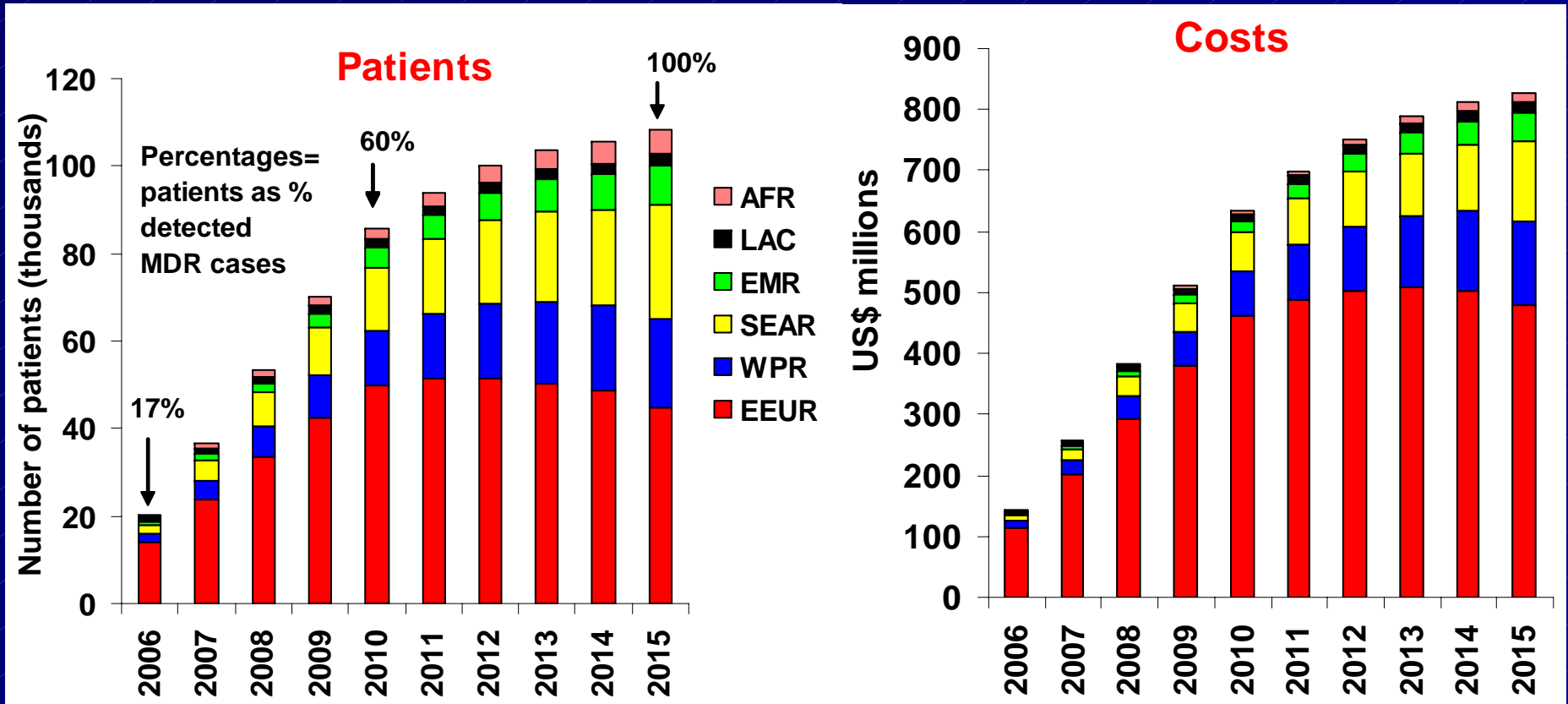
- 60% of 1.3 m detected culture-positive MDR-TB patients will be treated
- 75% of the 778 000 MDR-TB cases under treatment will be treated successfully
- The proportion of re-treatment cases will decrease from 20% in 2005 to 11% in 2015
- The number of MDR-TB cases will be reduced from an estimated 533 000 in 2005 to 193 000 in 2015
- 142 000 deaths from MDR-TB will be averted

# Costs for MDR-TB in Global Plan

## Compiled available evidence on costs of managing MDR-TB in pilot projects/programmes



# Financial costs for MDR-TB in Global Plan

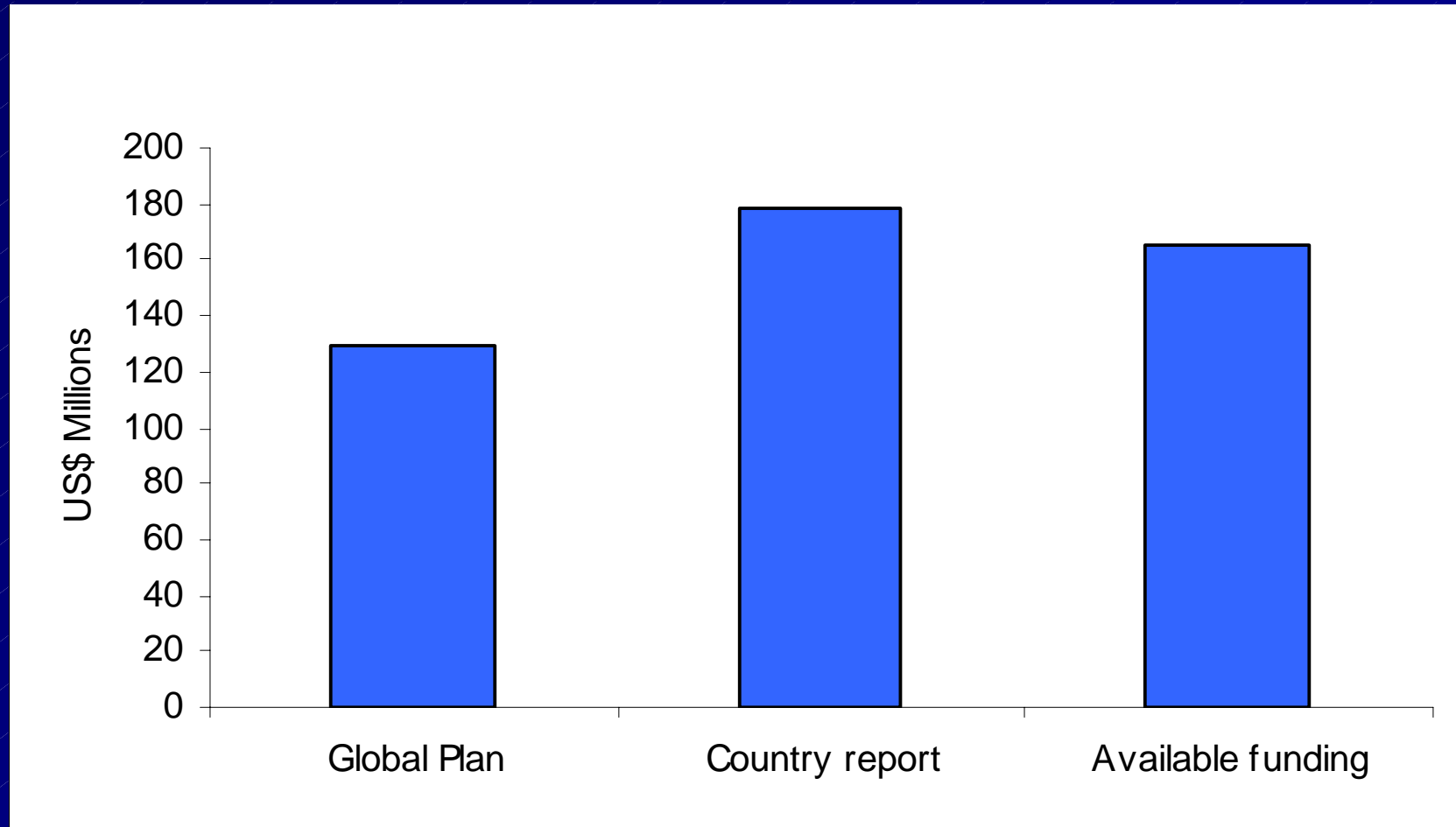


- ◆ Total patients = 778,000, total costs = US\$5.8 billion
- ◆ Patients and costs dominated by EEUR, SEAR, WPR regions

# Total needs for MDR-TB management in 2007

## Global Plan and country reports

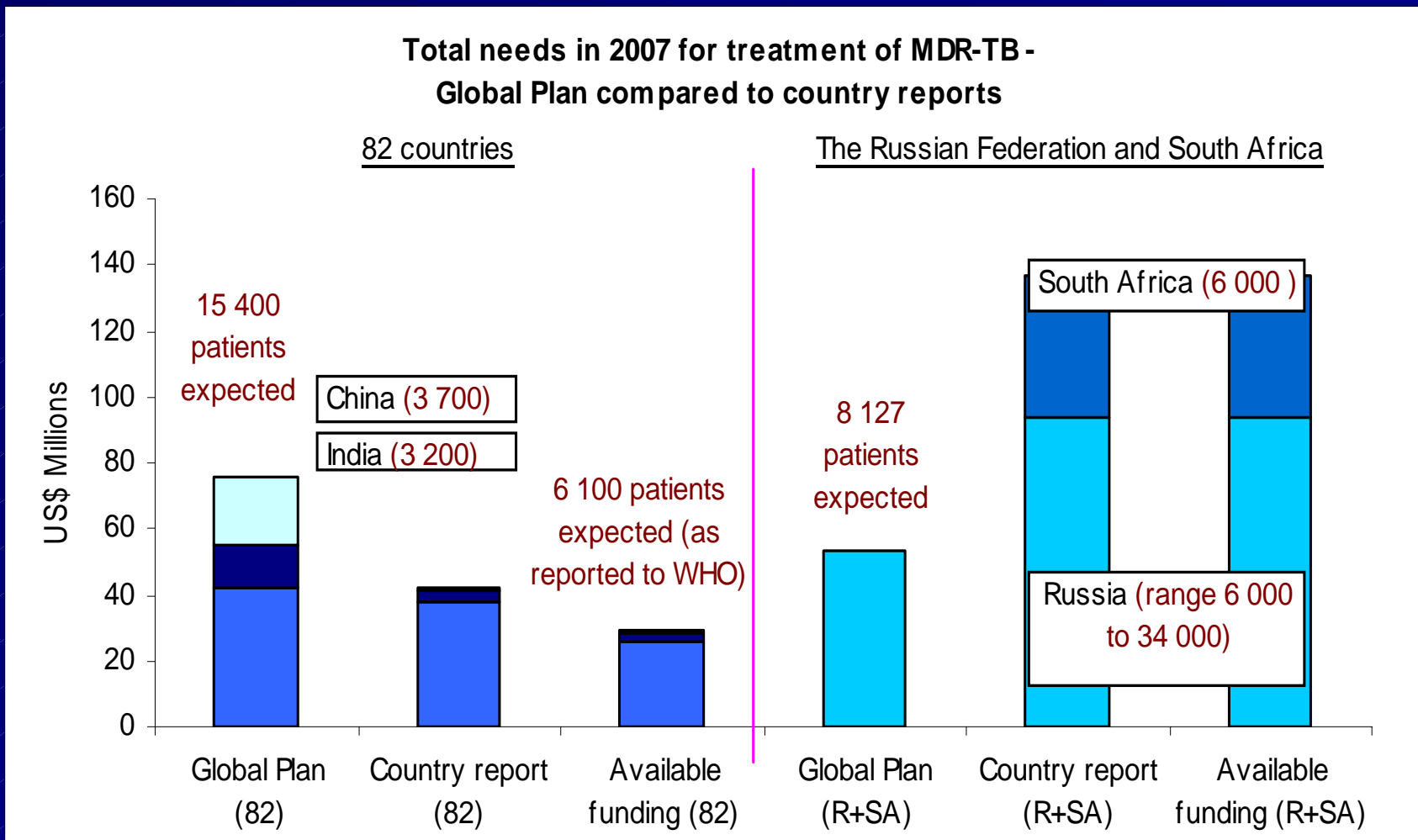
### 84 Countries



# Total needs for MDR-TB management in 2007

## Global Plan and country reports

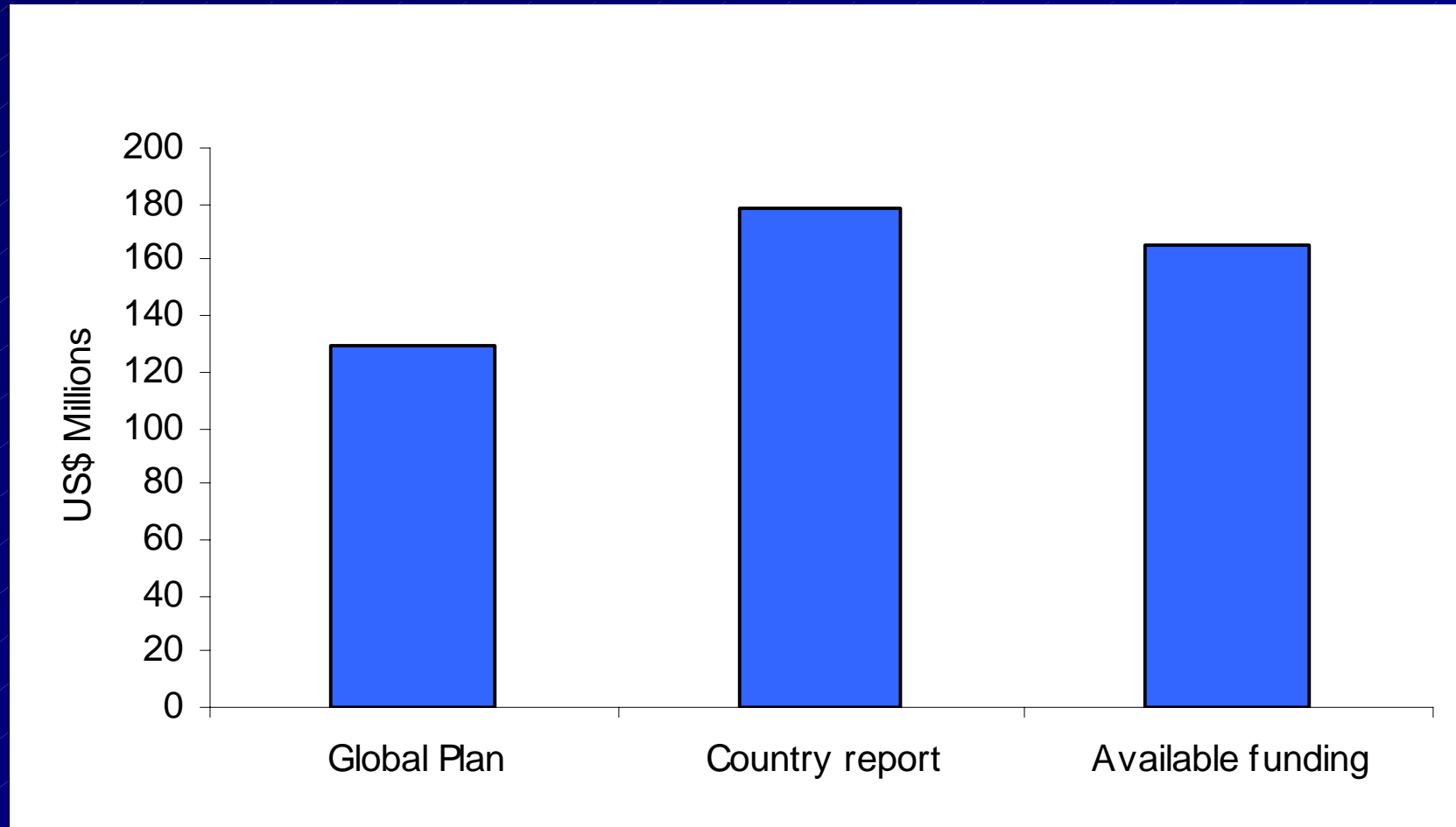
### 84 Countries



# Total needs for MDR-TB management in 2007

## Global Plan and country reports

### 84 Countries



# International response to the XDR-TB emergency



## Global Task Force on XDR-TB, October 2006

[http://www.who.int/tb/xdr/globaltaskforce\\_update\\_feb07/en/index.html](http://www.who.int/tb/xdr/globaltaskforce_update_feb07/en/index.html)

"Priority for the immediate strengthening of TB control in countries"

- Accelerate access to rapid tests for *rifampicin* resistance
- Ensure adherence to WHO drug resistance guidelines, improve programme management, access to MDR-TB drugs under proper conditions including direct observation. Ensure all patients with HIV are adequately treated for TB and started on antiretroviral therapy
- Accelerate implementation of infection control measures to reduce transmission especially among those HIV positive
- Strengthen laboratory capacity to diagnose, manage and survey drug resistance. Commence rapid survey so that the size of the XDR-TB epidemic can be determined
- Initiate information-sharing strategies that promote prevention, treatment and control of XDR-TB

# Green Light Committee Reform

## Review

- GLC members increased from 6 to 9
- Each application is reviewed by 2 members of the committee
- Fast-tracking of projects enrolling < 50 patients
- Secretariat strengthened

## Procurement

- Converged with the GDF
- Procurement team strengthened
- New MOU with the procurement agent
- Funds available to establish global buffer stock
- GFATM / UNITAID

# The good, the less good and...

- **DOTS-Plus for MDR-TB is now matured**
- **Revision of the Global Plan underway**
- **Several countries ready to scale up**
- **GLC strengthened and revised**
- **UNITAID/GFATM funding available**

- **MDR scale up from levels far below GP**
- **Universal access and XDR-TB not yet in the GP**
- **Funding gap not yet fulfilled**
- **Political and financial will at country level to manage MDR-TB is still insufficient in some powerful countries**