Catalysing HIV/TB research: innovation, funding and networking

Cape Town, July 19, 2009

MDR, XDR TB and HIV: global data, approaches and operational research issues

Paul Nunn, WHO

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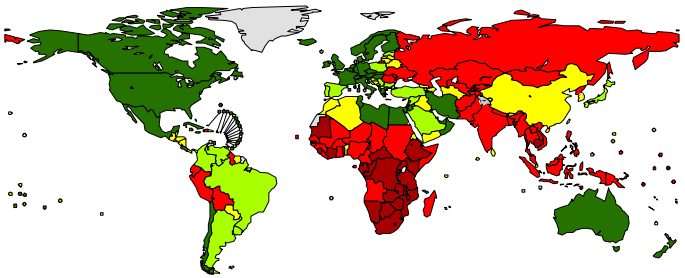
Latest global TB estimates - 2007

(Updated Mar 2009)



	Estimated number of cases	Estimated number of deaths
All forms of TB **Greatest number of cases in Asia; greatest rates per capita in Africa**	**9.27 million** **(139 per 100,000)**	**1.77 million** **(27 per 100,000)**
Multidrug-resistant TB (MDR-TB)	**511,000**	**~150,000**
Extensively drug-resistant TB (XDR-TB)	**~50,000**	**~30,000**
HIV-associated TB	**1.37 million** 15% of TB cases	**456,000** 26% TB deaths 23% HIV deaths

Definitions

- MDR (multi-drug resistance) = Resistance to at least INH and RIF
- XDR (eXtensively drug resistant) = MDR plus resistance to fluoroquinolones, and one of the second-line injectable drugs (amikacin, kanamycin, or capreomycin)

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Global approaches

- Anti-TB drug resistance surveillance
- Normative WHO functions.
  - Analytical work and policy development
  - Technical support
  - Monitoring and evaluation
- 2nd line drug management – Green Light Committee
- Advocacy and partnerships

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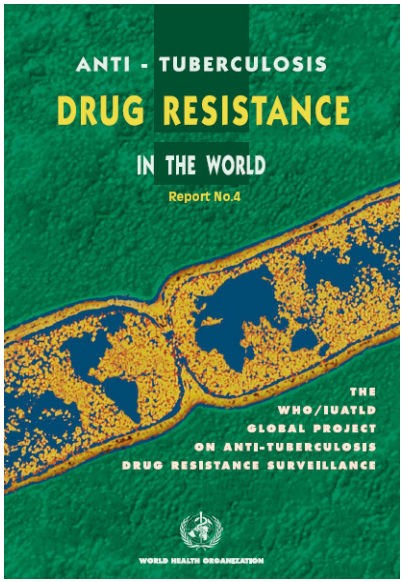
Global estimate of MDR-TB



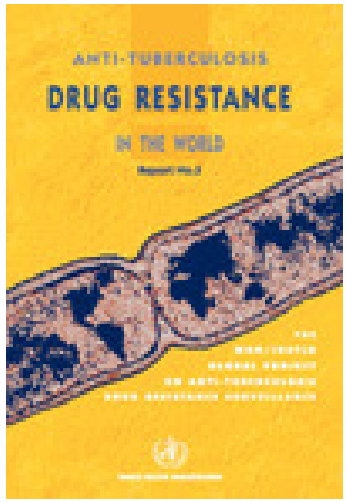
511,000

incident cases MDR-TB in 2007

289,000 among all new cases (3.1%), and

221,000 among previously treated cases (19%).

- Based on 138 settings surveyed in 116 countries between 1994-2007
- WHO drug resistance surveillance project with the Supra-national reference laboratory network
- Now including 2nd line drug susceptibility testing



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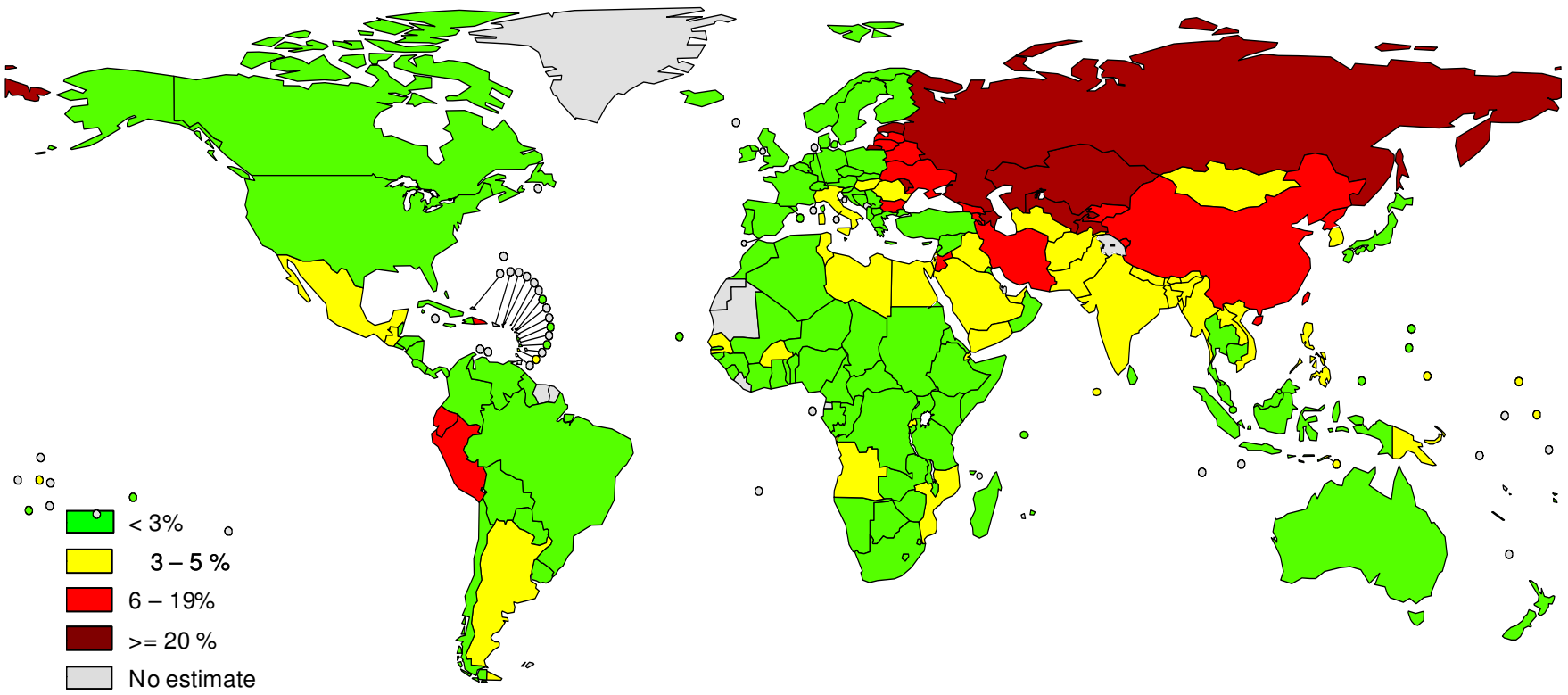
MDR cases among new and retreatment cases, 2007



Countries that had reported at least one XDR-TB case by end April 2009

World Health Organization

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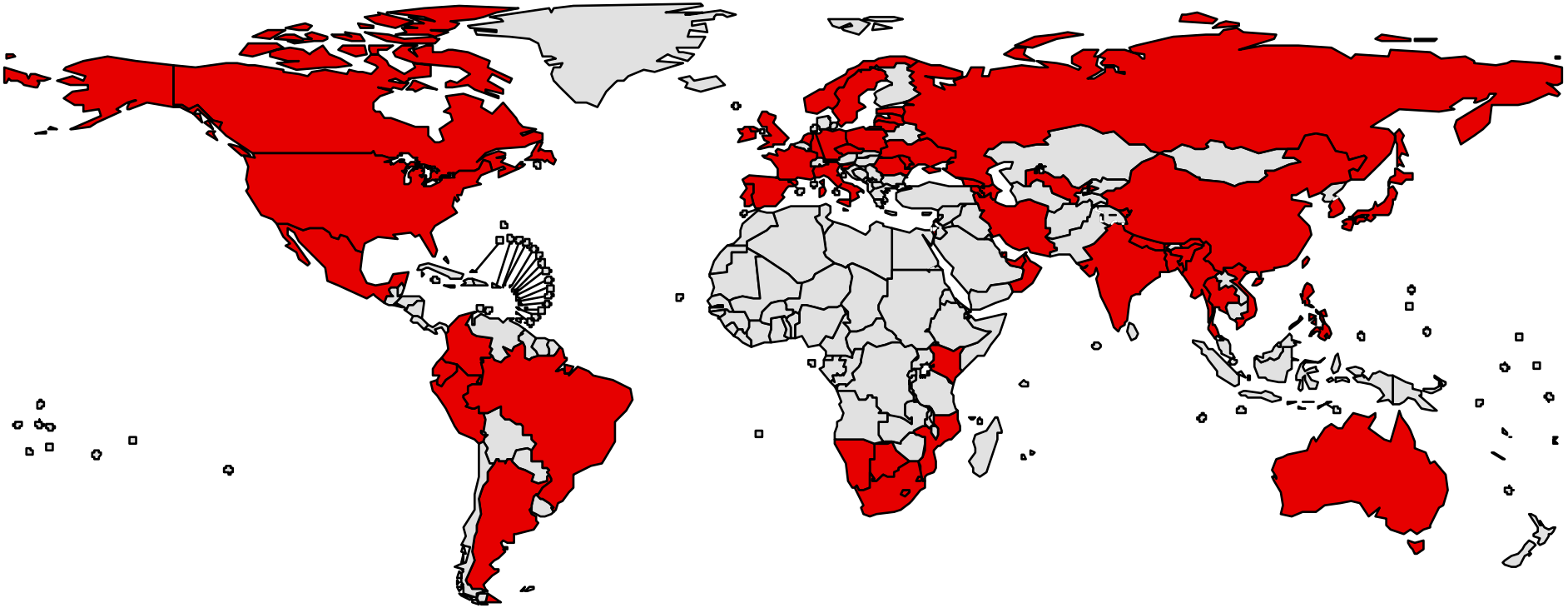

Argentina	Canada	Georgia	Japan	Myanmar	Philippines	Russian Federation	Ukraine
Armenia	China	Germany	Kenya	Namibia	Poland	Slovenia	United Arab Emirates
Australia	Colombia	India	Latvia	Nepal	Portugal	South Africa	United Kingdom
Azerbaijan	Czech Republic	Iran (Islamic Republic of)	Lesotho	Netherlands	Qatar	Spain	United States of America
Bangladesh	Ecuador	Ireland	Lithuania	Norway	Republic of Korea	Swaziland	Uzbekistan
Botswana	Estonia	Israel	Mexico	Oman	Republic of Moldova	Sweden	Viet Nam
Brazil	France	Italy	Mozambique	Peru	Romania	Thailand	

MDR-TB & HIV in institutions in the West

	Reference	Patients with MDR-TB			
		Total no.	HIV infected %	Died %	Time to death, median, weeks
Hospital (Florida), 1988–1990	MMWR 1991;40:585-91	**65**	**93**	**72**	**7**
Hospital (New York City), 1989–1990	MMWR 1993;42:427-34 JAMA 1996;276:1229-35	**51**	**100**	**89**	**16**
Hospital (New York City), 1990–1991	JAMA 1996;276:1229-35 NEJM 1992;326:1514-21	**70**	**95**	**77**	**4**
Hospital (New York City), 1991–1992	JAMA 1996;276:1229-35 JID 1993;168:1052-5	**32**	**91**	**83**	**4**
Two hospitals (Italy), 1991–1995	AIDS 1998;12:1095-102	**116**	**98**	**95**	**6-8**
Hospital (Madrid, Spain), 1991–1995	EID 1996;2:125-9	**48**	**100**	**98**	**7**
Hospital (Buenos Aires, Argentina), 1994–1995	JID 1997;176:637-42	**68**	**100**	**93**	**5**
Prison system (New York State), 1990–1991	JID 1994; 170:151-6	**42**	**98**	**79**	**4**

JID 2007;196 Suppl 1:S86-107

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Epidemiology of MDR and HIV in Africa

	Patients tested for HIV and DR	Place	Association between HIV status and any R
Githui, 1989	271	Nairobi, Kenya	No association
Chum, 1996	1164	Tanzania	No association
Kenyon, 1999	240	Botswana	No association
Churchyard, 2000	1913	South Africa	No association
Warndorff, 2000	836	Malawi	No association
Espinal, 2001	463	Multicentre	No association
Mac-Arthur, 2001	709	Mozambique	Association with HS
Weyer, unpublished	762	South Africa	No association
			Association with MDR among retreatments

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MDR-TB and HIV in Ukraine

	Civilian sector		Penitentiary sector	
	New cases n=924	Previously treated cases n=369	New cases n=78	Previously treated cases n=125
MDR rates (95% CLs)	15.5 (13.1 to 17.8)	41.5 (36.4 to 46.5)	21.8 (12.4 to 31.2)	52.8 (43.9 to 61.7)

- Independent predictors for MDR-TB
  - History of previous treatment: OR: 4.0 (95%CLs 3.1-5.1)
  - Imprisonment: OR: 1.5 (95%CLs 1.1-2.0)
- **HIV status: OR: 1.7 (95%CLs 1.3-2.3)**

Dubrovina I, et al. Int J Tuberc Lung Dis. 2008; 12: 756-62.

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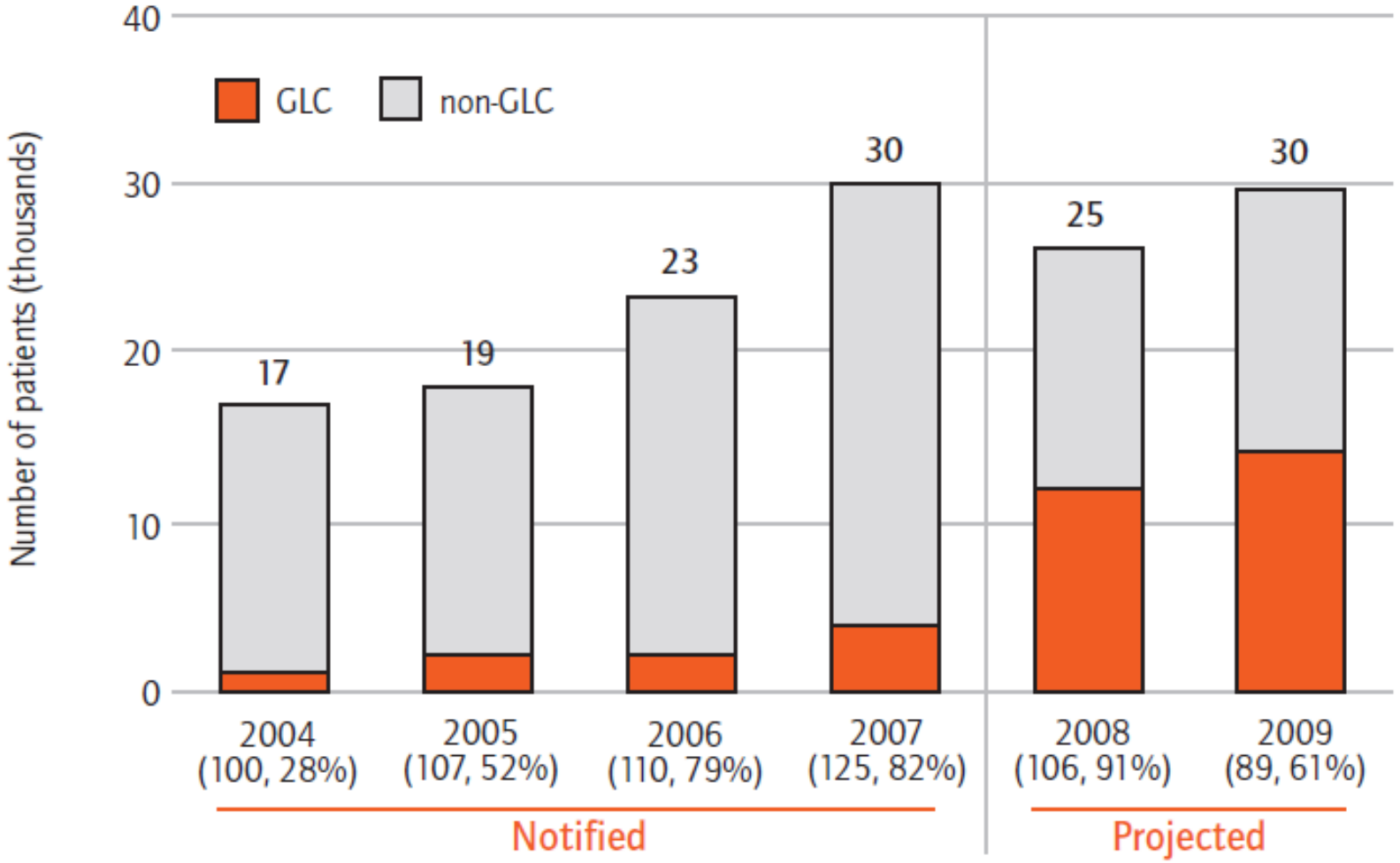
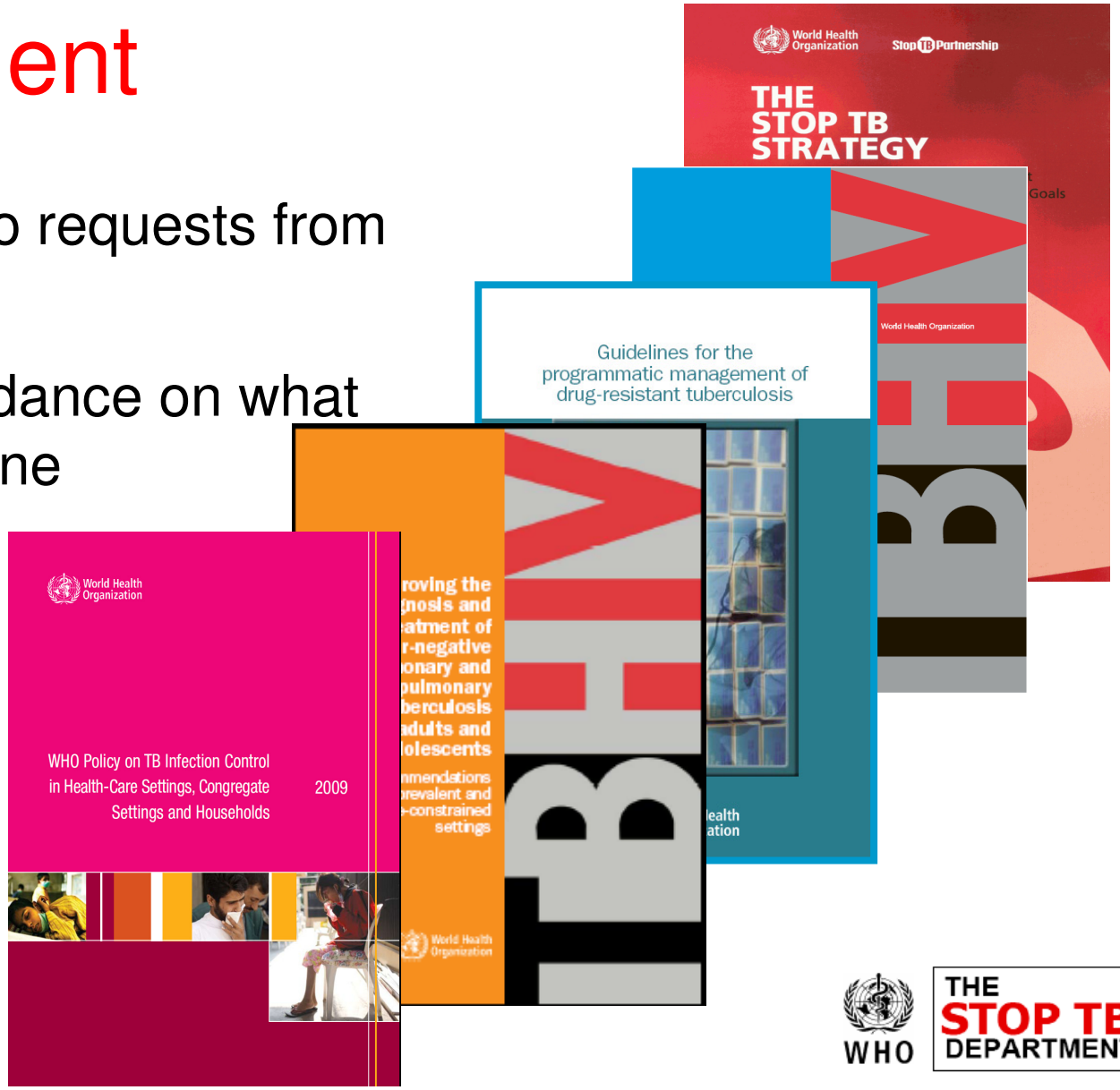
Notified cases of MDR-TB (2004–2007) and projected numbers of patients to be enrolled on treatment (2008–2009). The numbers under each bar show the number of countries reporting data, followed by the percentage of total estimated cases of MDR-TB accounted for by reporting countries.



Analytical work and policy development

- Responding to requests from countries
- Essential guidance on what needs to be done



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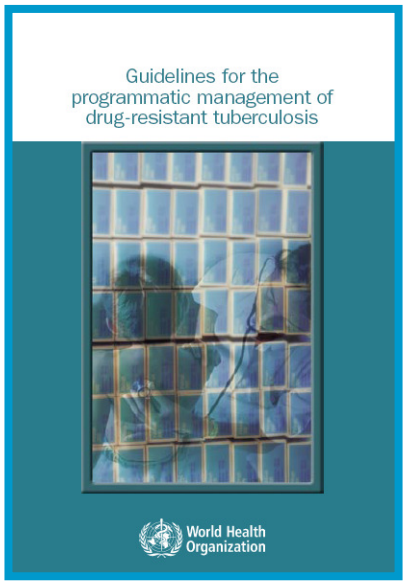
Key recommendations for HIV associated MDR/XDR-TB patients

- Diagnosis
  - Culture and DST, or, preferably, LPAs
  - Provider-initiated HIV testing
- Treatment
  - Empirical for HIV+ with suspected M/XDR-TB
  - Include CPT and ART (with closer monitoring)
  - At least 4 drugs (not cipro) including injectable
  - Never thioacetazone
  - Treat 18/12 beyond culture conversion
  - Nutrition and socioeconomic support
- Recording and reporting
  - Include HIV data
- Infection control

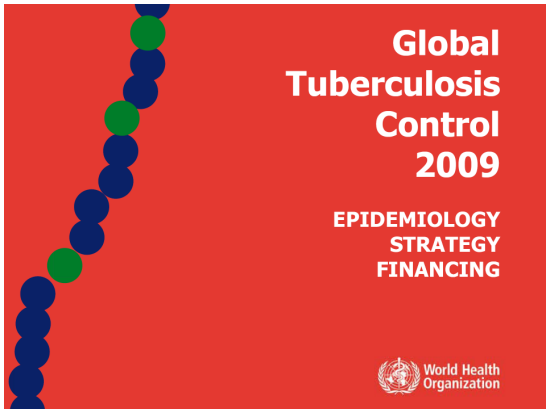


Technical support, M&E

Platform of coordination and communication laboratory strengthening, to provide:

- Global policy guidance
- Human capacity development
- Interface with lab networks,
- Quality assurance
- Coordination of tech support
- Knowledge sharing
- Advocacy and resource mobilisation

- Monitoring and evaluation
  - Drug resistance surveillance data
  - Performance data from Green Light Committee projects
  - Performance data from national laboratories
  - Infection control performance data



2nd line drug management - The Green Light Committee Initiative

- Multi-partner initiative (CDC, KNCV, MSF, MSH, PiH, WHO etc)
- Provides concessionally-priced drugs, with technical support, monitoring and evaluation
- 56,374 patients approved by Green Light Committee (GLC) since 2002 – 14,790 started on treatment
- Drugs procured by

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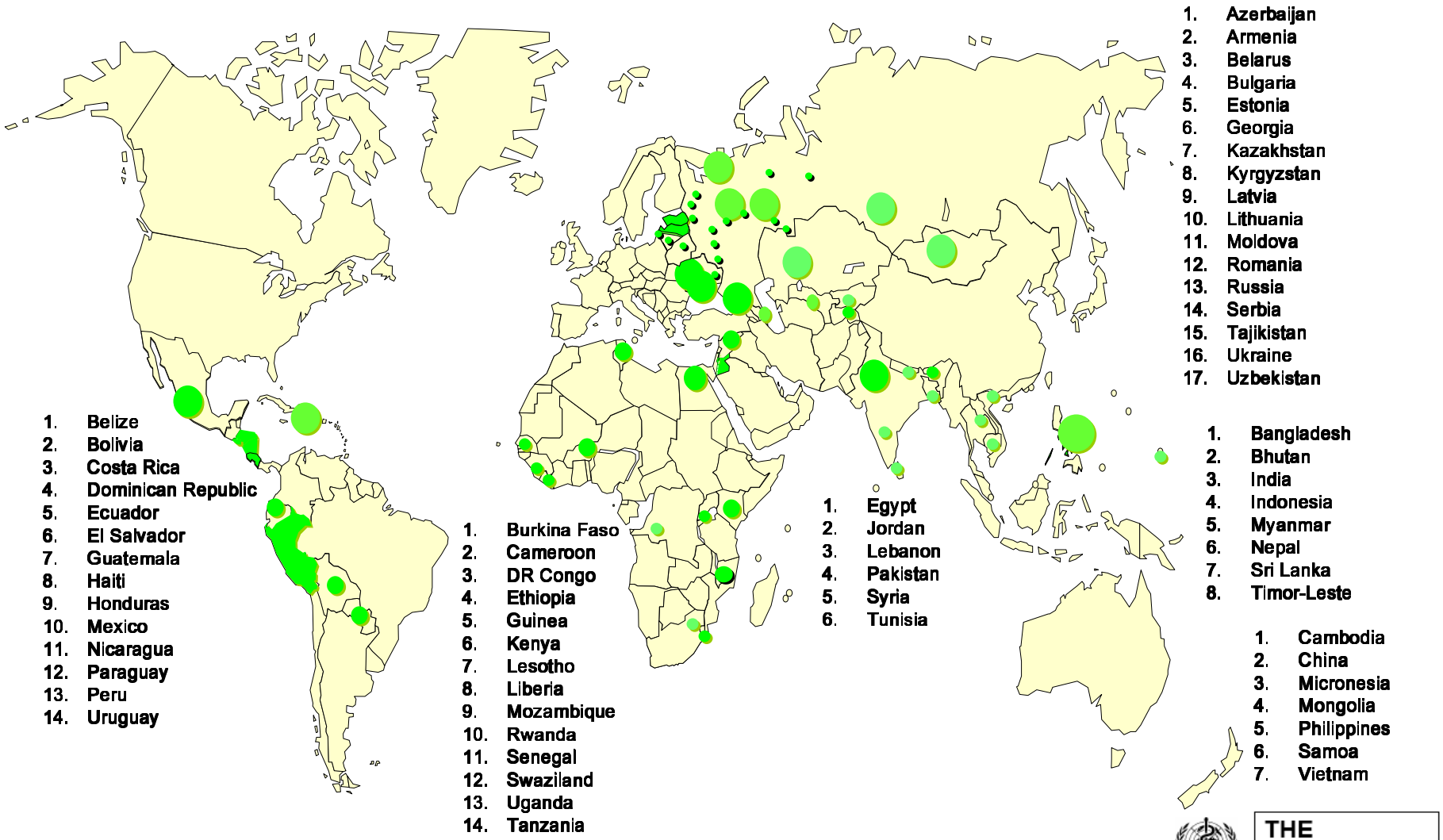
GLC approved projects through June 2009



GLC-approved projects in 66 countries

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Advocacy, partnership building and resource mobilization

- Addressing drug resistance is a major element of the Global Plan to Stop TB and Global MDR and XDR-TB Response Plan
- Community representatives crucial
- GFATM and UNITAID supplying commodities
- Ministerial meeting of 27 high MDR-TB burden countries, Beijing, April, 2009
- World Health Assembly, 2009, Resolution 62.15

Key operational questions

(assumes better TB and HIV collaboration)

- Causes/prevention
  - How and where is drug resistance being created/transmitted?
    - Drug quality?
    - Health system/patient management failures?
    - Transmission in health care facilities, eg ART clinics, community?
- Diagnosis
  - What are the best diagnostic algorithms for MDR-TB patients with HIV?
  - What is the impact of new diagnostic technologies, eg LPA, GenXpert?
  - What is the best model of ICF for TB in VCT and ART clinics, and in the community?
  - How can cell phones be used to accelerate diagnosis?
  - What impact can SMS boxes have to get patients on to treatment faster?

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Key operational questions - II

- Treatment
  - Where and how can MDR-TB be best managed? Hospital vs community.
  - How can TB patients, especially those with MDR-TB, better access ART?
  - What drug interactions occur between 2nd line anti-TB drugs and ARVs?
- Infection control
  - What are the best methods for separating infectious cases from susceptible contacts in a health facility/at home?
  - Do surgical masks on patients work?
  - Do respirators on staff and visitors work?
  - How can behaviour change in HCWs be encouraged and maintained?
  - What indicators should be used?

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Conclusions

- M/XDR-TB is 5.1% of total cases and rising
- The response is insufficient
- Operational research can relieve some of the bottlenecks and could drive progress

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