



Drug resistance TB in People Living with HIV: research questions and priorities.

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Outline of presentation

- Definition and magnitude
- Diagnosis & treatment
- Prevention and transmission
- Additional key operational research issues
- Conclusion

TB HIV

Catalysing HIV/TB Research: innovation, funding and networking

*Desmond Tutu HIV center
Cape Town, South Africa, July 18-19, 2009*

Organized by the World Health Organization and the TB/HIV Working Group of the Stop TB Partnership in collaboration with the International AIDS Society and Consortium to Respond Effectively to the AIDS/TB Epidemic, Treatment Action Group and the Desmond Tutu HIV Center



Definitions of MDR and XDR-TB

- **MDR (Multi drug resistance) TB**
 - Resistance to at least **INH** and **Rifampicin**
- **XDR (Extensively drug resistant) TB**
 - **MDR**, and
 - Resistance to **fluoroquinolones**, and
 - One of the second-line **injectable** drugs (amikacin, kanamycin, or capreomycin)

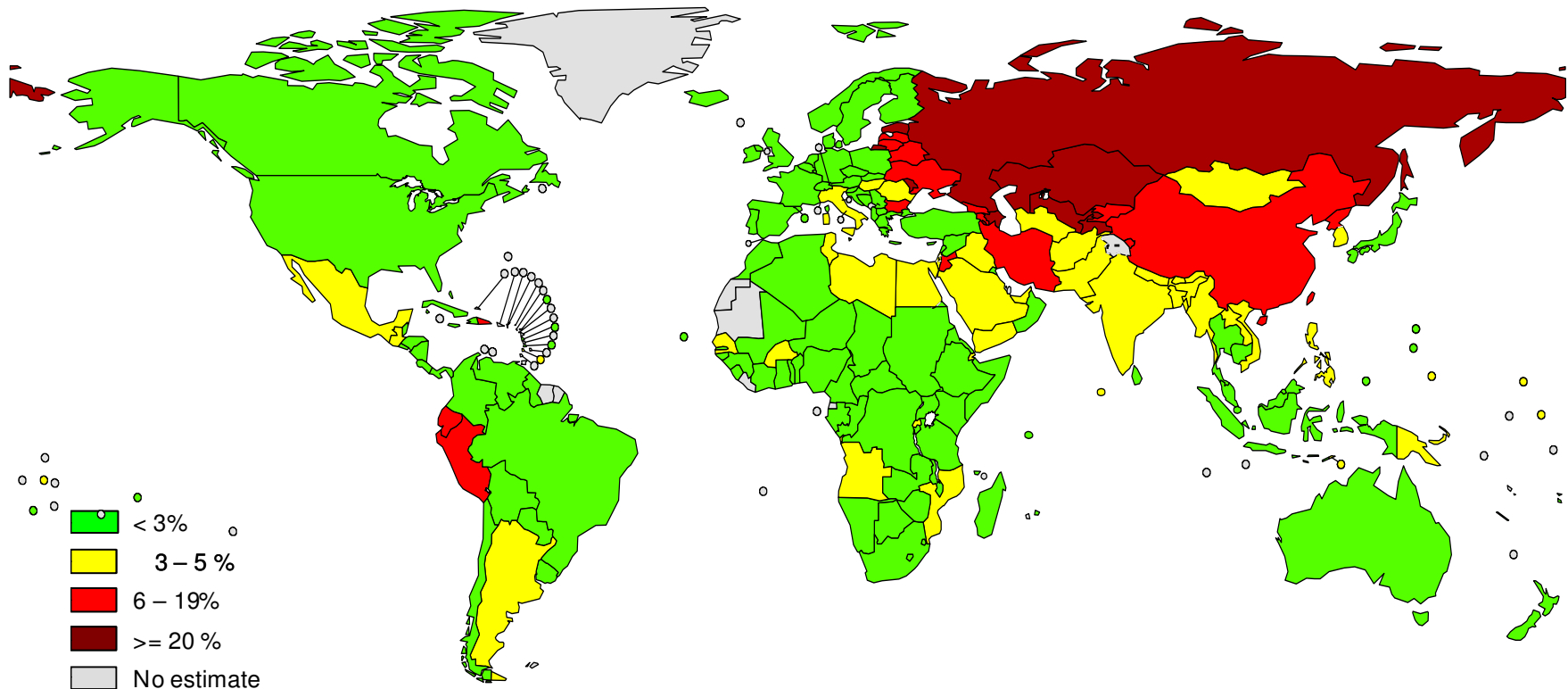
Latest global TB estimates - 2007

	Estimated number of cases	Estimated number of deaths
All forms of TB	9.27 million	1.77 million
MDR-TB	511,000	~150,000
XDR-TB	~50,000	~30,000
HIV-associated TB	1.37 million	456,000

How many of the MDR and XDR cases are also PLHIV?

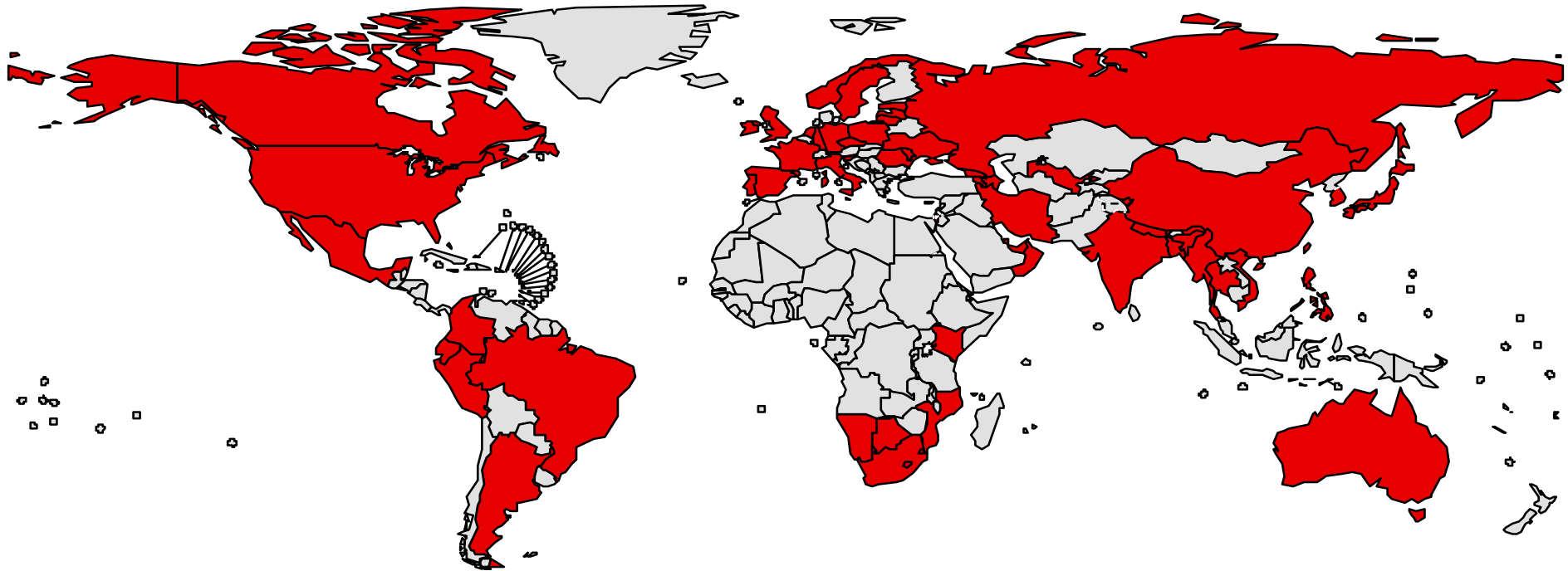
"I don't want to see TB statistics without HIV" Ken Castro, CDC.

Estimated MDR cases among new and retreatment cases, 2007



"Is this the tip of the iceberg?"

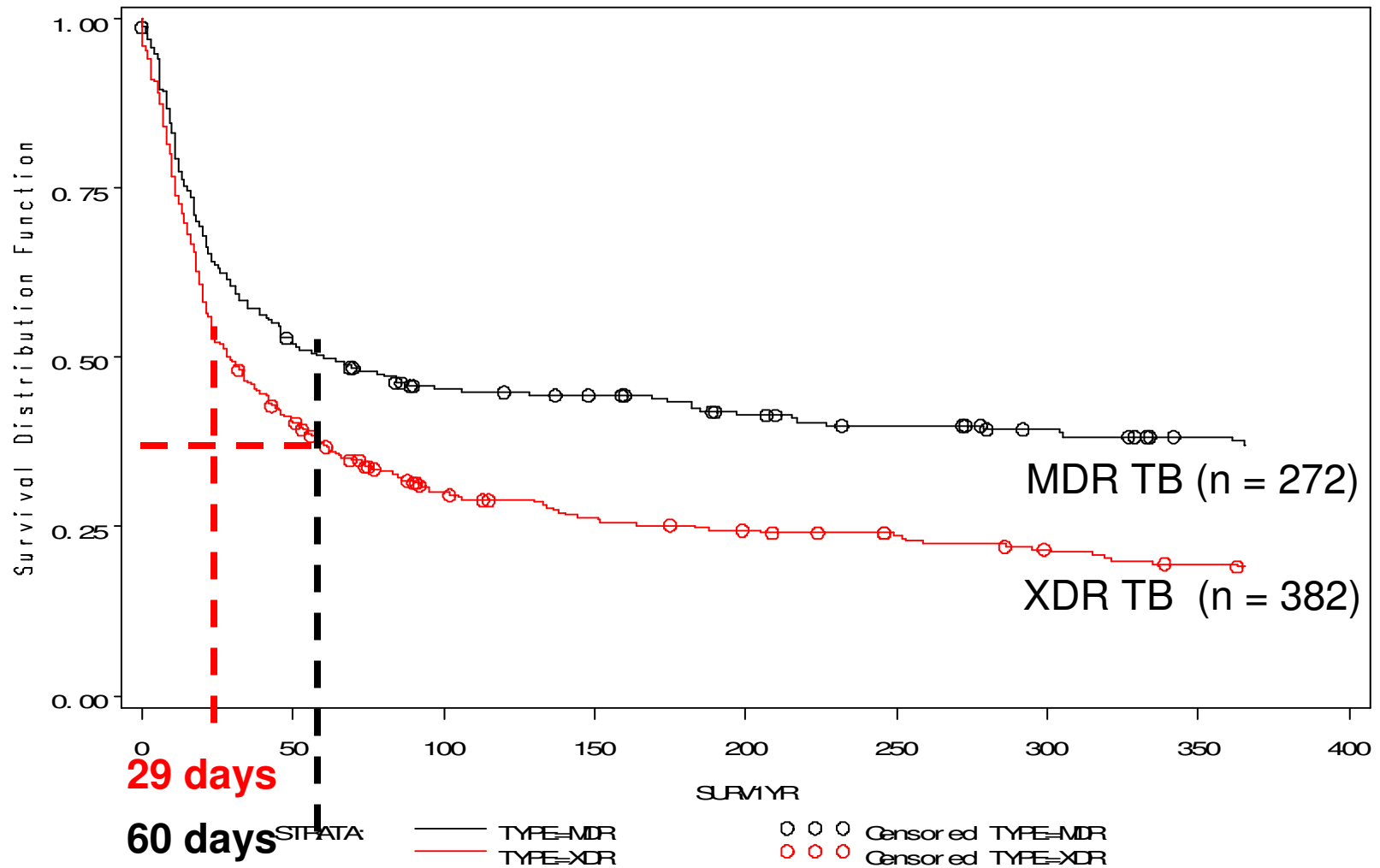
Countries with at least one XDR-TB case April 2009 (n=55)



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	

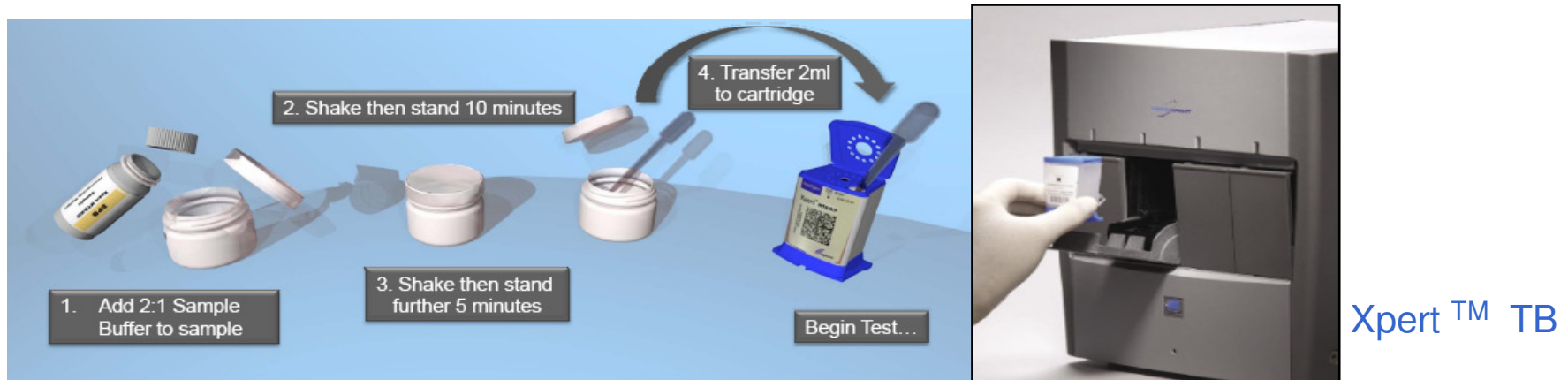
Are there clinical predictors for MDR and XDR TB?

HIV-Associated MDR (>70%) & XDR (>85%)



Why higher mortality in PLHIV? What about in HIV - ?

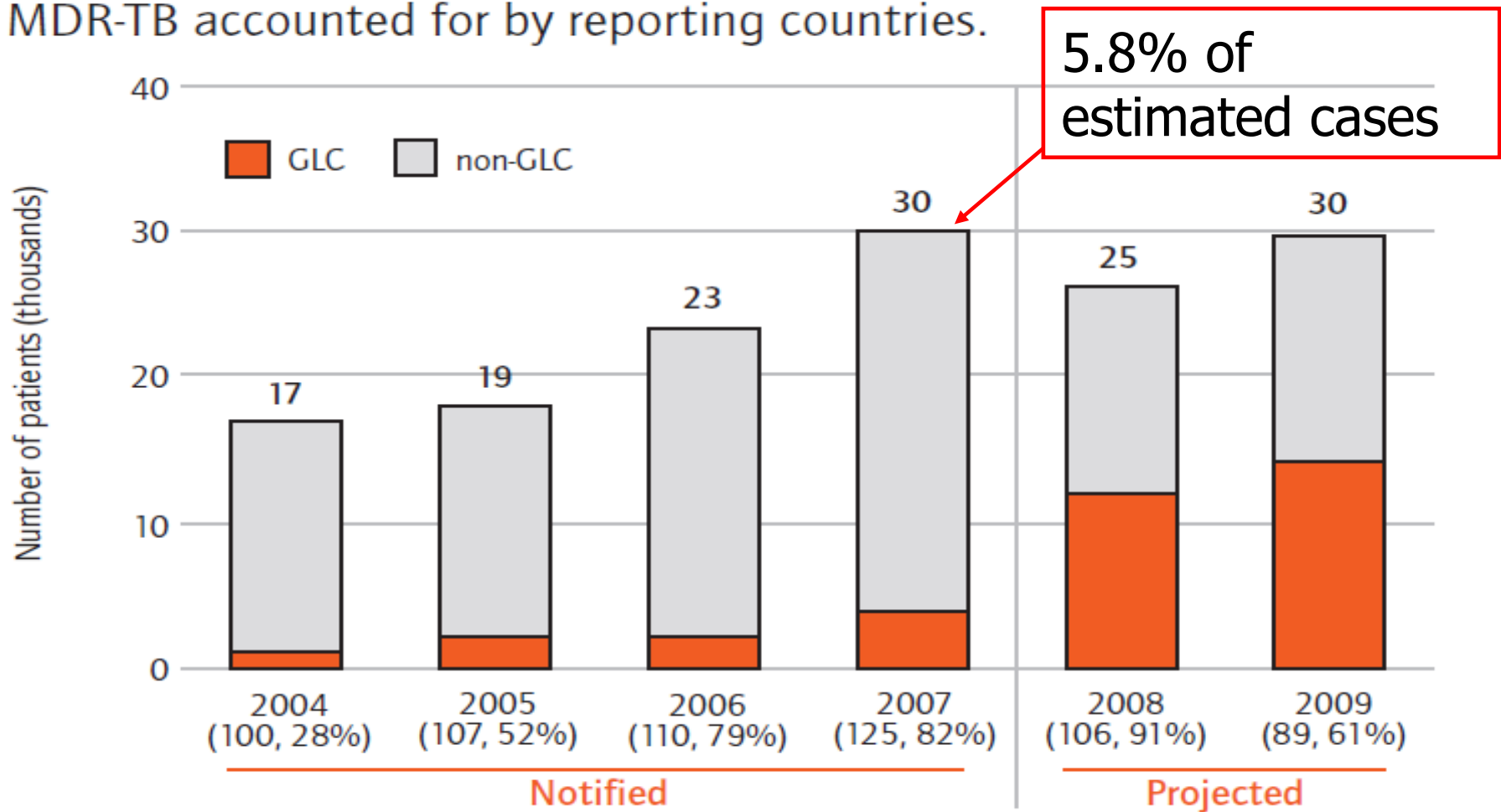
Integrated NAAT for TB and Rif resistance



- A common platform:
 - *TB and Rifampicin (MDR)*
 - *TB and quinolones (XDR)*
 - *HIV viral load*
- Time to result less than 2 hours
- Closed system (no contamination)

What about EP TB? Children? Dipstick TB test?

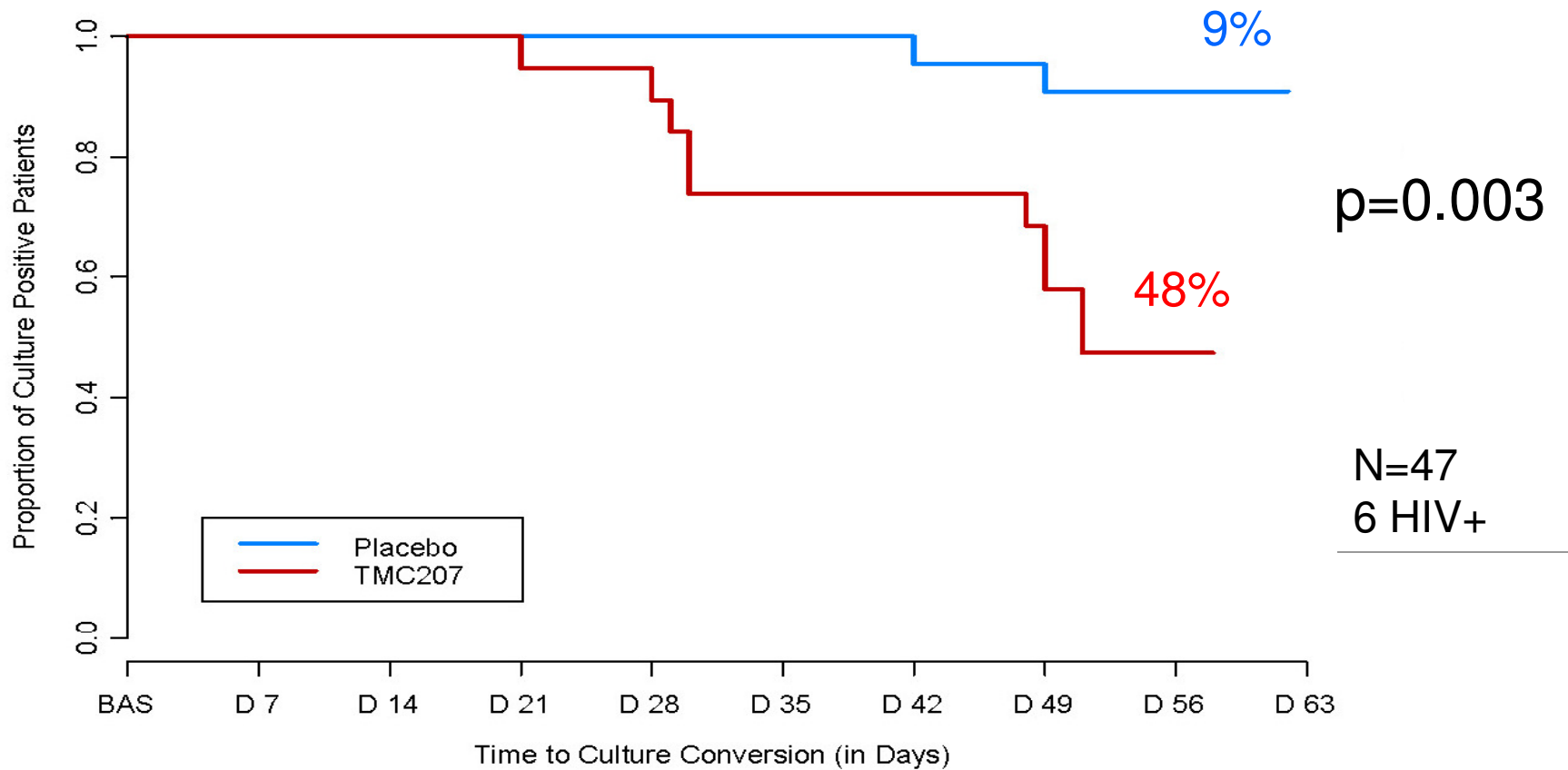
Notified cases of MDR-TB (2004-2007) and projected numbers of patients to be enrolled on treatment (2008-2009). The numbers under each bar show the number of countries reporting data, followed by the percentage of total estimated cases of MDR-TB accounted for by reporting countries.



Where to treat patients best? Hospital or in the community? Enablers of treatment including ART?

TMC207 shortens time to culture conversion in MDR cases

Diacon, NEJM, 2009



Safety, effectiveness and drug-drug interactions of concomitant use of ART and SLD-TB drugs?

Prevention and transmission

Four TB strains in single patient



- Susceptible TB → MDR TB → XDR TB
(percentage of transmission reduced as disease progresses)
- 86% of XDR TB acquired from MDR TB (Van Helden)

XDR TB in PLHIV: transmission or generation? How to stop it?

Prevention and transmission

- How and where MDR and XDR being created?
 - Drug quality
 - Health care delivery failure
 - Patient failure
- Treatment of latent MDR and XDR infection?
- What are the best methods for separating infectious cases from susceptible contacts?
- Do surgical masks on patients work?
- Do respirators on staff and visitors work?
- What indicators should be used?

Additional Operational issues

- Diagnosis
 - What are the best diagnostic algorithms?
 - What is the best model of case finding?
- Treatment
 - What are the best treatment models? Hospital or community?
 - How can TB patients, especially those with MDR-TB, better access ART?

Conclusion

- MDR/XDR TB and HIV are converging and increasing in magnitude and challenge.
- Huge paucity of evidence in the understanding and magnitude of the disease .
- Research to ease the bottlenecks (patient, delivery) for the diagnosis and treatment of MDR and XDR TB among PLHIV is a priority.
- New drugs and vaccines!
- New drugs research to include PLHIV with TB

Living with HIV, Dying of TB



Thembu Ngubane
1985-2009