

Outcomes of XDR-TB in SA

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Conflict of interest: none



“If TB and AIDS are a snake, then the head is in South Africa while the tail is quickly moving through other African countries... And if the head of the snake is in South Africa then the teeth are in Durban”

Dr Aaron Motaledi (SA minister of Health)
World TB Day, 24 March 2011

**1 in 100 South Africans have TB
500 000 cases per annum (1000 new
cases every day!)**

Overview

- ❑ Outcomes in MDR and XDR-TB
- ❑ Ominous threat of pan-resistant TB
- ❑ Summary and conclusions

What is the size of the problem globally?

- Worldwide **650 000 prevalent cases of MDR-TB in 2010** (5.4% of the 12 million prevalent cases)

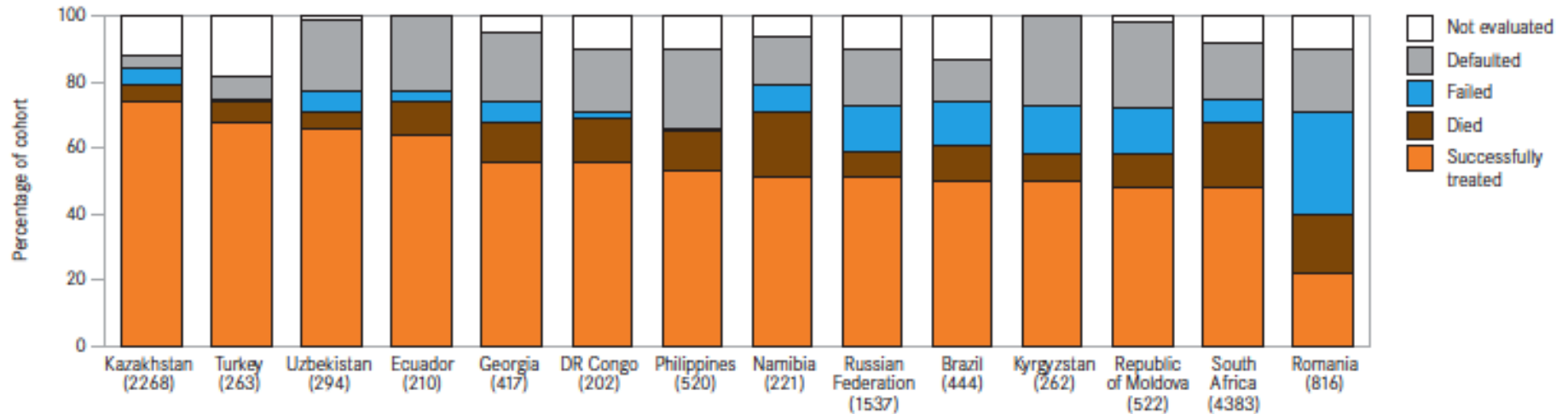
(**490 000 new** cases; 3.4% of new cases and 20% of retreatment cases)

WHO. Global TB Control. 2011.

- XDR-TB: globally ~ **25000 XDR-TB** cases annually
-

MDR-TB outcomes in different settings

Treatment outcomes for patients diagnosed with MDR-TB in 14 countries, 2008 cohorts. The total number of patients starting treatment in each cohort is shown under each country.^a



WHO. Global TB Control. 2011

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- ❑ Initial optimism of encouraging outcomes in XDR-TB

Mitnick C, NEJM, 2008;

Keshavjee S, Lancet, 2008;

Sotgiu G, ERJ, 2009

Early treatment outcomes and HIV status of patients with extensively drug-resistant tuberculosis in South Africa: a retrospective cohort study



Keertan Dheda, Karen Shean*, Alimuddin Zumla*, Mubasim Badri*, Elizabeth M Streicher, Liesl Page-Shipp, Paul Willcox, Melanie Anne John, Gary Reubenson, Darshini Govindasamy, Michelle Wong, Xavier Padanilam, Alicia Dziwiecki, Paul D van Helden, Sweetness Siwendu, Julie Jarand, Colin N Menezes, Avnil Bums, Thomas Victor, Robin Warren, Martin P Grobusch, Martie van der Walt*, Charlotte Kvasnovsky**

Review of 199 patients with XDR-TB

Dheda K, Shean K, Warren R, Willcox P; Lancet; 2010

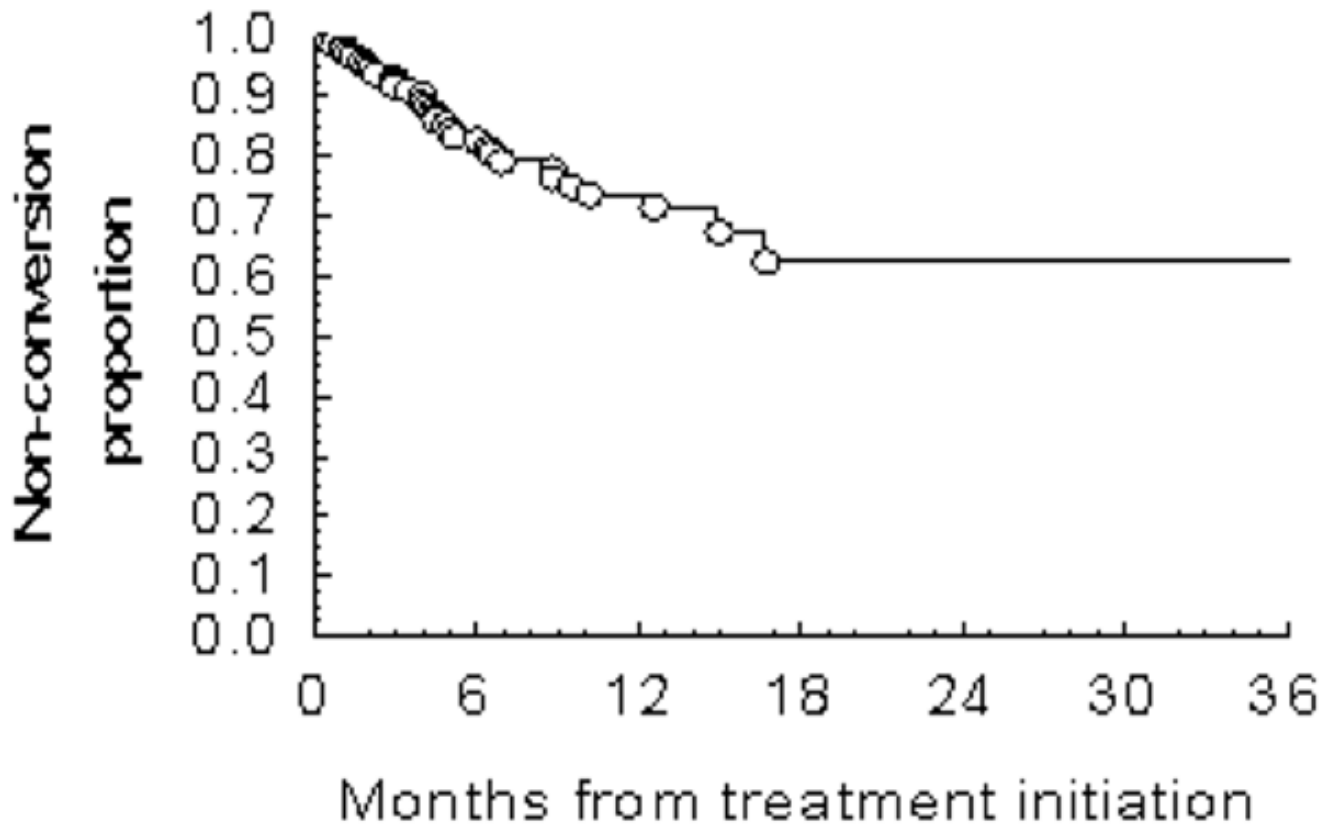
- Become apparent that outcomes in high burden settings like South Africa are poorer than in intermediate to low burden settings

Gandhi N, Lancet, 2006

O'Donnell M, IJTLD, 2009

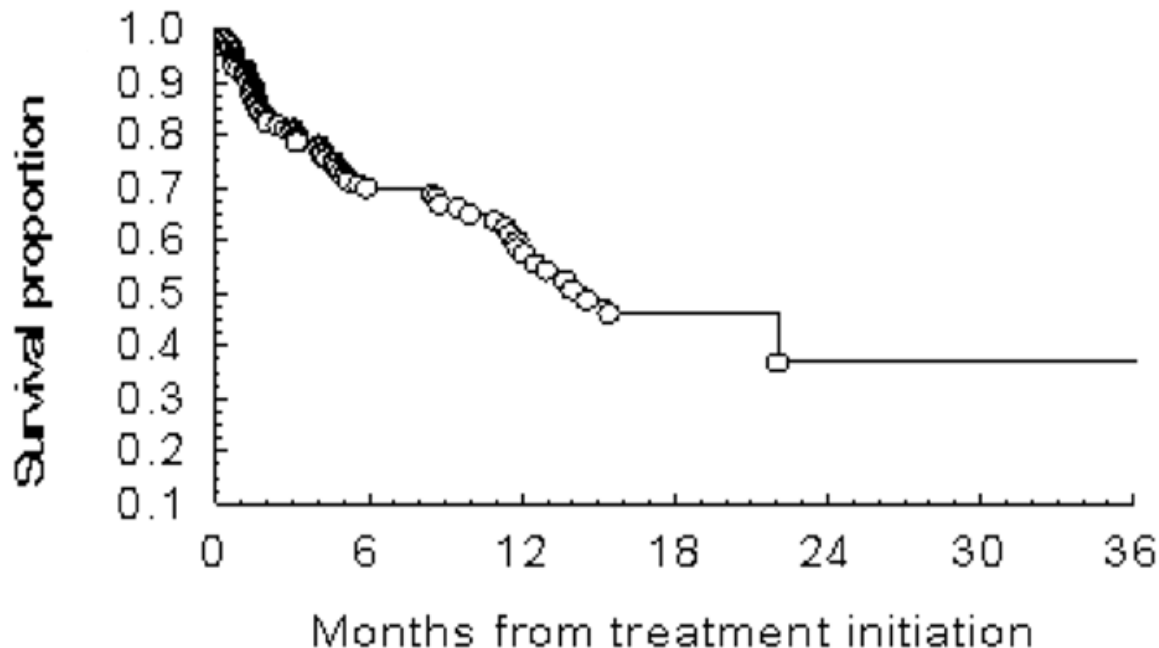
Kaplan-Meier probabilities of XDR-TB culture-conversion (n= 174)

- The overall culture-conversion rate was 19% (33/174)



Death in the whole cohort of patients from the date of treatment-initiation

- ❑ Overall and 12-month mortality rates were 42%, 36% (n= 174)
- ❑ Contrast [Mitnick et al, NEJM, 2008](#); median time to conversion was 90 days, and mortality in 48 XDR-TB patients was only 23% (11/48)



Conclusion

- ❑ Treatment related outcomes for XDR-TB were poor both in HIV- infected and uninfected patients. ART improves outcomes in HIV-infected persons. Low body weight, previous treatment for MDR-TB, and major ADRs were adverse prognostic indicators.
 - ❑ Strengthening the National TB Programme and addressing the underlying social determinants of health remains is of paramount importance.
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Why is MDR and XDR-TB a threat?

- **Mortality rates are substantially higher** (annual mortality in patients with XDR TB approaches 40%)

Dheda K, Lancet, 2010

O'Donnell M, IJTLD, 2010

Gandhi N, Lancet, 2006

- **Drastically increases the costs** of running a TB program (despite annually treating 500 000 cases of drug-susceptible TB and < 10 000 MDR/XDR-TB, the latter eats up > 50% of the annual TB drug budget).

Pooran and Dheda, PLoS One, submitted

High Incidence of Hospital Admissions With Multidrug-Resistant and Extensively Drug-Resistant Tuberculosis Among South African Health Care Workers

Max R. O'Donnell, MD, MPH; Julie Jarand, BSc, MD; Marian Loveday, BSc, MPhil; Nesri Padayatchi, BSc, MBChB, DCH, DTM+H, DHSM, DPH, MS(Epi); Jennifer Zelnick, MSW, ScD; Lise Werner, MSc; Kasavan Naidoo, MSc, BSc; Iqbal Master, MBChB; Garth Osburn, MBChB; Charlotte Kvasnovsky, MD, MPH; Karen Shean, MSc; Madhukar Pai, MD, PhD; Martie Van der Walt, PhD; Charles R. Horsburgh, MD, MUS; and Keertan Dheda, MBBCh, PhD

(23 XDR-TB and 208 MDR-TB HCWs in KZN)

	HCWs	General Population	Incidence Rate Ratio (95% C.I.)*
Annual MDR or XDR-TB Incidence	66.8/100,000	11.7/100,000	5.71 (4.96-6.69)
Annual MDR-TB Incidence	62.3/100,000	10.7/100,000	5.82 (5.03-6.87)
Annual XDR-TB Incidence	4.5/100,000	1.04/100,000	4.33 (2.69-8.18)

O' Donnell, Padayachi, Dheda; Annals Intern Med; 2010
Jarand J & Dheda K, TMIH, 2010

Sondalo (1938)- 3500 beds



St Helliere






- ❑ Surgical techniques promoting partial or complete lung collapse were also used.
- ❑ With the advent of effective anti-TB therapy, the need for sanatoria dwindled.

What is happening to these many culture non-converters?

- Given the poor conversion rates, there are large numbers of treatment failures (defined as failure to culture-convert after twelve months of intensive in-patient XDR treatment with regimens including an injectable drug like capreomycin).
 - While some patients die within weeks or months, a significant proportion of patients do survive for months or years.
 - How should these living treatment failures be dealt with?
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Places of isolation and palliative care for XDR-TB treatment failures

Viewpoint 
HC

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**The global rise of extensively drug-resistant tuberculosis:
is the time to bring back sanatoria now overdue?**

Keertan Dheda K, Giovanni B Migliori

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- Community stay facilities with multi-disciplinary teams for treatment failures
- Palliative care facilities

[Dheda K, Lancet, 2012](#)

Summary

- ❑ There is a significant and increasing burden of DR-TB globally. The burden of XDR-TB is increasing worldwide
- ❑ XDR-TB treatment outcomes are poor
- ❑ Tuberculosis has now evolved into a therapeutically destitute disease, which is virtually untreatable
- ❑ New drugs but must be protected and regulated
- ❑ TB is a good example of how a MDR pathogen can become a global threat
- ❑ Time to build sanatoria now overdue!



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