

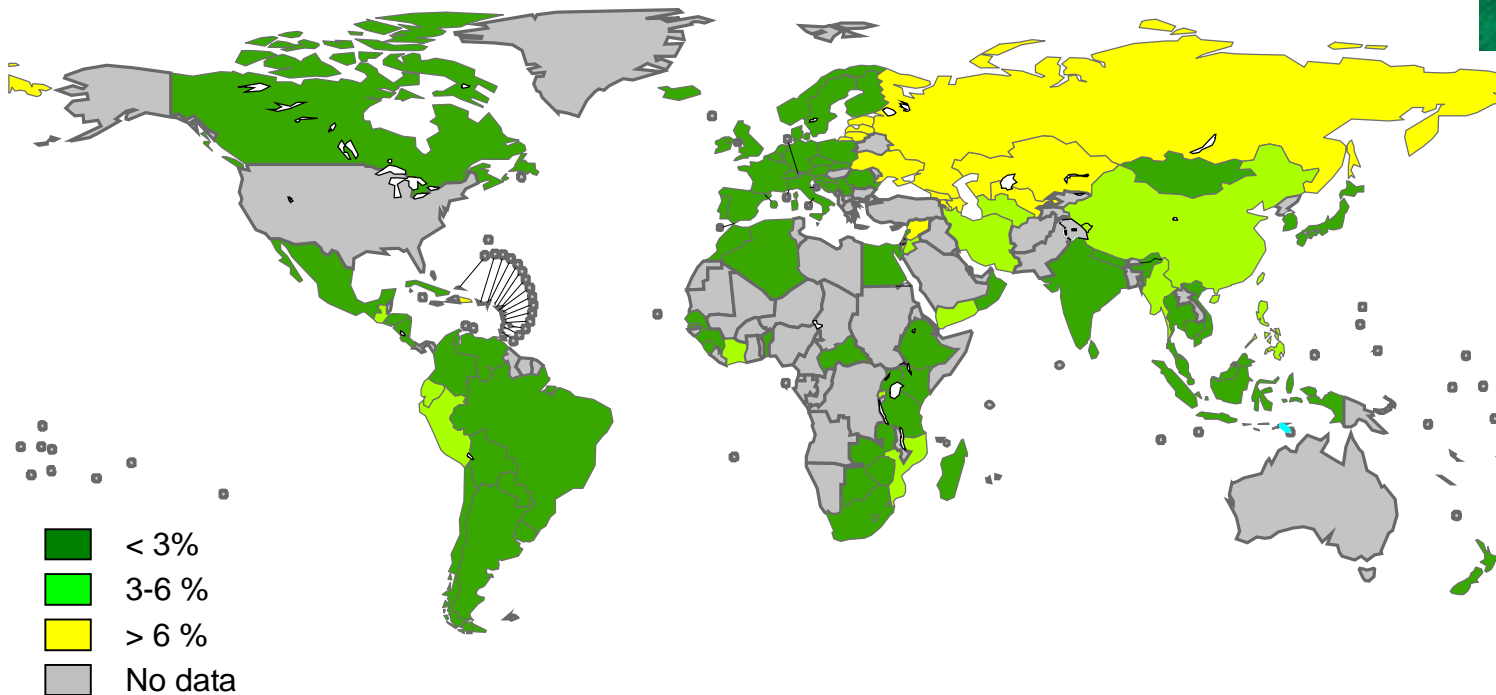
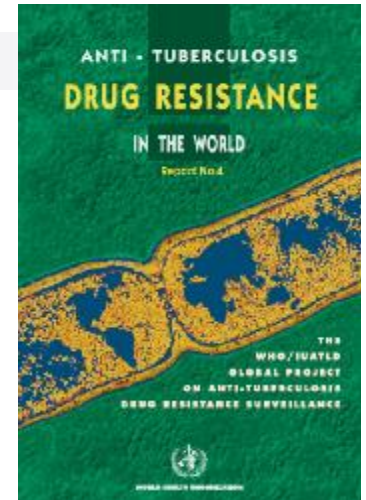
# Underreported threat of MDR-TB in Africa

Forum on Drug Discovery,  
Development and Translation

Yanis BEN AMOR

# MDR-TB among new cases 1994-2007

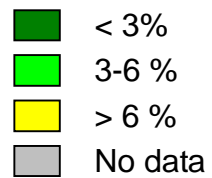
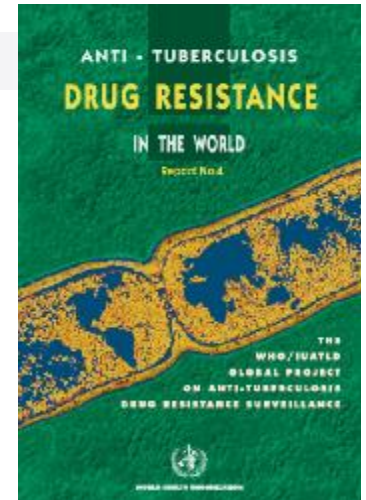
\* Sub-national averages applied to China, Russia, Indonesia



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# MDR-TB among new cases 1994-2007





# Countries with no data

- n Despite high TB incidence and prevalence, and high HIV prevalence, MDR-TB is considered low in Africa
- n NTP are operating well
- n Rifampicin introduced later



# Performance of NTP (1997-2008)

	<b>Case Detection</b>	<b>Treatment Success</b>
<b>Estonia</b>	69%	68%
<b>Kazakhstan</b>	76%	76%
<b>Latvia</b>	73%	70%
<b>Lithuania</b>	78%	78%
<b>Russian Federation</b>	43%	64%
<b>Uzbekistan</b>	42%	79%
<b>AFRO</b>	51%	70%

*Source: WHO reports 1997 - 2008*



# Introduction of Rifampicin

<b>Country</b>	<b>Year</b>
<b>South Africa</b>	1979
<b>Tanzania</b>	1982
<b>Botswana</b>	1986
<b>Gambia</b>	1986
<b>Mozambique</b>	1986
<b>Zambia</b>	1989



# Countries with no data

- n One might speculate that the countries capable of providing DRS data may have been the ones most likely to have a well functioning NTP, laboratory structures and transport networks.
- n MDR-TB rates are likely higher in the African countries which were never surveyed than in the countries already surveyed

# Countries with known MDR-TB rate

## Underreported Threat of Multidrug-Resistant Tuberculosis in Africa

Yanis Ben Amor, Bennett Nemser, Angad Singh, Alissa Bankin, and Neil Schluger

Multidrug-resistant tuberculosis (MDR TB) in Africa may be more prevalent than previously appreciated. Factors leading to development of drug resistance need to be understood to develop appropriate control strategies for national programs. We gathered estimates of MDR TB rates for 39 of 46 countries in Africa. The relationship between MDR TB rates and independent factors was analyzed by using correlation and linear regression models. Our findings indicate that drug resistance surveys in Africa are critically needed. MDR TB rates must be assessed in countries without these surveys. In countries that have conducted a drug resistance survey, a new survey will determine evolution of drug resistance rates. We found no correlation between high MDR rates and TB incidence, HIV/TB co-infection rates, or year of introduction of rifampin. Results show that the retreatment failure rate was the most predictive indicator for MDR TB. Current category II drug regimens may increase MDR TB.

Global control of tuberculosis (TB) has been jeopardized by 2 major threats: HIV/AIDS and multidrug-resistant TB (MDR TB). MDR TB is defined as strains of *Mycobacterium tuberculosis* that are resistant to at least isoniazid and rifampin (1). Drug resistance has reached alarming levels with the emergence of strains that are virtually untreatable with existing drugs. The recent report of an outbreak of extensively drug-resistant TB (XDR TB) in South Africa (2), with its extremely high case-fatality rate, has drawn wide attention. However, the more general problem of MDR TB, with an estimated 450,000 cases worldwide annually, has been recognized since the first World Health Organization (WHO) global survey on drug resistance in the late 1990s (3).

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According to the WHO Global Report on Anti-tuberculosis Drug Resistance in the World (4), MDR TB strains have emerged in all regions of the world. However, despite the dramatic increase in TB rates in Africa, MDR TB appears nearly absent from this continent, which, until recently, reported the lowest median levels of drug resistance.

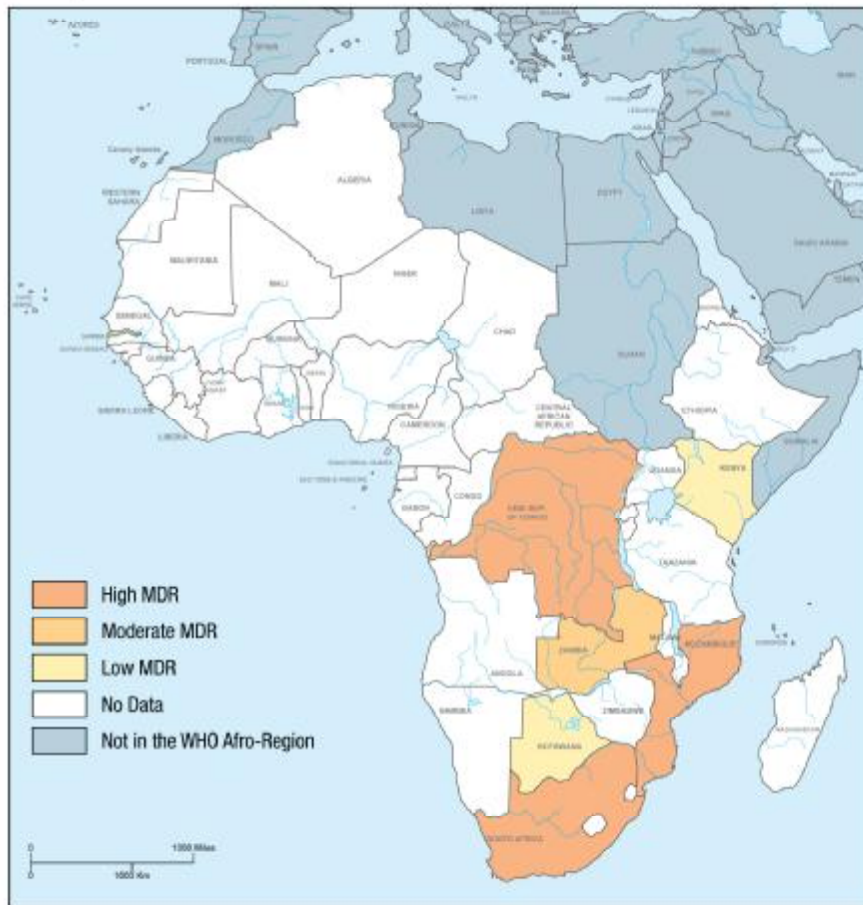
Two explanations have been most commonly put forward to explain these reported low levels of MDR TB in Africa. The first explanation is the presence of well-functioning control programs in Africa. Eighty-nine percent of the population in the WHO-defined region of Africa is covered by directly observed therapy, short course (DOTS), which is similar to the global average (4). However, there is discordance between purported DOTS coverage and national TB program (NTP) efficacy. Each year, countries with the lowest case detection and cure rates are clustered in the WHO-defined Regional Office for Africa (AFRO) region (4). This suggests that NTPs in Africa are not performing better than their Eastern European or South American counterparts, where MDR TB rates have already reached alarming levels. The functional status of many programs in Africa is difficult to assess with certainty, and the high incidence rates on that continent indicate that programs may not be functioning well. Low case-detection rates alone may not lead to development of MDR TB. Other factors that might favor development of MDR TB include the availability of drugs on the open market and a private sector that delivers drugs to the population in an unregulated fashion.

The second explanation is the recent introduction of rifampin in Africa. It is often stated that because rifampin was only recently introduced in Africa on a large scale, there has been relatively little time for resistance to develop. However, development of rifampin resistance may be spurred by HIV infection, and such resistance appears to develop rapidly (5–10).

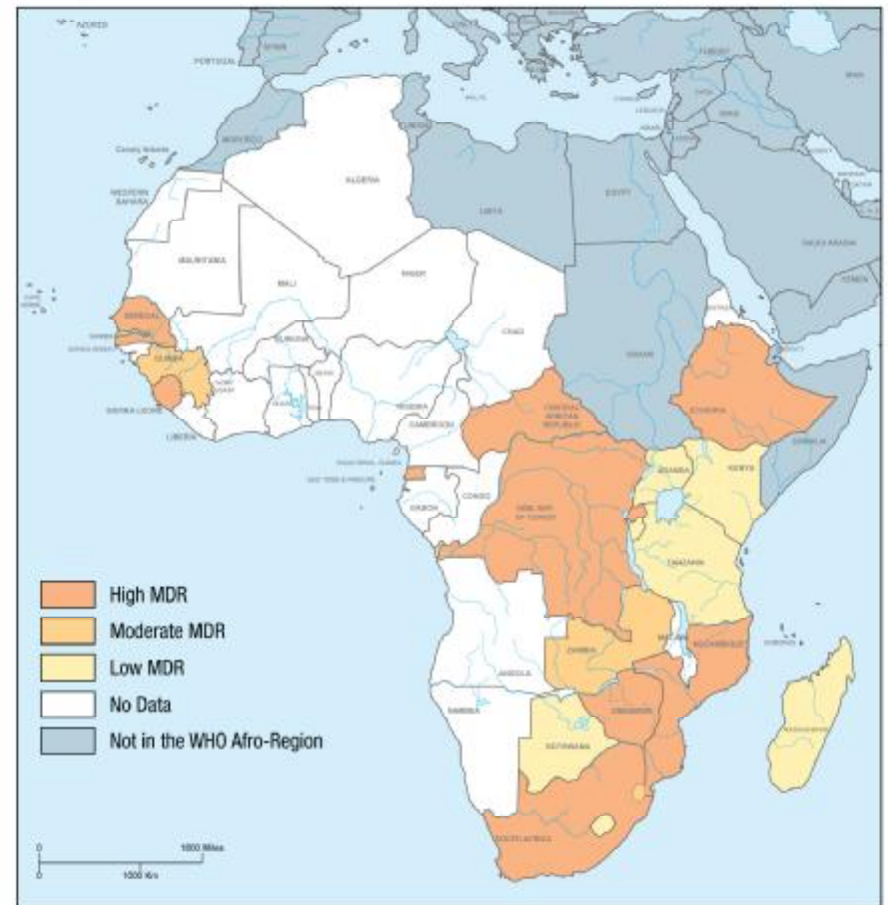


# Countries with known MDR-TB rate

Map 1



Map 2



**Most new countries surveyed are either moderate or high MDR levels**

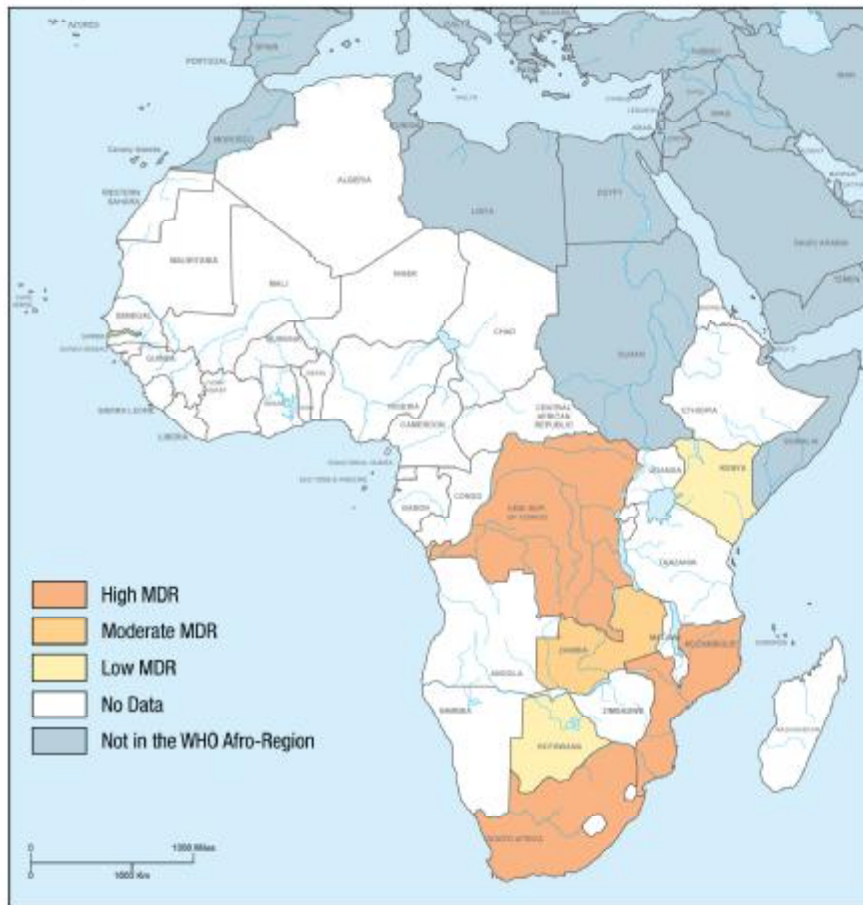


## Countries with known MDR-TB rate

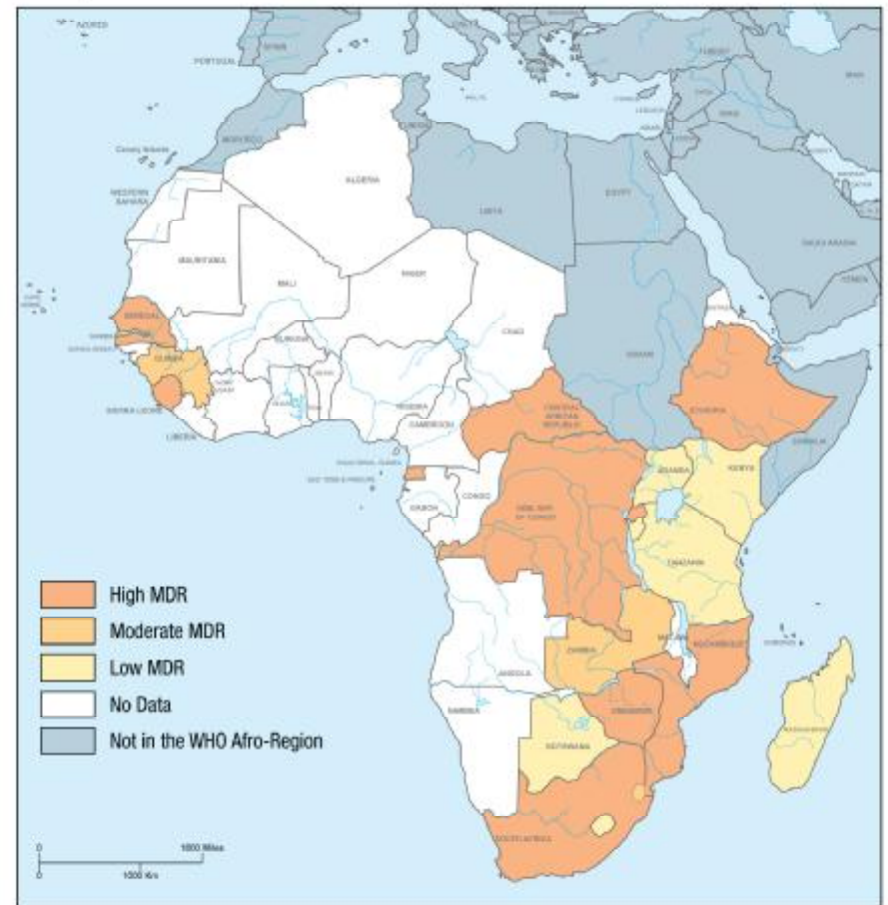
- n 14 /21 surveys are older than 5 years
- n Few settings in Africa with repeat surveys show rising MDR-TB rates (Botswana)
- n We can assume that current rates of MDR-TB in repeat surveys would be higher

# Countries with known MDR-TB rate

Map 1



Map 2



Matteo Zignol, Paul Nunn J. Infect Dis 2006



## Countries with known MDR-TB rate

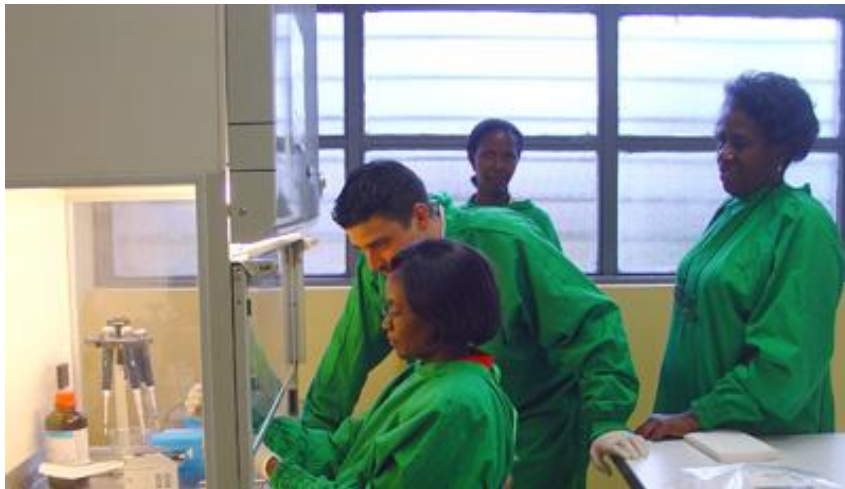
- n Current DRS only include SS+ TB cases
- n 2 countries (Latvia and Ukraine) with MDR-TB rates segregated based on HIV status show significant association between HIV+ and MDR-TB
- n HIV + are more likely to be SS-
- n In high HIV prevalence settings, current DRS protocol may underestimate actual MDR-TB levels



# Indicators of MDR-TB rates

- n Investigate association between country specific factors and MDR-TB levels in Africa
- n No linear relationship between MDR-TB rates and average case detection rate, average TB incidence rate or TB prevalence
- n Retreatment failure rate was the most predictive indicator of MDR-TB rates
  - .. Association without causation
  - .. Current retreatment regimen may cause MDR-TB

# Conclusions



- n MDR-TB likely to be underestimated
- n Diagnosis of MDR-TB not widely available
- n Second line drugs not available
- n Current Category II regimen may be creating MDR-TB



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