



# Epidemiology

TB Infection Control Training



**ICAP**

International Center for AIDS  
Care and Treatment Programs

MAILMAN SCHOOL OF PUBLIC HEALTH  
Columbia University

# Objectives of this session

- Provide an overview of epidemiological concepts relevant to TB and HIV
- Provide an overview of global, regional and local epidemiology of TB and HIV
- Give an update on the global and local epidemiology of multi-drug resistant TB

# Global TB and HIV Epidemiology



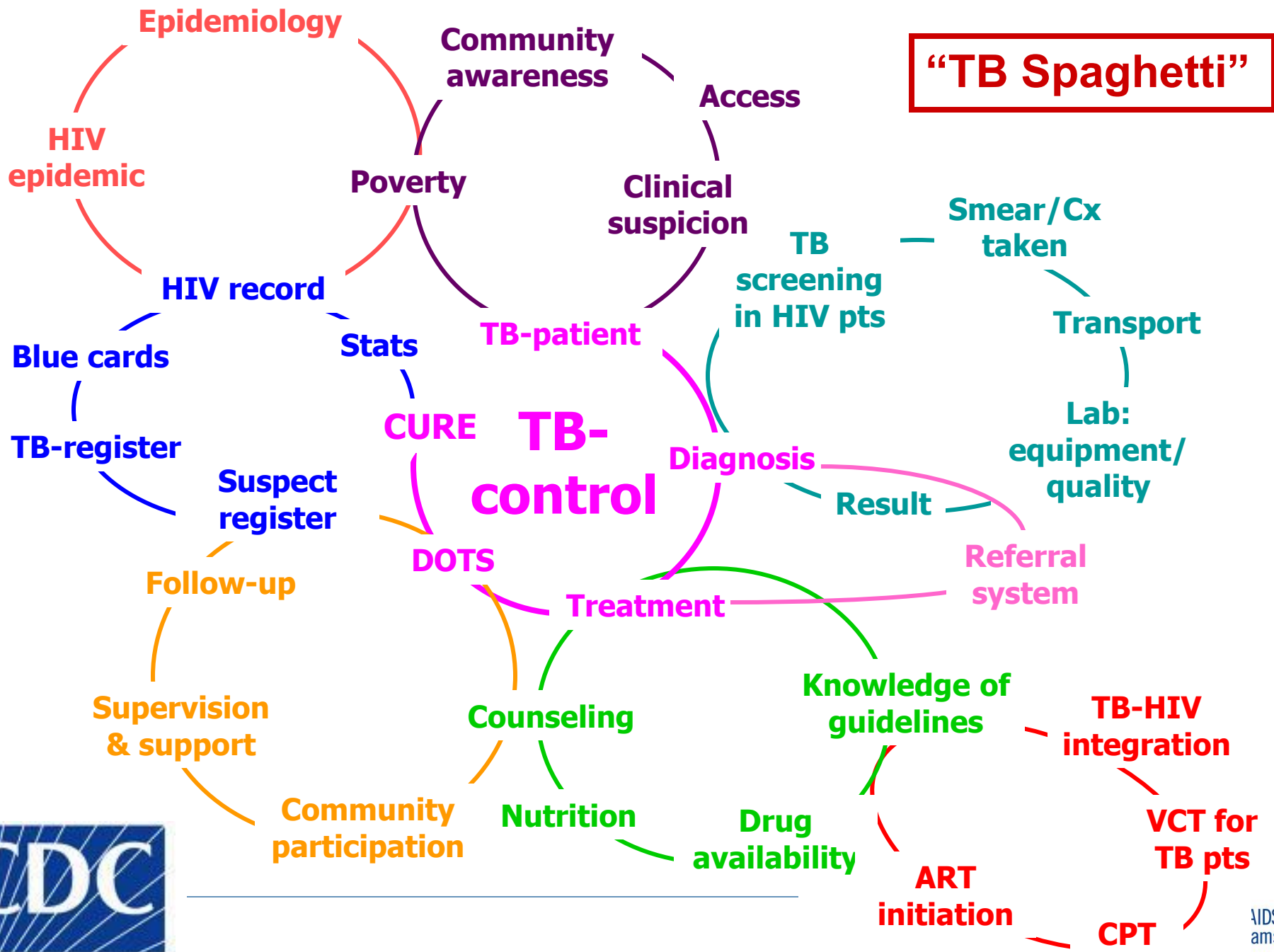
# Paradigm Shift in TB/HIV Advocacy



***" We can't fight AIDS unless we do much more to fight TB as well "***

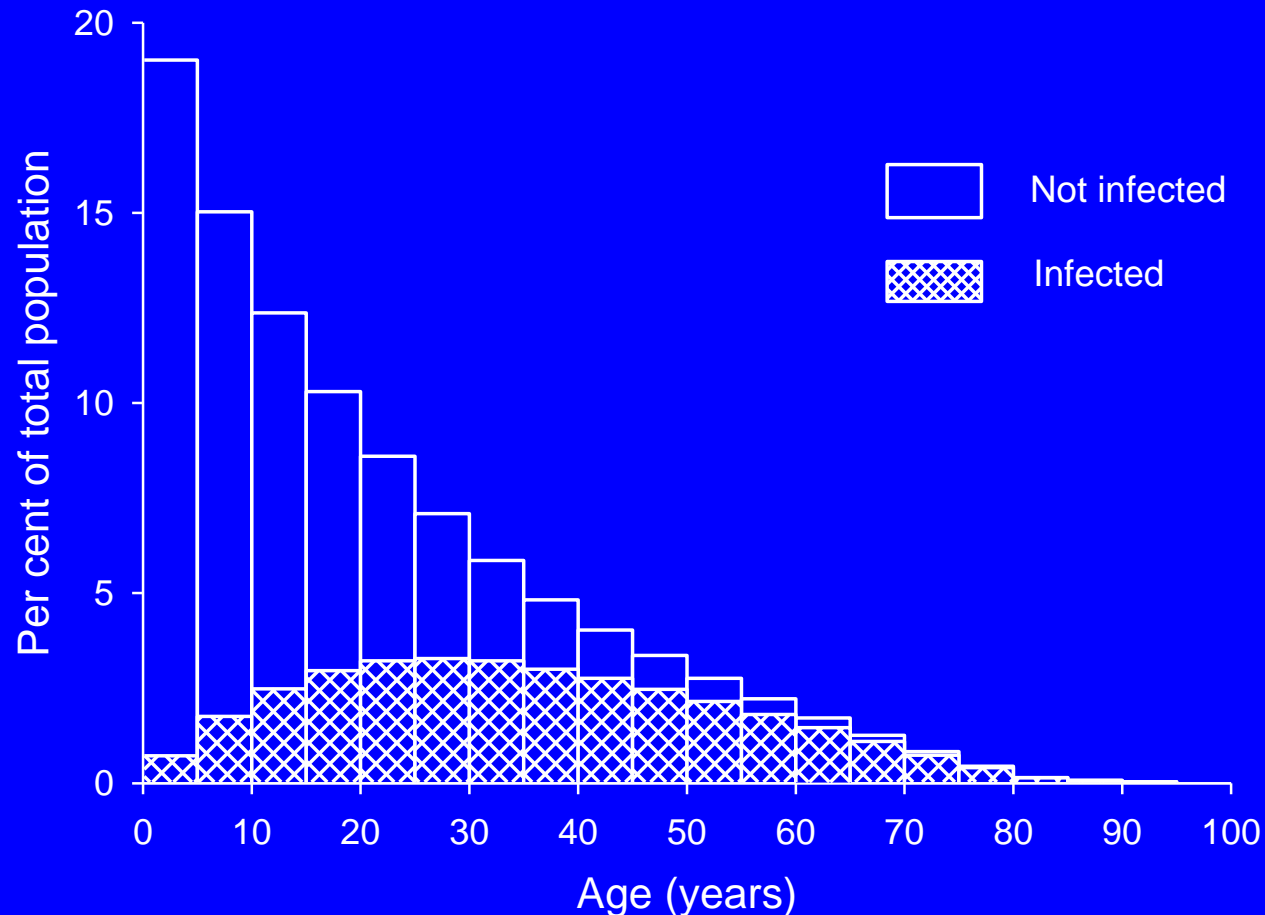
Nelson Mandela, Bangkok, July 2004

**“TB Spaghetti”**



# Epidemiology Concepts in TB

Age-specific Prevalence of Tuberculous Infection  
in Tropical and Southern Africa



Data courtesy: ten Dam HG, World Health Organization, 1990

# When TB is Epidemic (Incidence $>1000/100,000$ )

- Most TB cases are from recent infection
- Disease is most common in young people
  - Exposure happens early in life
- Smear positive cases are not contained by early diagnosis and treatment
- There is no predilection for ‘high-risk’ groups
  - Everyone is at risk

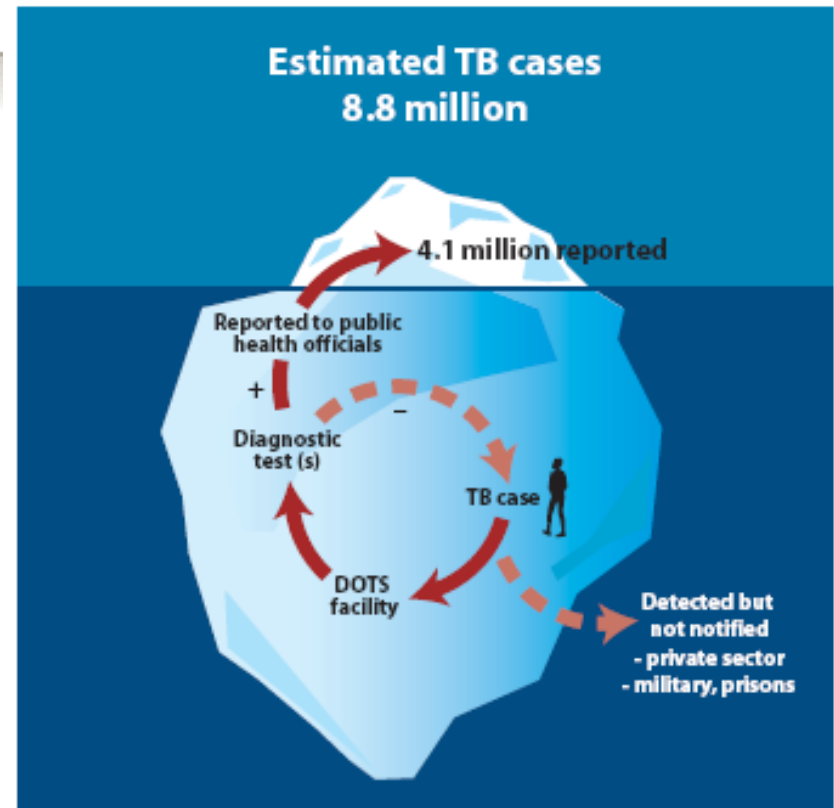
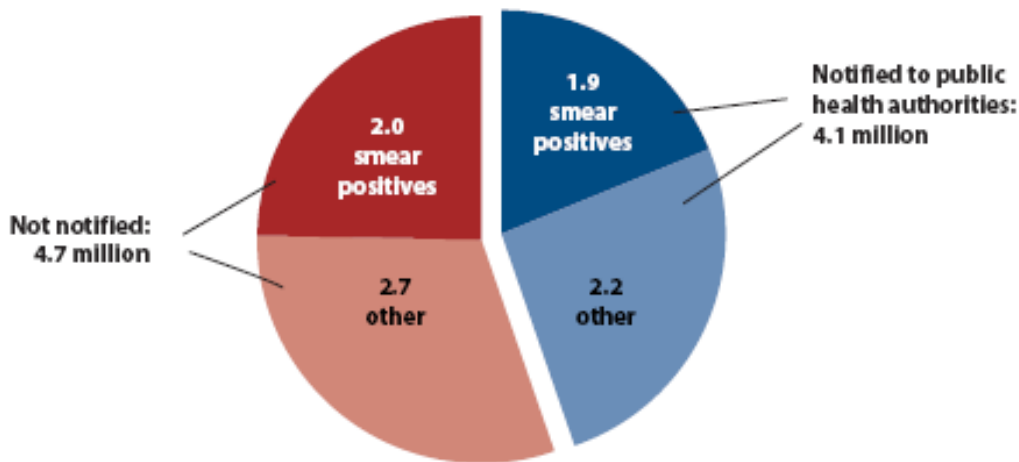
# When TB Disease is Uncommon (Incidence $<1000/100,000$ )

- Most TB cases are from reactivation
- Disease is more common in older people
- Smear-positive cases can be contained by early diagnosis and treatment
- High risk groups can be identified
  - Contacts of TB cases
  - Silicosis
  - Residents of urban informal housing settlements

# TB in the World Today

## THE GAP BETWEEN ESTIMATED AND NOTIFIED CASES

GLOBAL CASELOAD OF NEW TB CASES STRATIFIED BY SMEAR AND NOTIFICATION STATUS



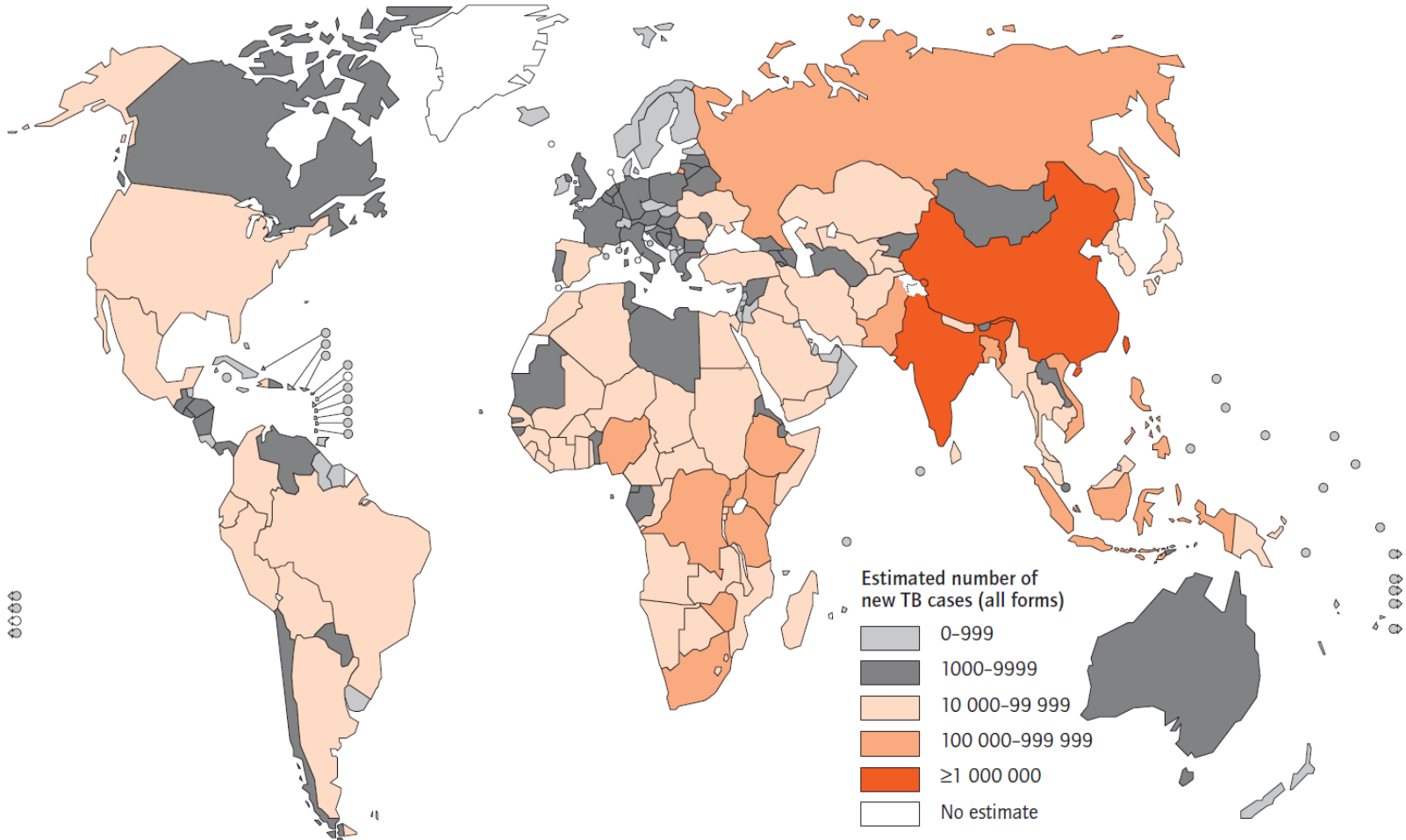
## Estimated epidemiological burden of TB, 2007

	POPULATION 1000s	INCIDENCE*				PREVALENCE*		MORTALITY				HIV PREV. IN INCIDENT TB CASES <sup>b</sup> %
		ALL FORMS		SMEAR-POSITIVE		ALL FORMS		HIV-NEGATIVE		HIV-POSITIVE		
		NUMBER 1000s	PER 100 000 POP PER YEAR	NUMBER 1000s	PER 100 000 POP PER YEAR	NUMBER 1000s	PER 100 000 POP PER YEAR	NUMBER 1000s	PER 100 000 POP PER YEAR	NUMBER 1000s	PER 100 000 POP PER YEAR	
1 India	1 169 016	1 962	168	873	75	3 305	283	302	26	30	2.5	5.3
2 China	1 328 630	1 306	98	585	44	2 582	194	194	15	6.8	0.5	1.9
3 Indonesia	2 31 627	528	228	236	102	566	244	86	37	5.4	2.4	3.0
4 Nigeria	148 093	460	311	195	131	772	521	79	53	59	40	27
5 South Africa	48 577	461	948	174	358	336	692	18	38	94	193	73
6 Bangladesh	158 665	353	223	159	100	614	387	70	44	0.4	0.3	0.3
7 Ethiopia	83 099	314	378	135	163	481	579	53	64	23	28	19
8 Pakistan	163 902	297	181	133	81	365	223	46	28	1.4	0.9	2.1
9 Philippines	87 960	255	290	115	130	440	500	36	41	0.3	0.3	0.3
10 DR Congo	62 636	245	392	109	174	417	666	45	72	6.0	10	5.9
11 Russian Federation	142 499	157	110	68	48	164	115	20	14	5.1	3.6	16
12 Viet Nam	87 375	150	171	66	76	192	220	18	20	3.1	3.5	8.1
13 Kenya	37 538	132	353	53	142	120	319	10	26	15	39	48
14 Brazil	191 791	92	48	49	26	114	60	5.9	3.1	2.5	1.3	14
15 UR Tanzania	40 454	120	297	49	120	136	337	12	29	20	49	47
16 Uganda	30 884	102	330	42	136	132	426	13	41	16	52	39
17 Zimbabwe	13 349	104	782	40	298	95	714	6.9	52	28	213	69
18 Thailand	63 884	91	142	39	62	123	192	10	15	3.9	6.0	17
19 Mozambique	21 397	92	431	37	174	108	504	10	45	17	82	47
20 Myanmar	48 798	83	171	37	75	79	162	5.4	11	0.9	1.9	11
21 Cambodia	14 444	72	495	32	219	96	664	11	77	1.8	13	7.8
22 Afghanistan	27 145	46	168	21	76	65	238	8.2	30	0.0	0	0
High-burden countries	4 201 761	7 423	177	3 245	77	11 301	269	1 058	25	339	8.1	14

# Estimated number of new TB cases, 2007

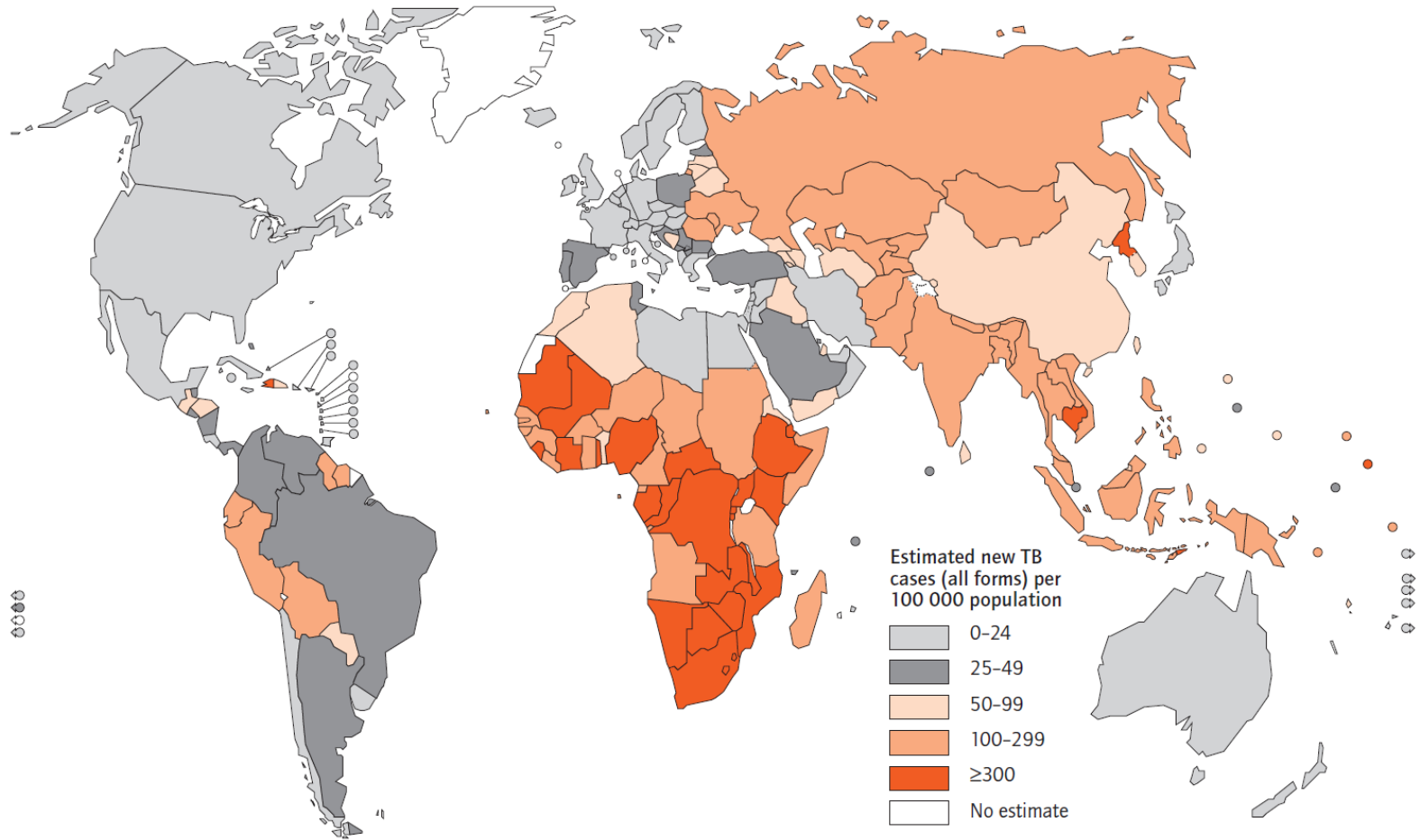
■ **FIGURE 1.1**

Estimated number of new TB cases, by country, 2007



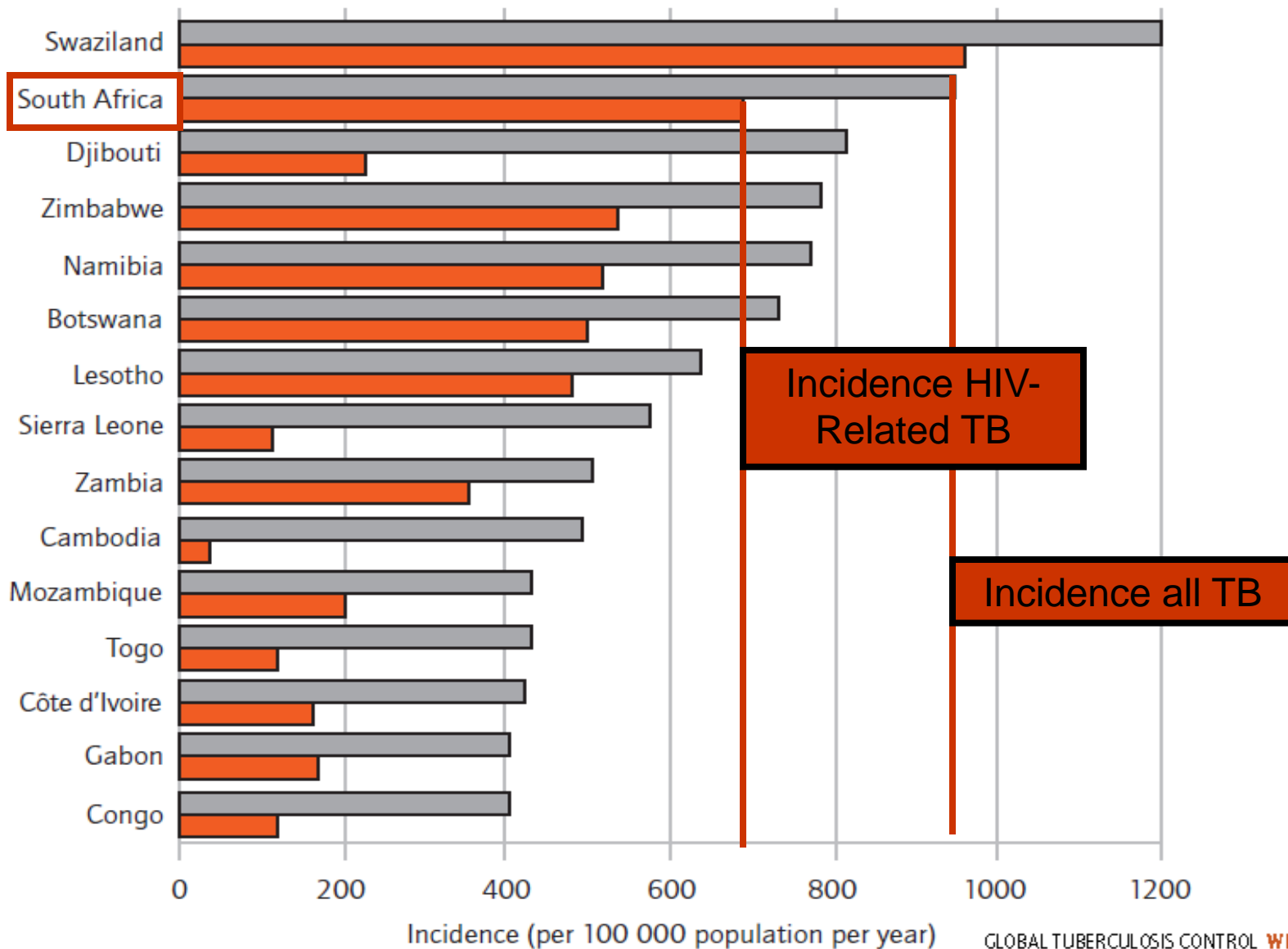
# Estimated TB incidence rates, 2007

■ **FIGURE 1.2**  
Estimated TB incidence rates, by country, 2007



## ■ FIGURE 1.4

Fifteen countries with the highest estimated TB incidence rates per capita (all forms; grey bars) and corresponding incidence rates of HIV-positive TB cases (red bars), 2007



# Trends in Tuberculosis – the last 30 years

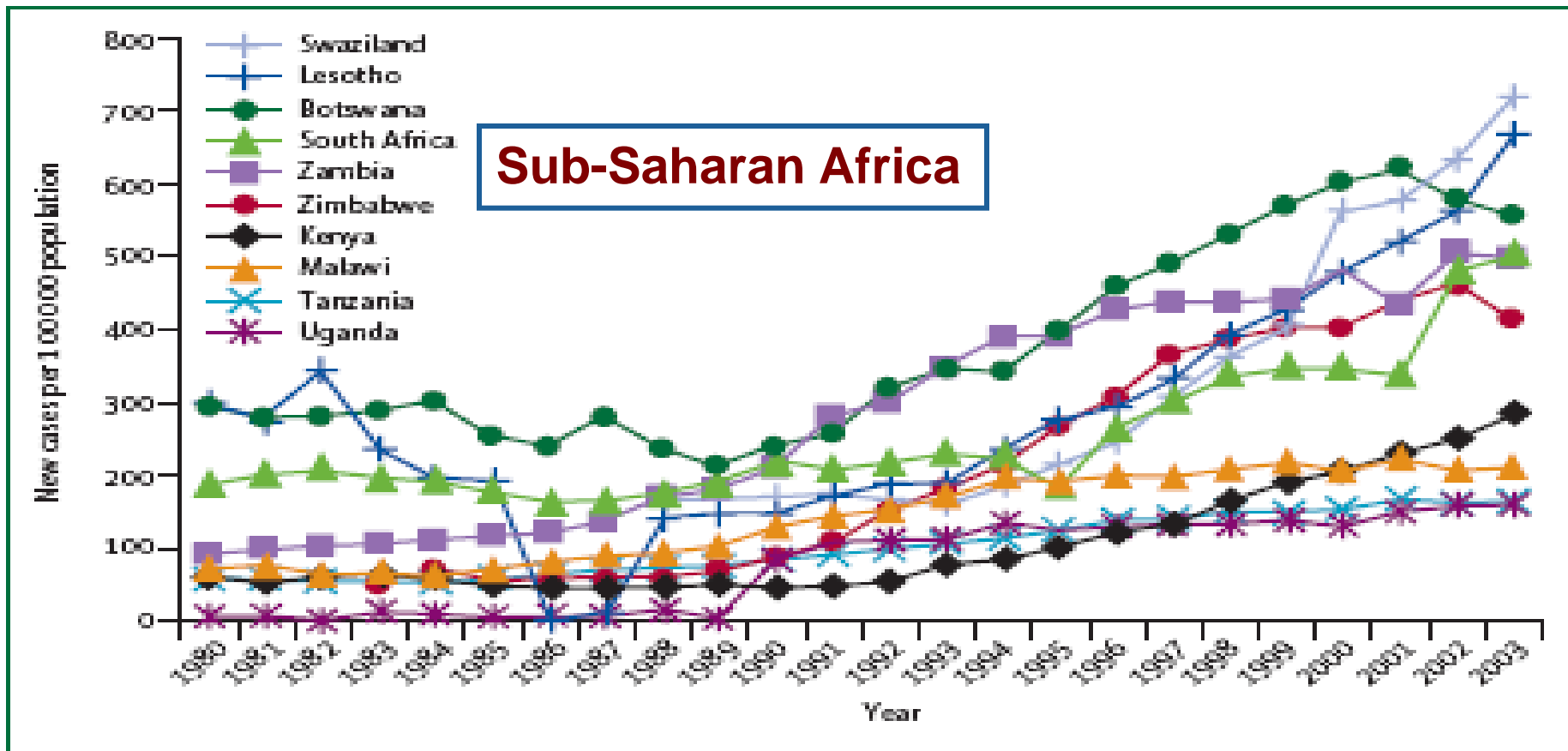
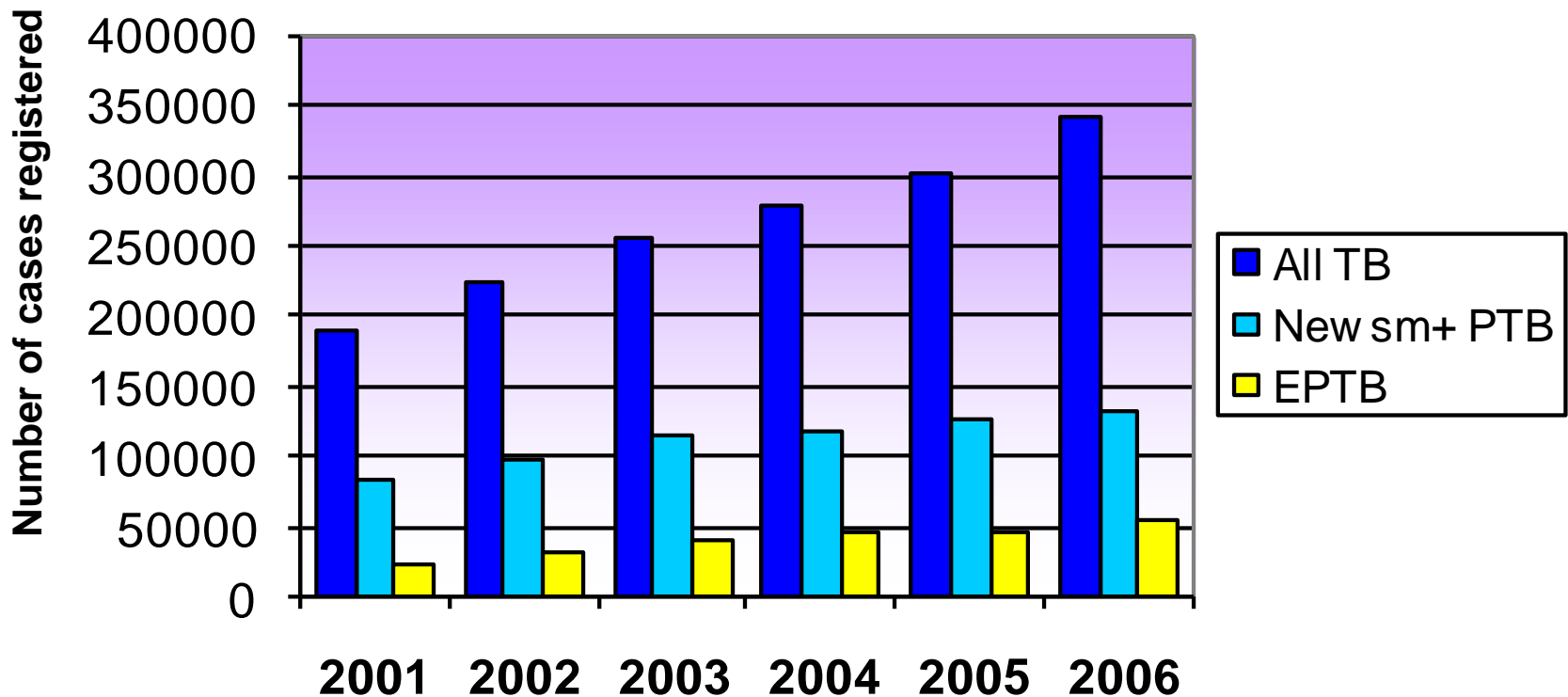
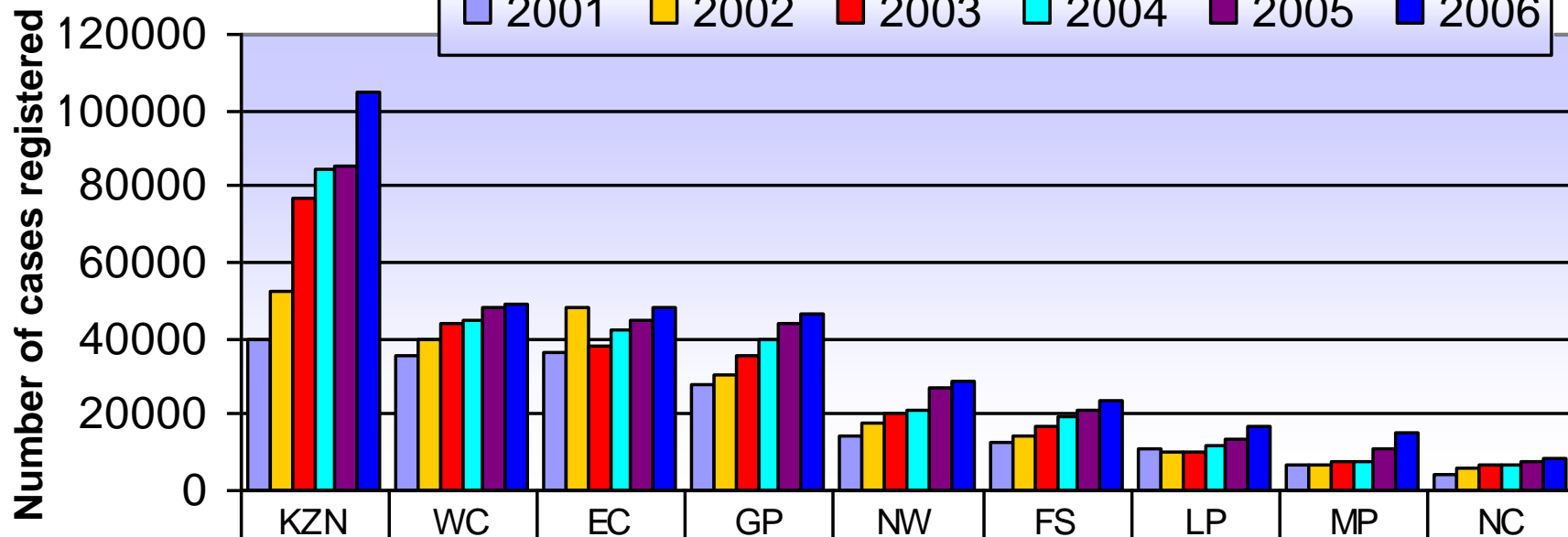


Figure 4: Time trends in tuberculosis case-notification rates in southern and east Africa  
As reported to WHO.<sup>18</sup>

# TB in South Africa 2001-2006



# All TB Cases by Province

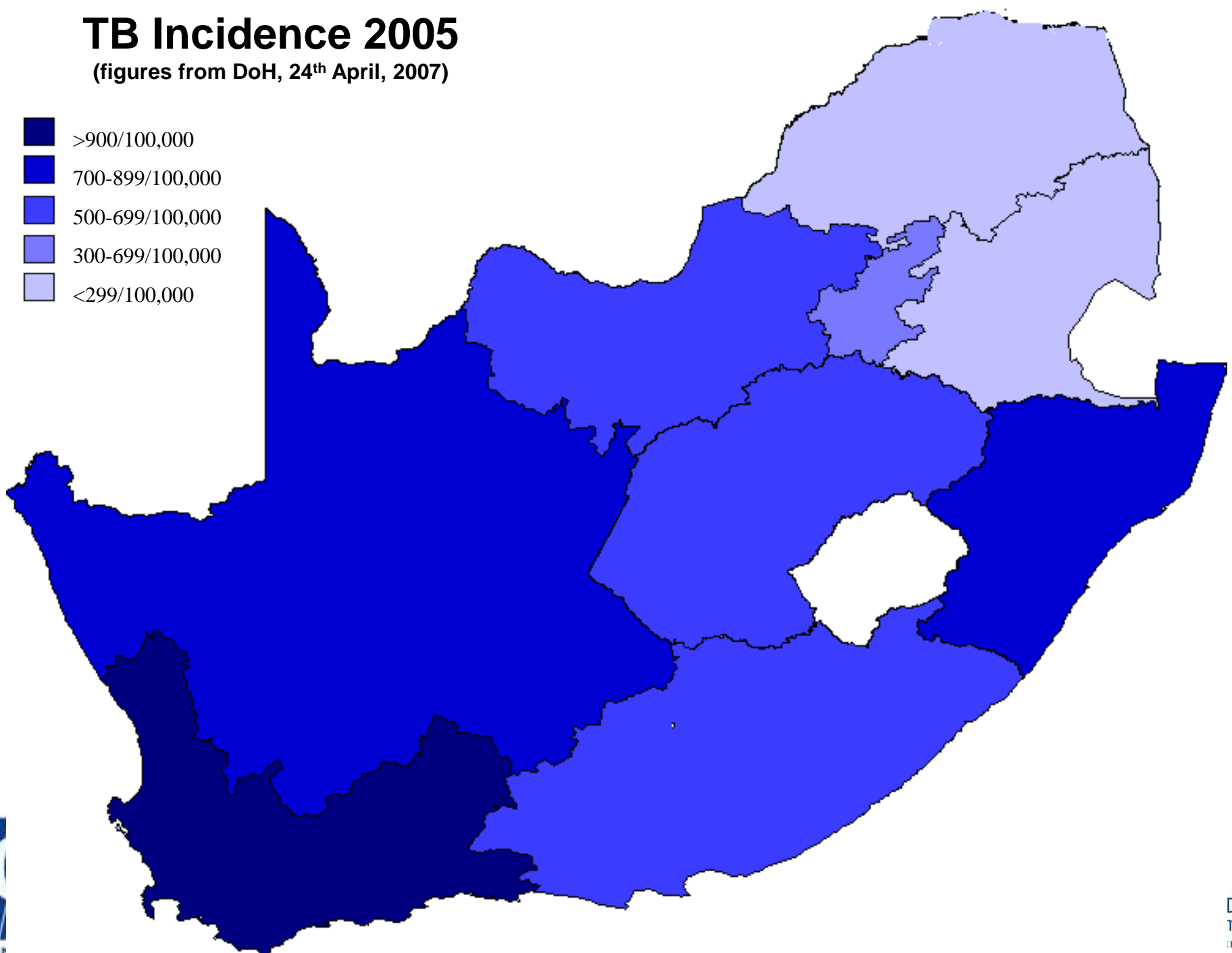
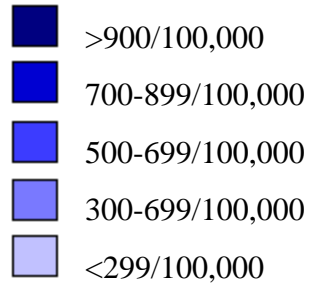


	KZN	WC	EC	GP	NW	FS	LP	MP	NC
2001	39586	35687	36520	27622	14277	13024	10619	6925	4435
2002	52016	39650	48130	30515	17612	14221	10098	6536	5642
2003	76838	44161	38430	35161	19918	16733	9797	7732	6652
2004	84794	45170	42026	39697	21119	19697	11879	7831	7047
2005	85507	48193	44909	43990	27208	20915	13366	10746	7633
2006	104705	49093	48512	46093	28421	23374	17301	15035	8631

Source: NTCP 2008

# TB Incidence 2005

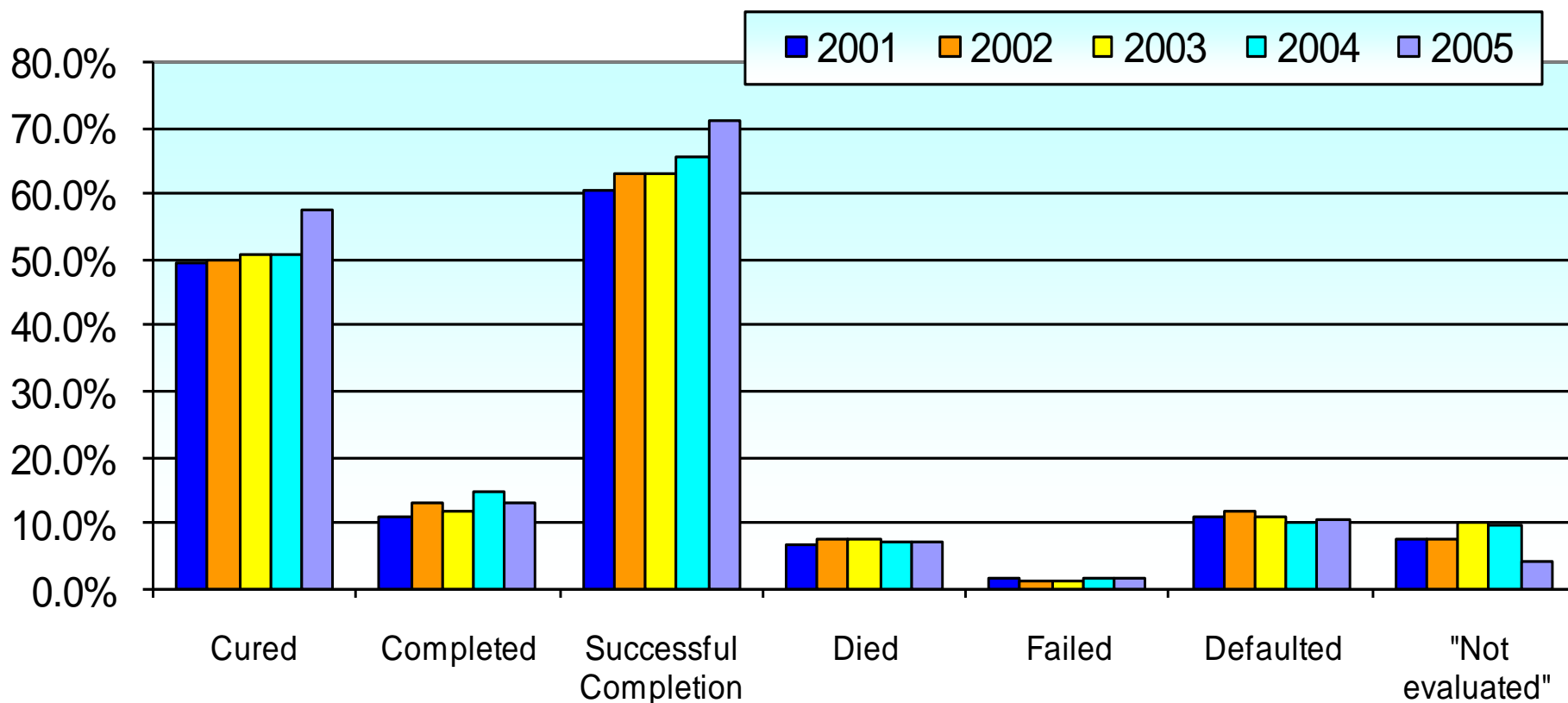
(figures from DoH, 24<sup>th</sup> April, 2007)



## Treatment Outcome (New Smear Positive Cases) for 2005

	Cured		Completed		Successful Completion		Died		Failed		Defaulted		Transferred		"Not Evaluated"	
	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#
EC	54.7	11239	20.0	4104	74.7	15343	7.0	1441	1.2	244	9.0	1846	3.6	750	4.5	927
FS	67.5	6572	9.3	907	76.9	7479	10.1	982	2.0	195	5.9	576	4.8	469	0.3	30
GP	66.7	15965	5.0	1195	71.7	17160	9.6	2288	1.5	361	6.9	1650	8.1	1932	2.2	530
KZN	42.5	16487	19.1	6971	64.2	23458	6.1	2235	1.2	446	14.7	5362	5.8	2127	7.9	2883
MP	51.8	3959	13.9	1065	65.7	5024	9.0	687	1.0	77	10.8	824	4.3	327	9.2	703
NW	57.6	7936	12.3	1700	70.0	9636	7.3	1004	2.9	396	9.5	1314	6.5	898	3.8	523
NC	50.1	1948	21.3	829	71.4	2777	6.8	266	3.2	123	13.1	511	2.8	109	2.6	102
LP	60.8	4142	9.2	625	70.0	4767	9.5	645	2.0	139	7.4	507	8.5	581	2.5	168
WC	71.9	13547	7.8	1472	79.7	15019	3.7	693	1.9	365	11.1	2096	3.2	606	0.4	66
SA	57.7	81795	13.3	18868	71.1	100663	7.2	10241	1.7	2346	10.4	14686	5.5	7799	4.2	5932

# Treatment Outcomes for Smear+ TB in SA

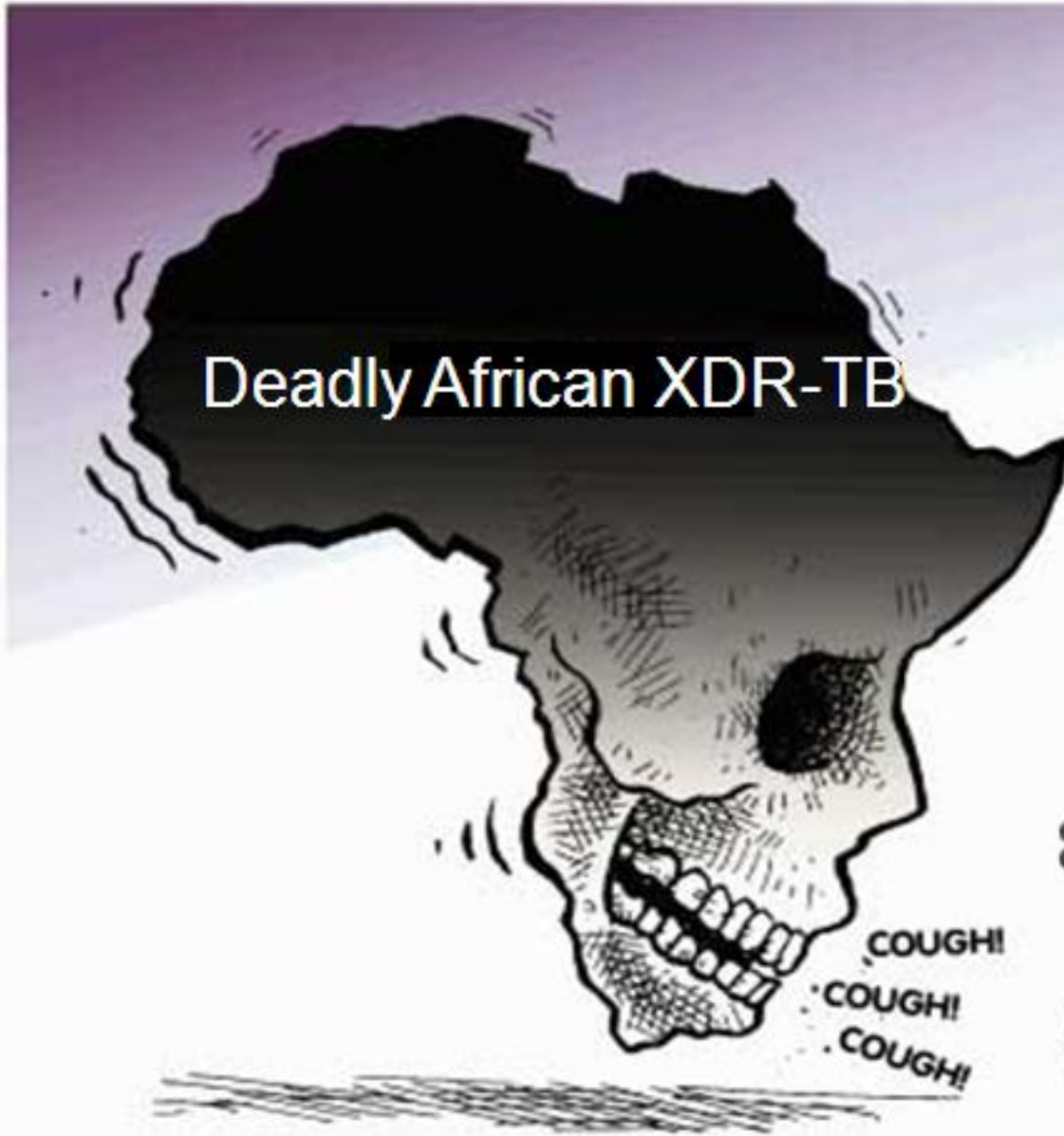


Source: NTCP 2008



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# Deadly African XDR-TB



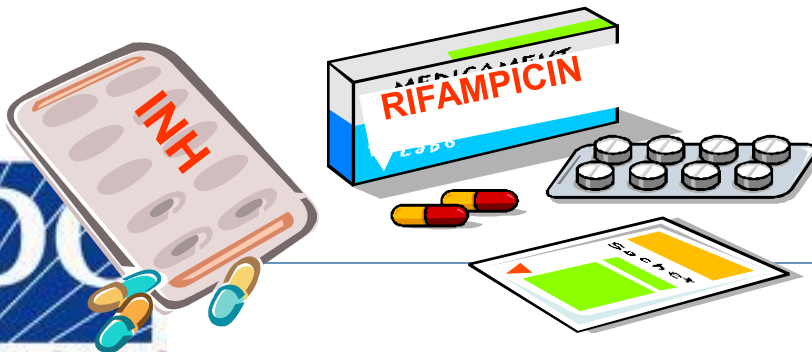
# Drug Resistant TB

- **MDR TB**

- **M**ulti-**D**rug **R**esistant TB
- “*in vitro*” resistance to both **isoniazid and rifampicin**, with or without resistance to other anti-TB drugs
- Estimated 8000 cases per annum in RSA

- **XDR TB**

- e**X**tremely **D**rug-**R**esistant TB
- MDR-TB **PLUS** “*in vitro*” resistance to any of the **fluoroquinolones** plus one or more of the **injectable second-line** anti-TB drugs, i.e. kanamycin, amikacin or capreomycin



# XDRTB in KZN

Articles

## The Lancet

Web: Lancet.com

Publication Early November

Extensively drug-resistant tuberculosis as a cause of death among patients co-infected with tuberculosis and HIV in a rural area in South Africa:



*Ned R Gandhi, Anthony McI, A Willem Sturm, Robert Pawinski, Thiloshini Govender, Umesh Lalloo, Kimberly Zeller, Jason Andrews, Gerald Friedland*



World Health  
Organization

# TUBERCULOSIS

## XDR-TB

## THE FACTS

### DEFINITION OF XDR-TB

- Extensively drug-resistant TB (XDR-TB) is a form of TB caused by germs resistant to all the most effective anti-TB drugs, and emerges through mismanagement of MDR-TB treatment. Once created, XDR-TB can spread from one person to another.
- XDR-TB is resistance to at least Isoniazid and Rifampicin (i.e. multidrug-resistant TB or MDR-TB), plus resistance to any fluoroquinolones, and any one of the second-line anti-TB injectable drugs (Amikacin, Kanamycin or Capreomycin).
- XDR-TB raises concerns of a future TB epidemic with restricted treatment options, and jeopardizes the major gains made in TB control and progress on reducing TB deaths among people living with HIV/AIDS.



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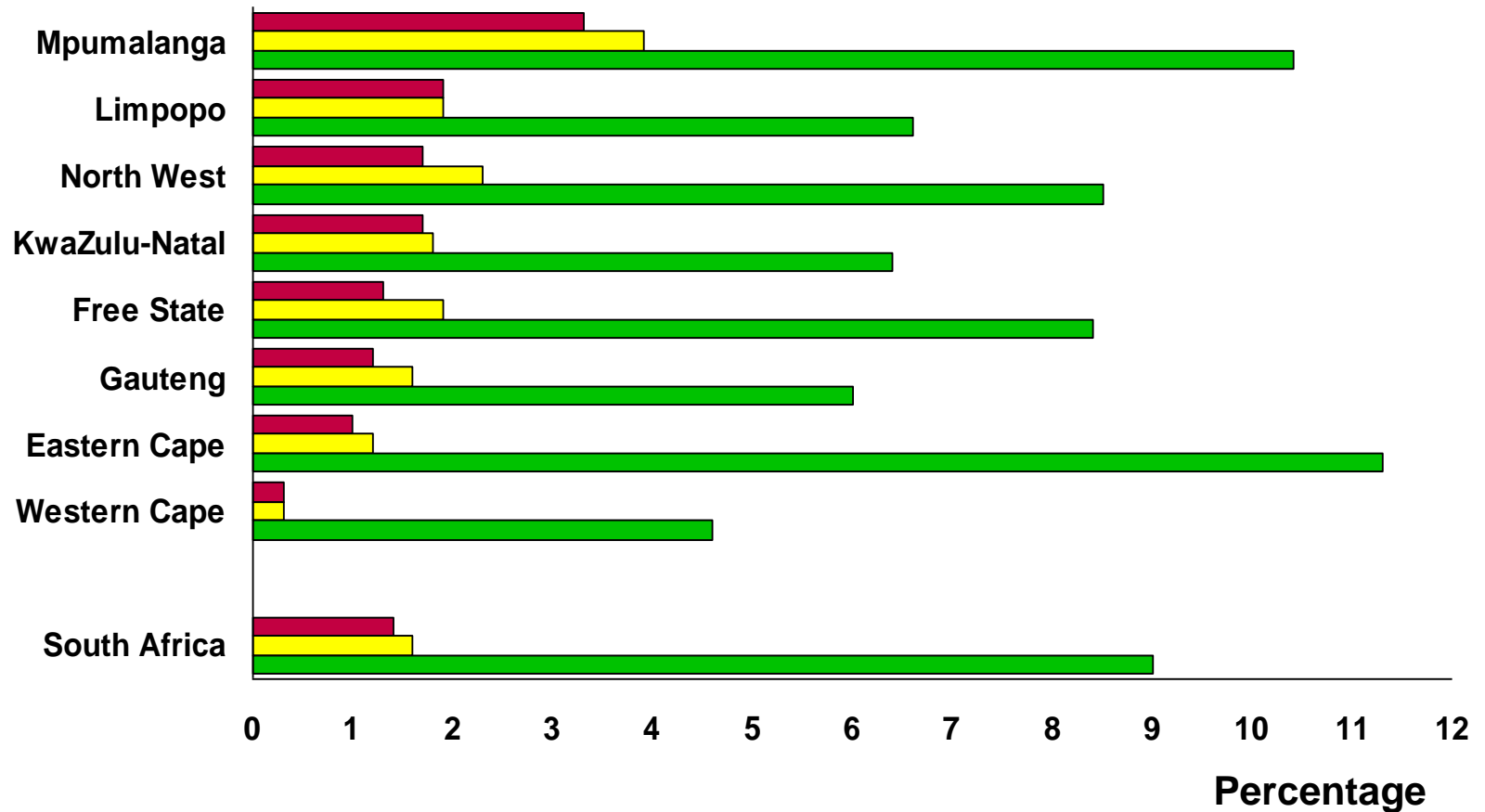
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# Drug-Resistant Tuberculosis Definitions

- Primary drug resistance
  - Patient is initially infected with a resistant strain of *M. tuberculosis*
- Acquired drug resistance
  - Patient develops drug resistance because of poor treatment or inadequate compliance
- National MRC susceptibility survey of TB drug resistance in 2001:
  - New: 1.6% (range 1.0% - 2.6%)
  - Retreatment: 6.6% (range 4.0% - 13.9%)

# Drug Resistance in New Patients

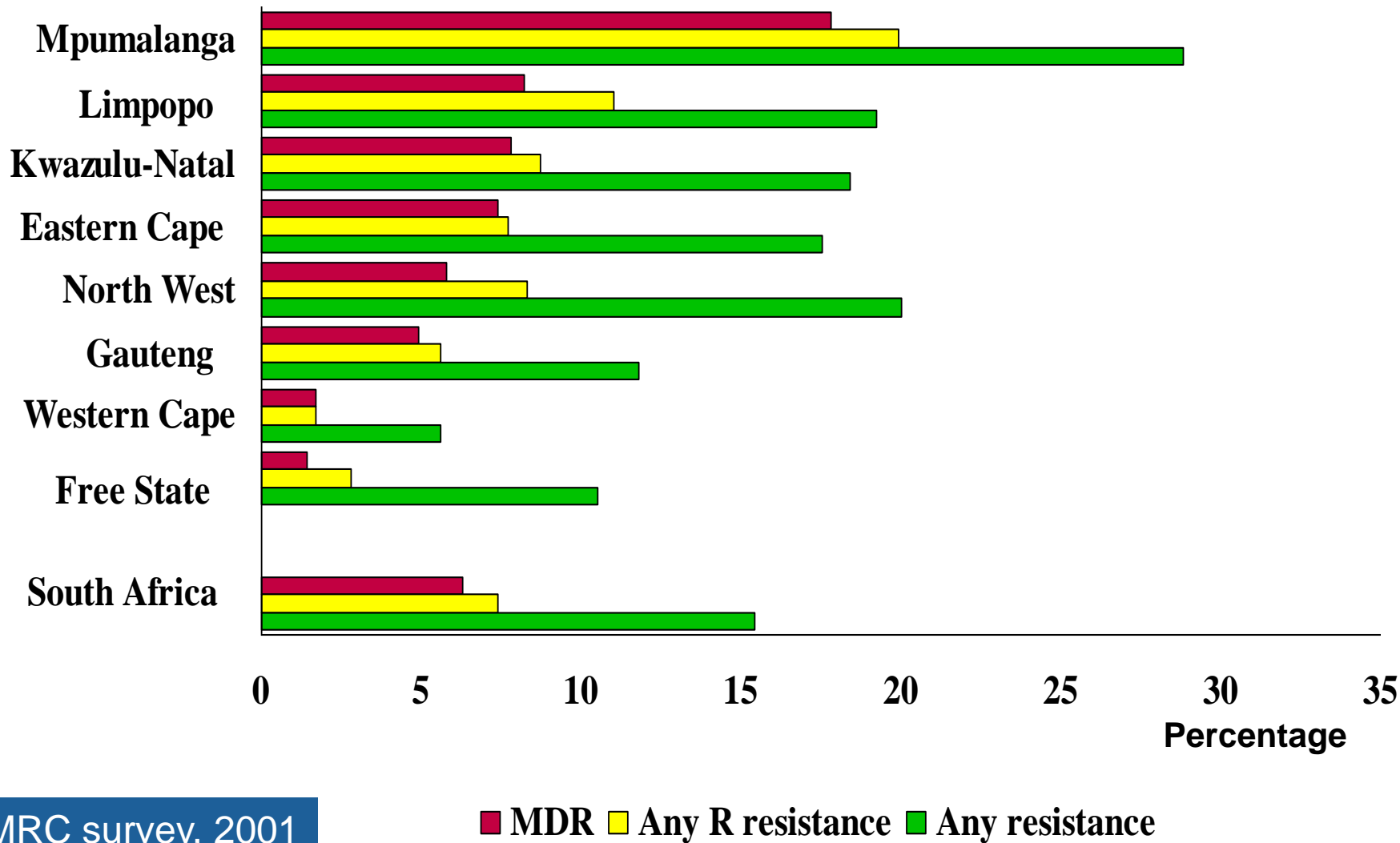


MRC survey, 2001

■ MDR ■ Any R resistance ■ Any resistance



# Drug Resistance in Re-treatment Patients



# XDR in RSA

- South Africa 2006
- MDR - 4422 of which 230 (5%) were XDR
- KwaZulu Natal
- MDR - 683 of which 113 (17%) were XDR
- Tugela Ferry
- MDR - 100 of which 87 (87%) were XDR!
  
- Tugela Ferry, KwaZulu Natal
  - 70% TB patients are HIV infected
- 53 of 544 TB patients defined as XDR-TB cases
  - 55% had never been treated for TB
  - 67% had recent hospital admission
  - 44 tested for HIV, all were HIV positive
  - 52/53 patients died on average within 15 days, including those on ART
  - **3 healthcare workers** affected
  - Genotyping of XDR isolates; 39 of 46 were similar strains



# Susceptibility pattern (Tugela Ferry XDR patients)

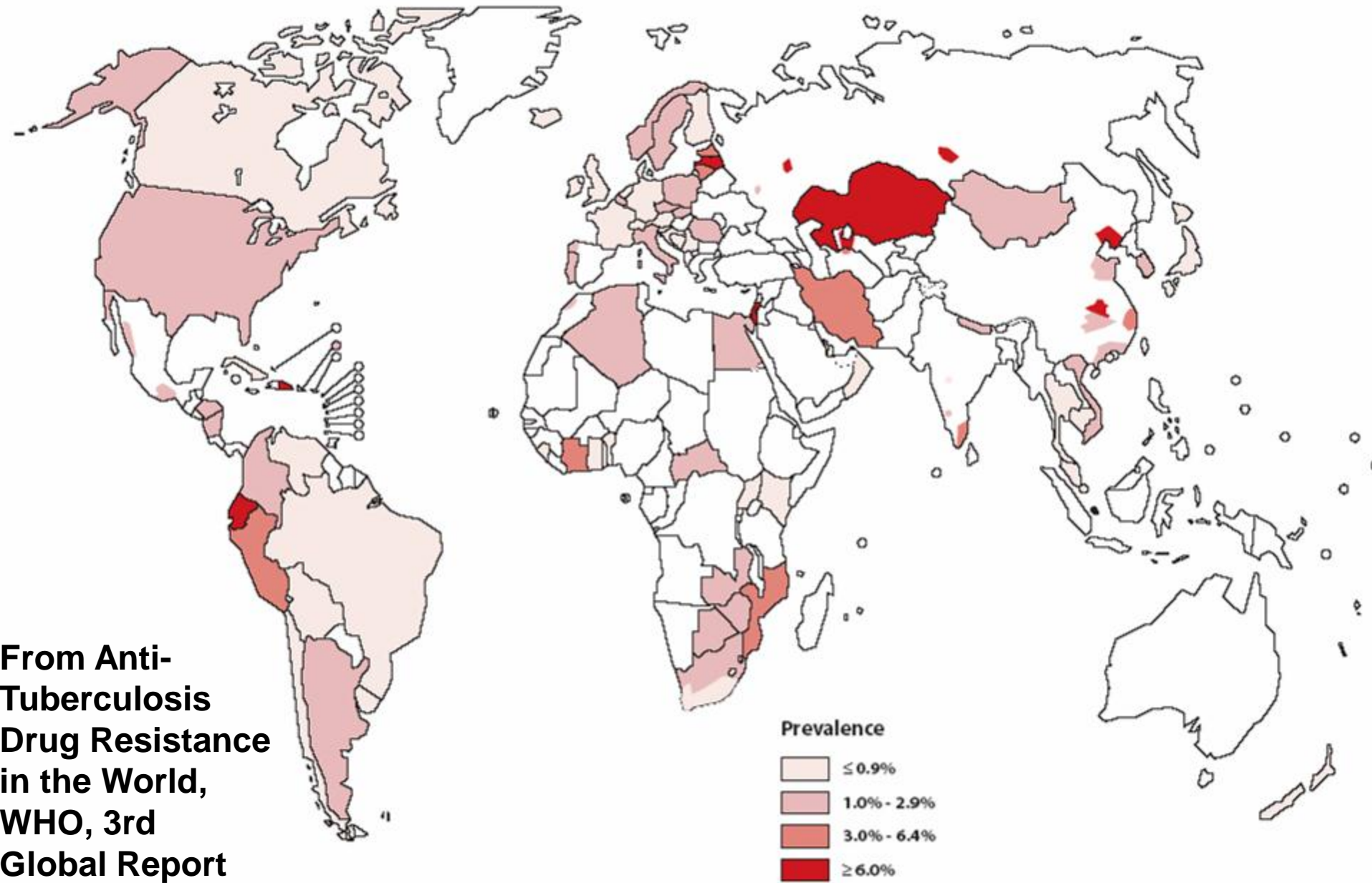
INH	<b>Resistant</b>
Rifampicin	<b>Resistant</b>
PZA	<b>Resistant</b>
Ethambutol	<b>Resistant</b>
Streptomycin	<b>Resistant</b>
Kanamycin/Amikacin	<b>Resistant</b>
Ciprofloxacin/Ofloxacin/Gatifloxacin/ Moxifloxacin	<b>Resistant</b>
Ethionamide	<b>Sensitive</b>
Cycloserine	<b>Sensitive</b>
Capreomycin	?
PAS (Para-aminosalicylic Acid)	?

# Determinants of MDR-TB in SA

(SAMRC National Survey 2002 - 2003; Multivariate Analysis)

- Previous TB treatment  
OR 5.1 (95% CI 2.8 - 6.9)       $p < 0.0001$
- Previous TB treatment in hospital  
OR 2.8 (95% CI 1.6 - 5.1)       $p = 0.001$
- Previous TB treatment failed/defaulted  
OR 2.2 (95% CI 1.3 - 1.9)       $p = 0.007$
- HIV co-infection (all)  
OR 1.3 (95% CI 1.0 - 1.7)       $p = 0.050$
- HIV co-infection (retreatment cases)  
OR 1.5 (95% CI 1.1 - 2.1)       $p = 0.032$

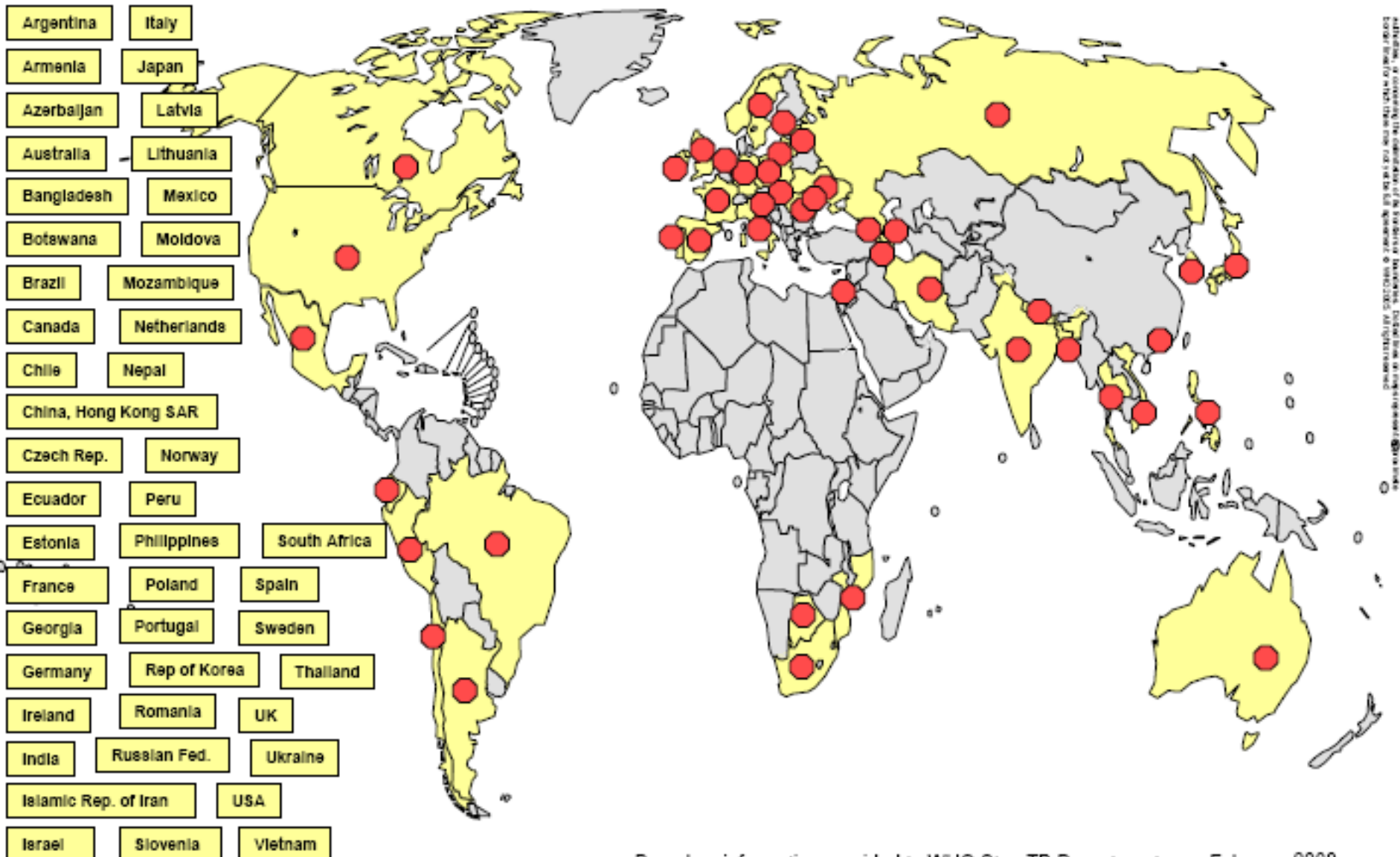
## Prevalence of MDR-TB among new TB cases, 1994-2002



From Anti-Tuberculosis Drug Resistance in the World, WHO, 3rd Global Report

The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area of its authorities, or concerning the delimitation of its frontiers or boundaries. Dashed lines represent approximate boundaries for which there may not be full agreement.

# Countries with XDR-TB confirmed cases as of February 2008



Based on information provided to WHO Stop TB Department - February 2008

The information on this page is for informational purposes only. It is not intended to be used for clinical or public health decision-making. The information is provided as a service to the public and is not intended to be used for clinical or public health decision-making.

# Current XDR Situation in SA

## October 2007

- 1068 cases identified
- 66% mortality (as per June 2007)
- KZN: 659 cases, 89% mortality
- EC: 132 cases, 35% mortality (incomplete data)
  - 2nd highest number of cases
  - Numbers increasing
  - Isolation units:
    - Jose Pearson (PE) – 35 beds
    - Fort Grey (EL) – 26 beds
    - Mthatha: 4 additional beds



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# Evidence for Nosocomial Transmission of XDR-TB, Tugela Ferry, KZN

- 55% had no prior TB treatment
- 30% with prior TB completion/cure
- Genotyping revealed similar strains
- 28/42 (67%) of patients hospitalized in prior 2 years
- Community contact tracing of XDR patients revealed no additional cases
- 2 health care workers died with confirmed XDR TB
- 4 other health care workers died with suspected XDR TB

# Infection Control Strengthening In Tugela Ferry

- **Administrative**
  - Staff information and training
  - TB screening & triage
  - Cough hygiene
  - Cultures and drug susceptibility testing
  - TB & HIV programs- communication/integration
- **Environmental**
  - Controlled natural ventilation
  - Aerosolization procedures outside
- **Personal**
  - N95 Respirator
  - HIV VCT for staff
- **Political**
  - Government strengthening of TB program-resources, prevalence survey
- **Effective???**

**“Outbreak” of MDR-TB among HIV-infected patients in rural KwaZulu Natal South Africa**

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Gerald Friedland, Tony Moll, Neel Gandhi, Theo van de Mere,  
Robert Pawinski, Umesh Laloo, Jason Andrews, AW Sturm

Yale University, Church of Scotland Hospital, Philanjalo, Tugela Ferry, South Africa, Nelson R Mandela School of Medicine, Department of Health, KwaZulu Natal, South Africa



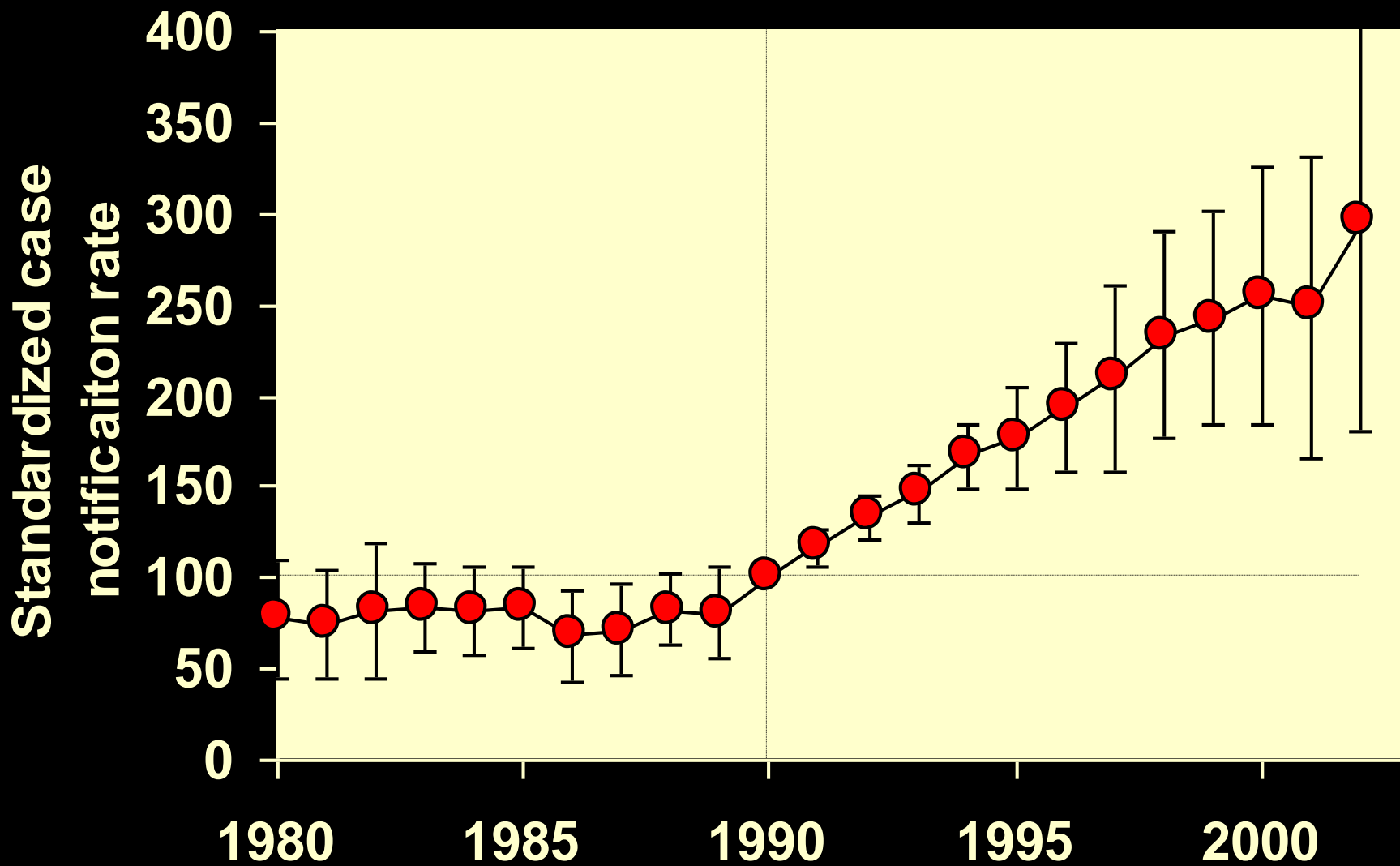
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# Africa's Dual Burden

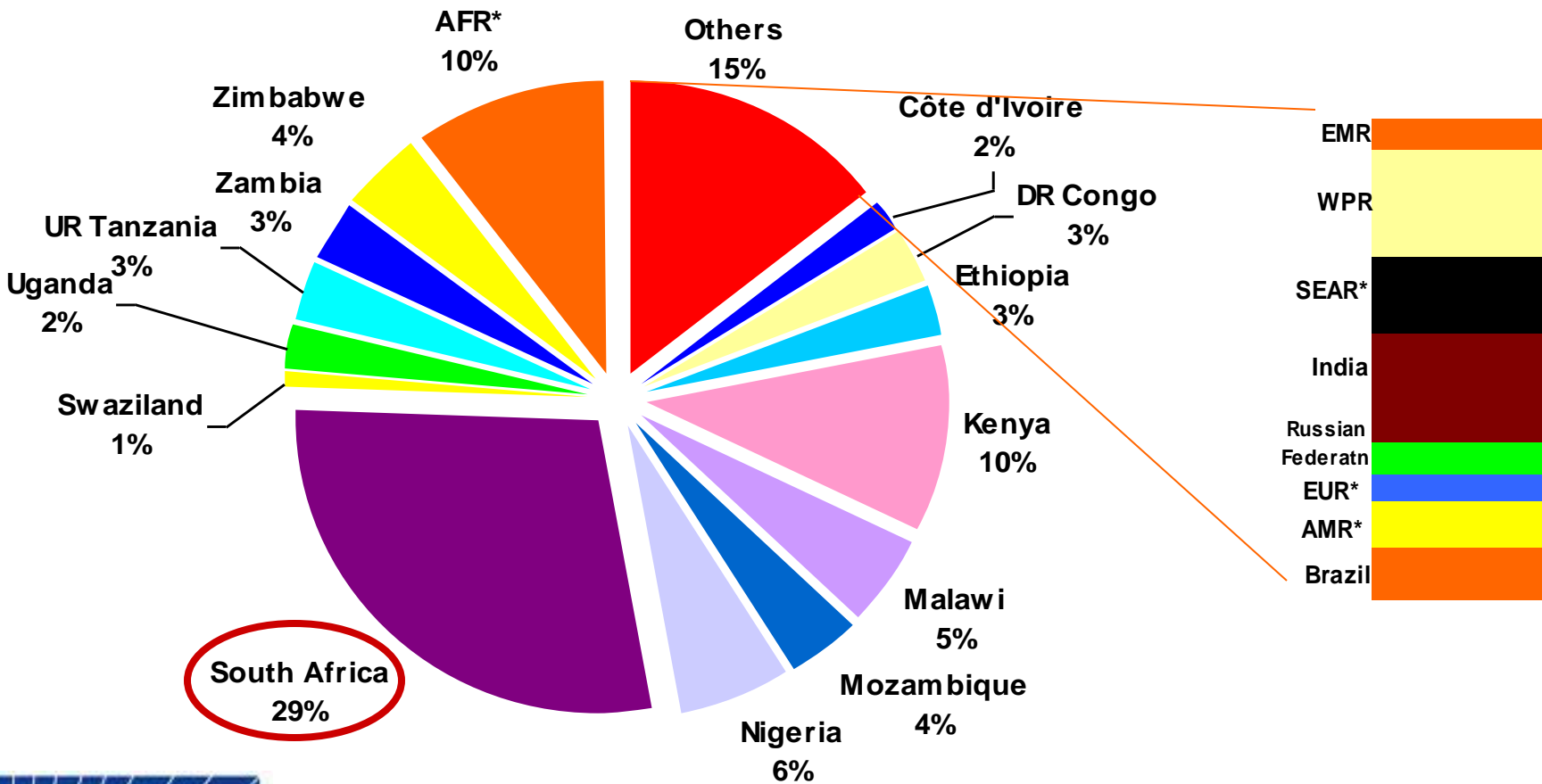


Every person represents 5% of the global total, with African people shown in **red** and the rest of the world in **blue**.

# The rise and rise of TB in Africa, linked to HIV



# Geographical distribution of HIV-positive TB cases, 2006



For each country or region, the number of incident TB cases arising in people with HIV is shown as a percentage of the global total of such cases. AFR\* is all countries in the WHO African Region except those shown separately; AMR\* excludes Brazil; EUR\* excludes the Russian Federation; SEAR\* excludes India.



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# Geographical distribution of HIV+ TB cases, 2007

**FIGURE 1.5**

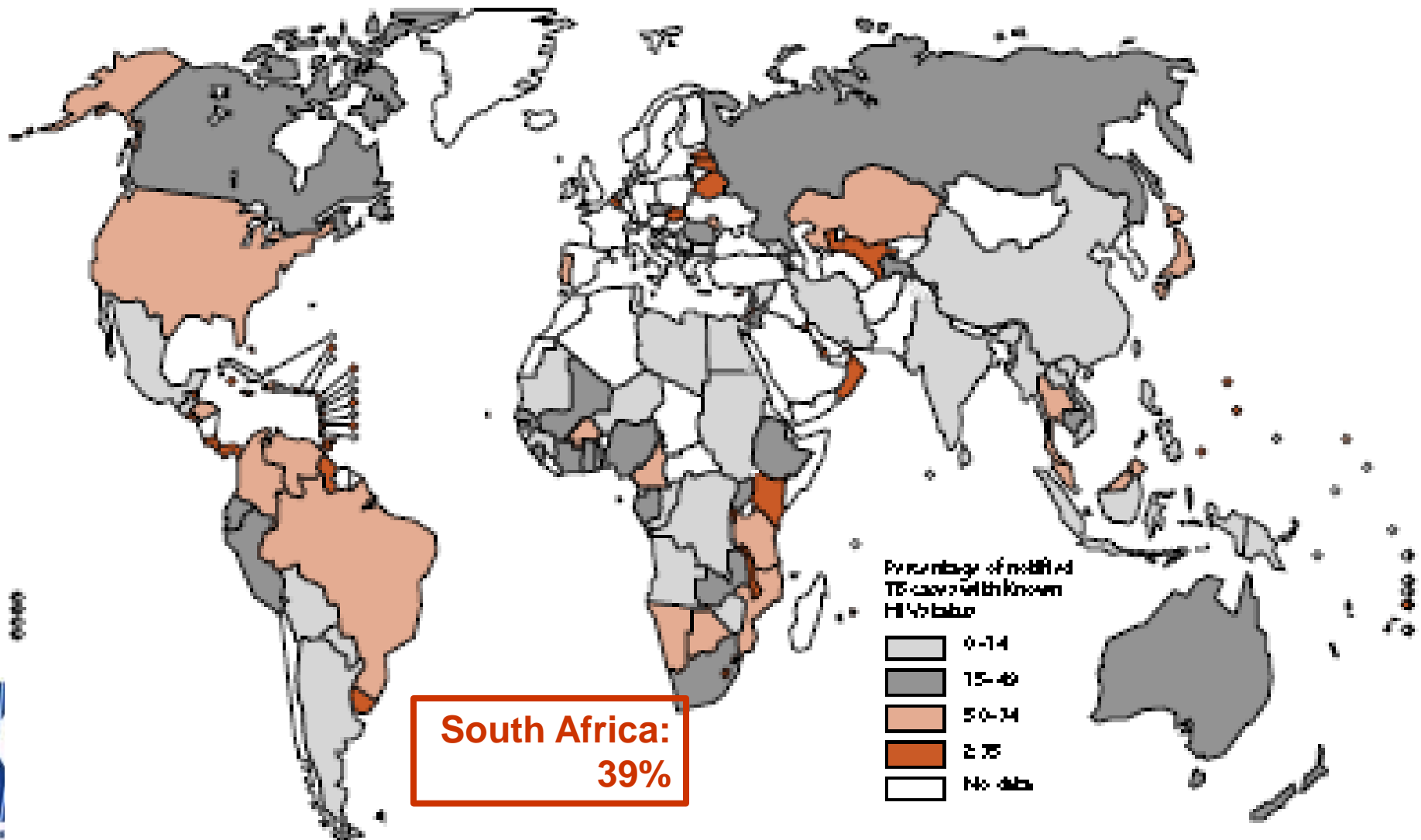
Geographical distribution of estimated number of HIV-positive TB cases, 2007. For each country (red circles) and WHO region (grey circles), the number of incident TB cases arising in people with HIV is shown as a percentage of the global total of such cases.



# HIV testing for TB patients 2006

■ FIGURE 26

HIV testing for TB patients, 2007



# Estimated HIV prevalence in new TB cases, 2007

■ **FIGURE 1.3**

Estimated HIV prevalence in new TB cases, 2007

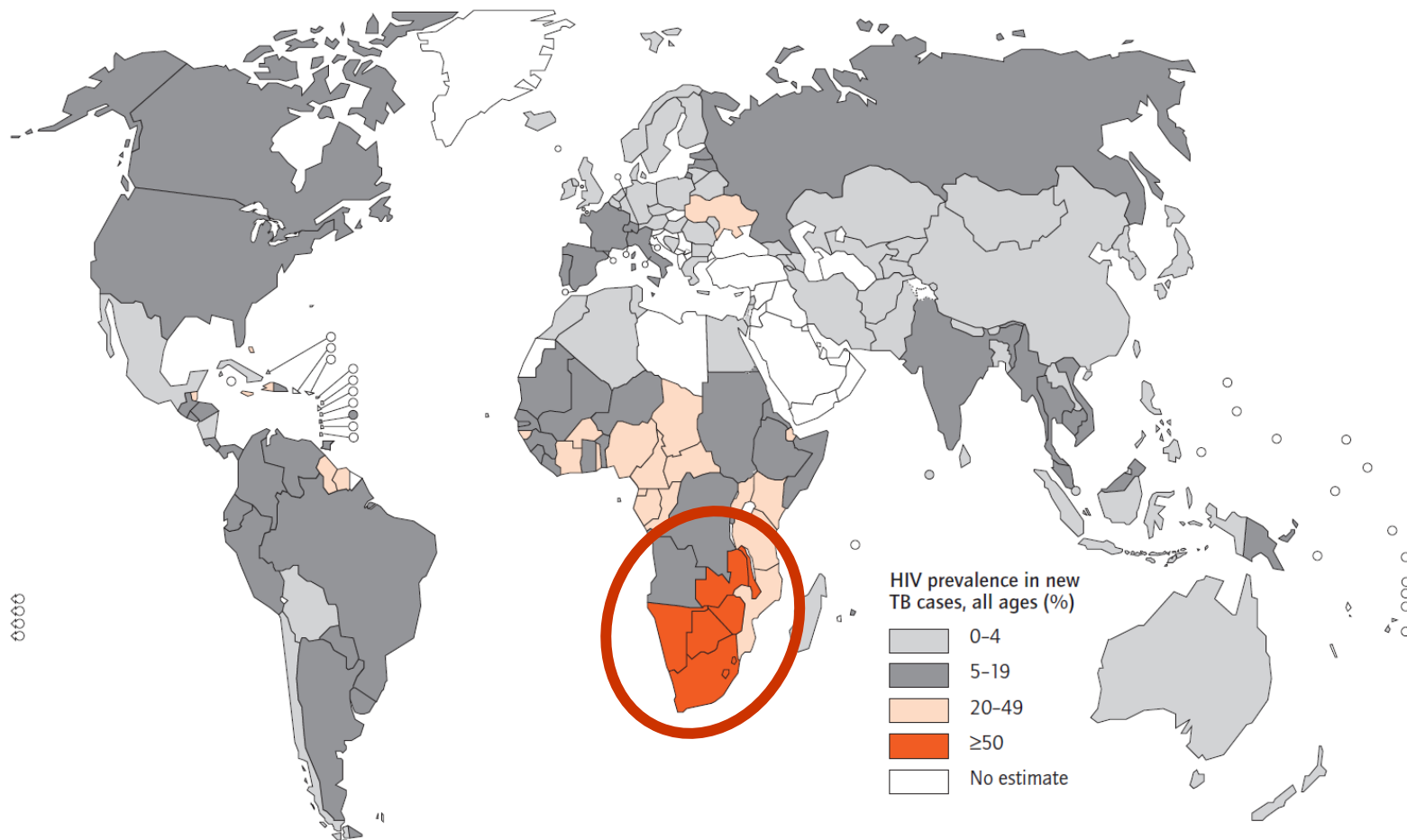
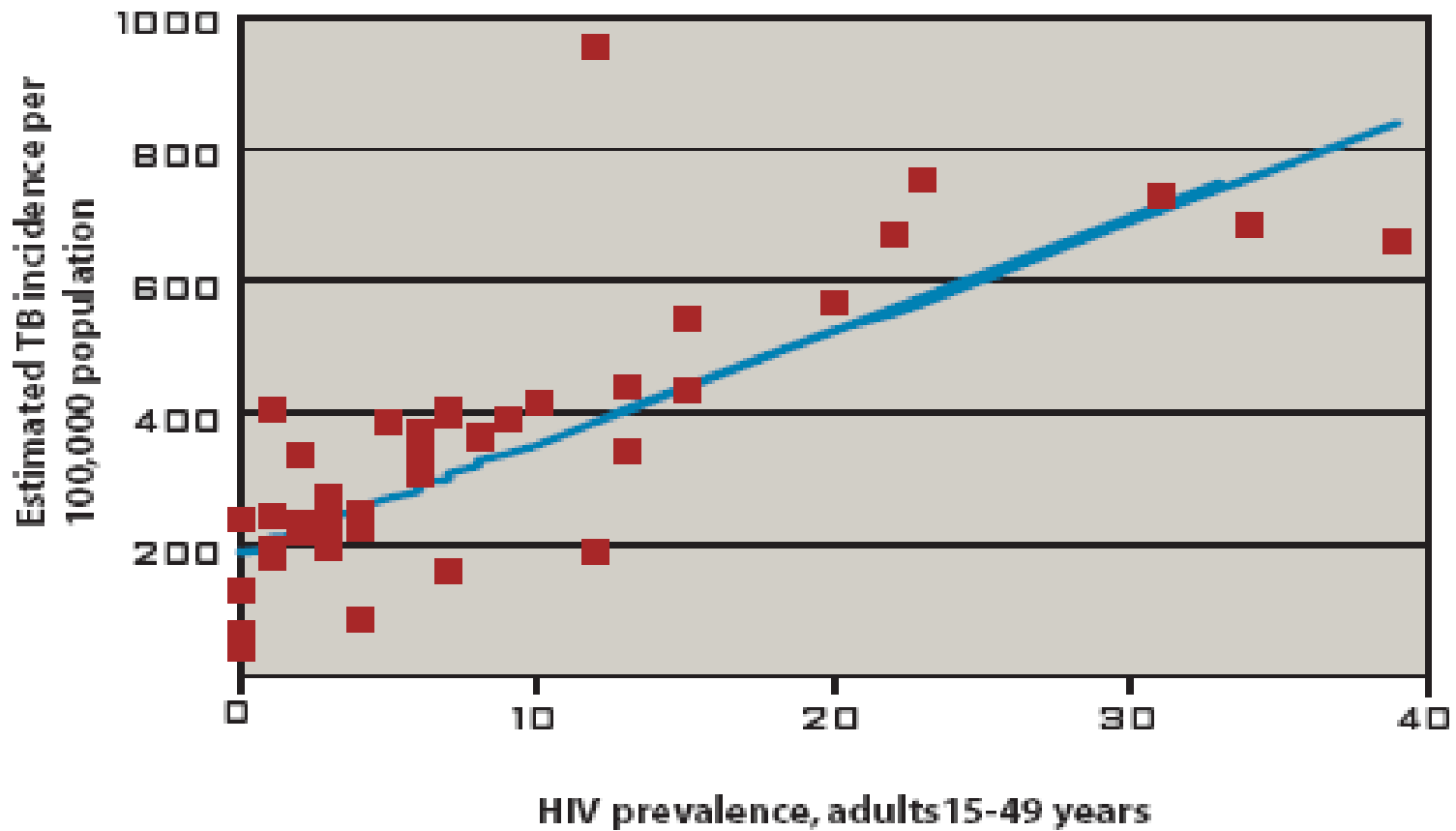


Figure 6

### TB INCIDENCE CLOSELY CORRELATED WITH HIV PREVALENCE IN AFRICA<sup>13</sup>



# Effect of HIV co-infection on TB epidemiology

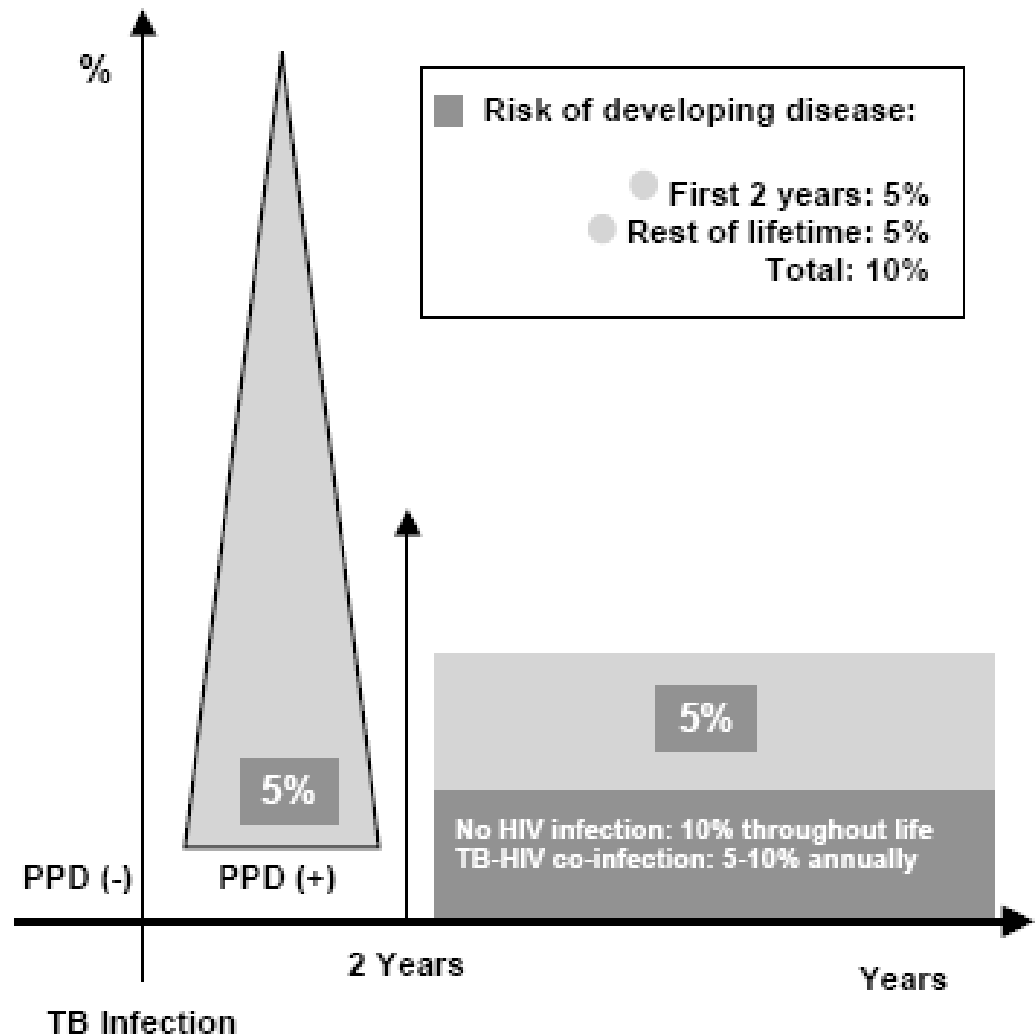
- Clustering of TB cases in HIV pts suggests recent exposure and early progression
  - In areas of high prevalence, this suggests re-infection (vs reactivation) is more important in HIV patients
- TB impacts on progression of HIV
  - Patients with TB have higher mortality and reduced survival compared to what is expected due to TB alone, due to complications of HIV/AIDS
  - TB: inflammatory condition, high levels of inflammatory cytokines (IL-1 and TNF $\alpha$ ) enhance viral replication

# Effect of HIV co-infection on TB epidemiology

- HIV impacts on progression of TB disease
  - HIV may make patient more susceptible to TB infection
  - HIV pts have reduced numbers of alveolar macrophages
  - HIV shifts the balance of immune system to TH2 response
    - Inadequate/inappropriate release of cytokines responsible for initiating sterilisation
    - Insufficient CD4 cells to effect killing
- HIV pts likely to acquire TB **nosocomially**

# Effect of HIV Co-Infection on TB Epidemiology

- HIV patients infected with TB have 5-10% annual risk of developing disease (reactivation)



# The Burden of TB and HIV in South Africa

- 5.6 million South Africans HIV-infected, 1.8 million of whom will get TB
- 1,700 new HIV infections per day
- 341,165 TB cases (720/100,000) in 2006 – more than 300% increase since 1989
- 55% of TB patients HIV+ (MRC)
- TB is the most common opportunistic infection and the biggest killer of people living with HIV/AIDS



# HIV ANC prevalence survey 2007

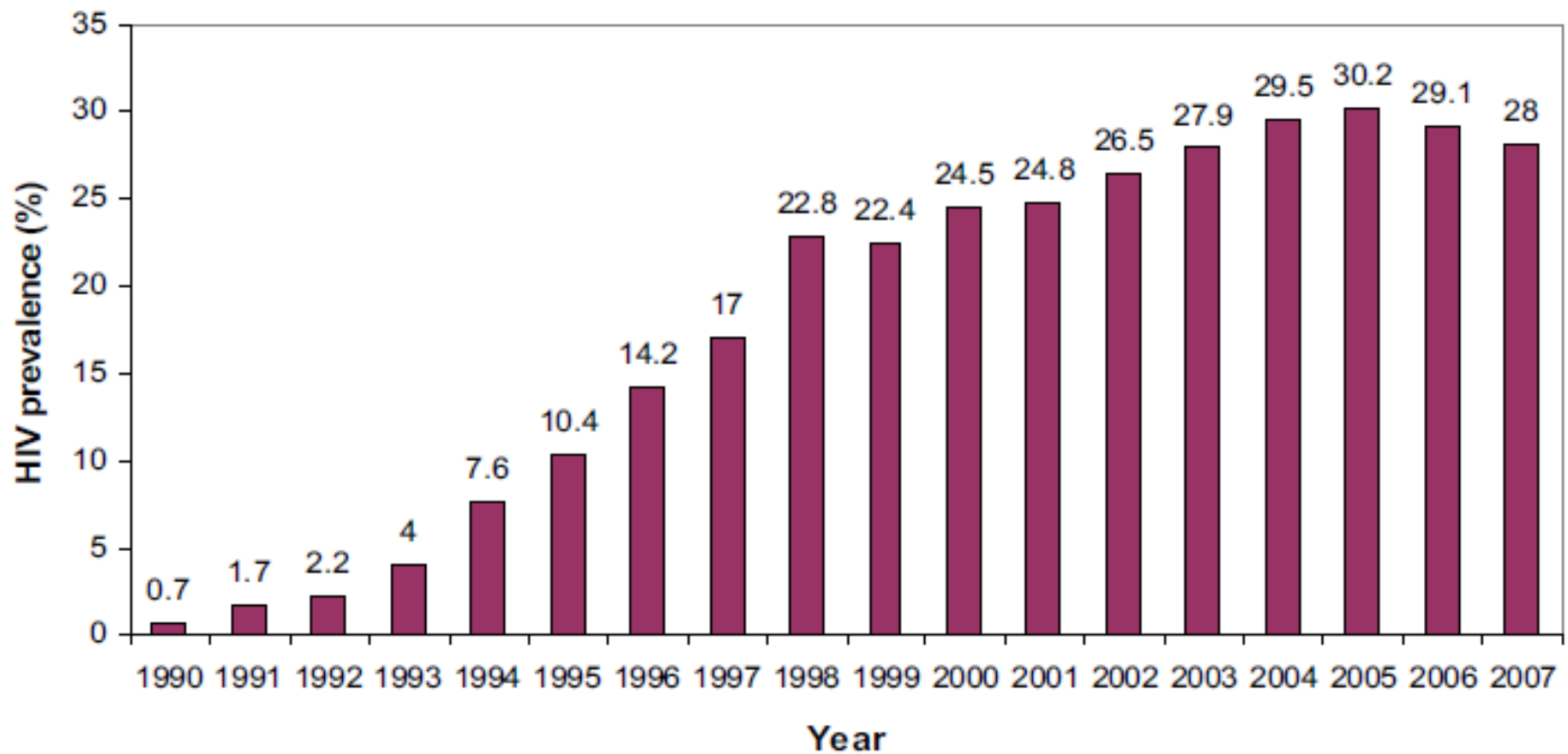


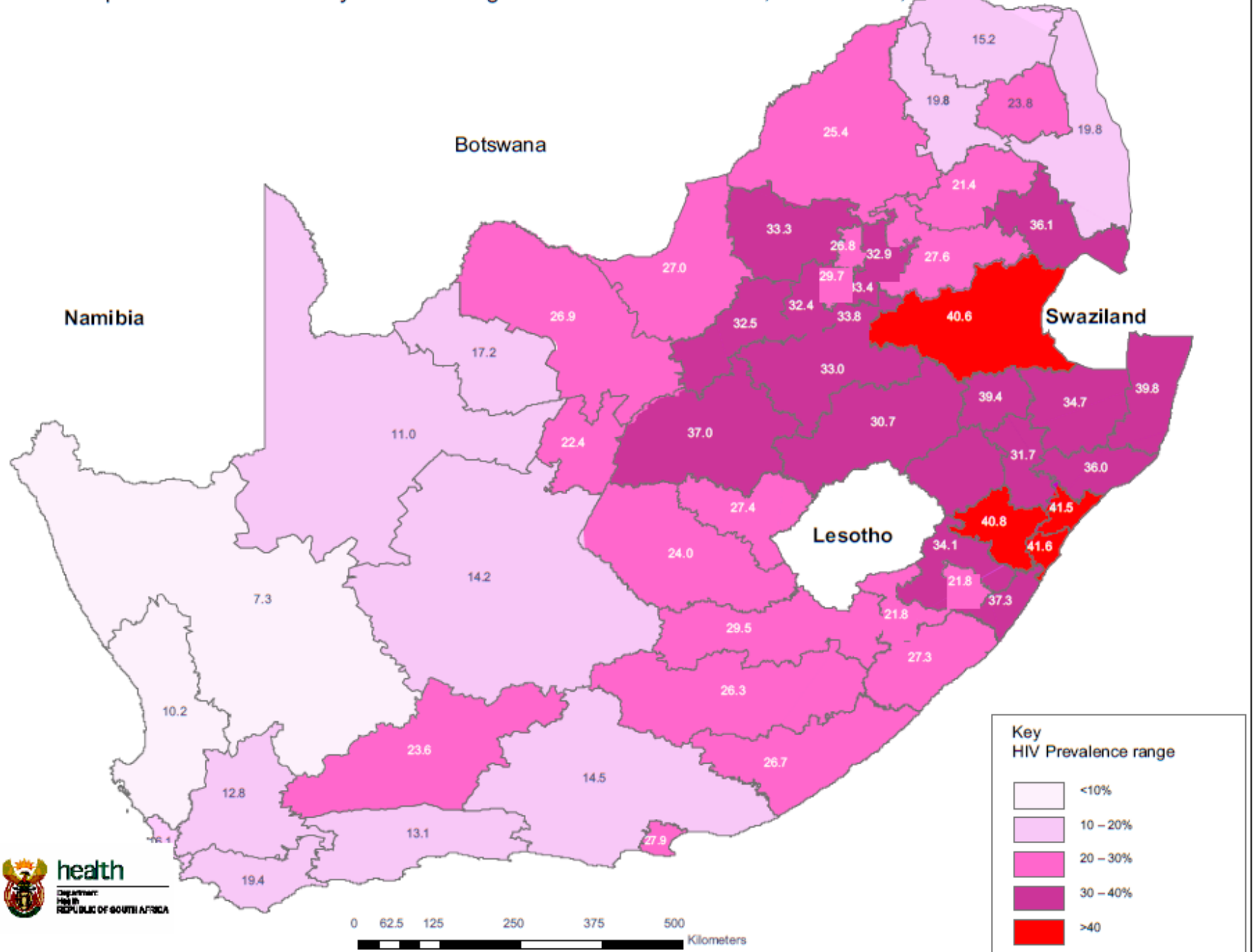
Figure 1: National HIV prevalence trends among antenatal clinic attendees, South Africa, 1990 to 2007.

# HIV ANC prevalence survey 2007

Province	HIV pos. 95% CI 2005	HIV pos. 95% CI 2006	HIV pos. 95% CI 2007
KwaZulu-Natal	39.1 (36.8 - 41.4)	39.1 (37.5 - 40.7)	37.4 (35.0 - 39.8)
Mpumalanga	34.8 (31.0 - 38.5)	32.1 (29.8 - 34.4)	32.0 (29.2 - 34.9)
Free State	30.3 (26.9 - 33.6)	31.1 (29.2 - 33.1)	33.5 (28.3 - 39.1)
Gauteng	32.4 (30.6 - 34.3)	30.8 (29.6 - 32.1)	30.3 (29.9 - 32.8)
North West	31.8 (28.4 - 35.2)	29.0 (26.9 - 31.1)	29.0 (24.8 - 33.5)
Eastern Cape	29.5 (26.4 - 32.5)	28.6 (26.8 - 30.4)	26.0 (24.0 - 28.1)
Limpopo	21.5 (18.5 - 24.6)	20.6 (18.9 - 22.3)	18.5 (16.7 - 20.4)
Northern Cape	18.5 (14.6 - 22.4)	15.6 (12.7 - 18.5)	16.1 (13.9 - 18.7)
Western Cape	15.7 (11.3 - 20.1)	15.1 (11.6 - 18.7)	12.6 (10.1 - 15.6)
<b>National</b>	<b>30.2 (29.1 - 31.2)</b>	<b>29.1 (28.3 - 29.9)</b>	<b>28.0 (26.9 - 29.1)</b>

*N.B. The 95% CI was used because statistically the true estimated value falls within the two confidence limits and therefore assures us that there is 95% certainty that the estimated value is not by chance.*

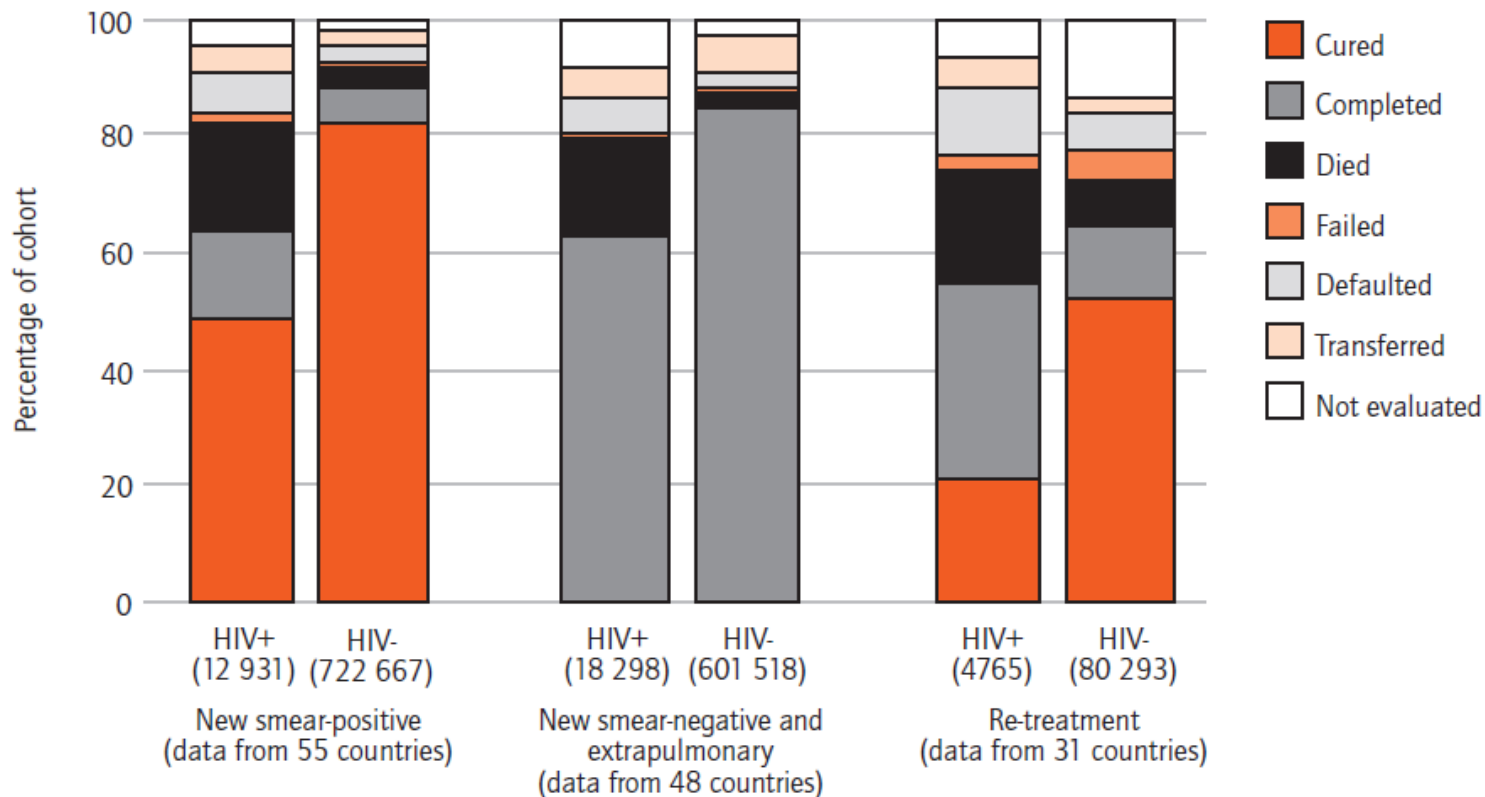
Figure 2: HIV prevalence estimates by district among antenatal clinic attendees, South Africa, 2007



# Treatment outcomes: HIV +ve versus HIV -ve

■ **FIGURE 1.26**

Treatment outcomes for HIV-positive and HIV-negative TB patients, 2006 cohort. The numbers under the bars are the numbers of patients included in the cohort.



**TB**

**DOTS  
+HIV C&T  
+condoms  
+HIV  
surveillance**

**TB/HIV**

**INH  
prophylaxis**

**Intensified  
TB case  
finding**

**TB  
Infection  
Control**

**HIV**

**C&T  
TB symptom  
screening  
IEC  
STI's  
ARV's**

**Co-trimoxazole Preventive Therapy**

**Home/community based care**

**General Health Services**