

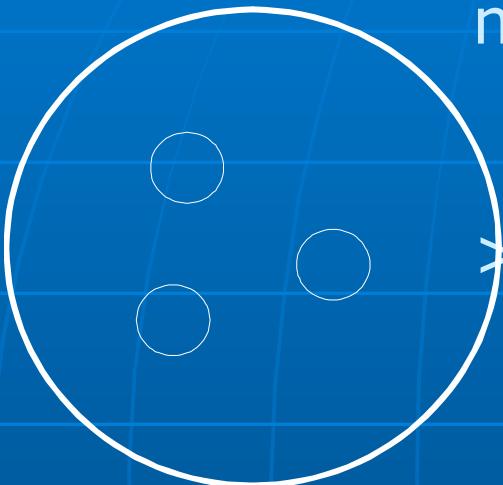
MDR Tuberkulose

Christian Wejse

Dep. Infectious Diseases,
Skejby

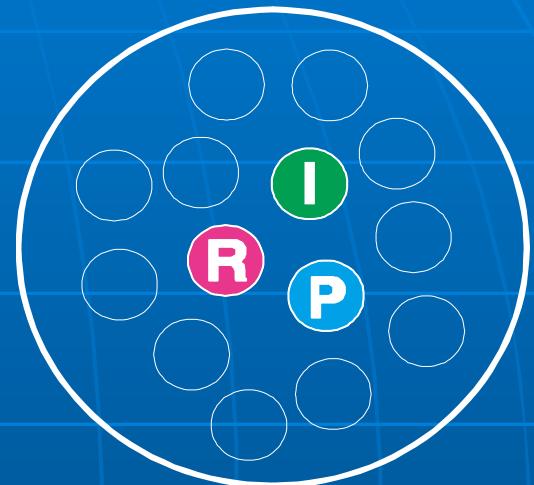
Drug resistant TB - definitions

- Drug resistant tuberculosis
 - TB resistant to any first line antituberculosis drug
- Multidrug resistant tuberculosis (MDR-TB)
 - TB resistant to at least isoniazid and rifampicin
- Extensively drug resistant tuberculosis (XDR-TB)
 - MDR TB + resistance to a fluoroquinolone and a second line injectable agent (aminoglycoside)



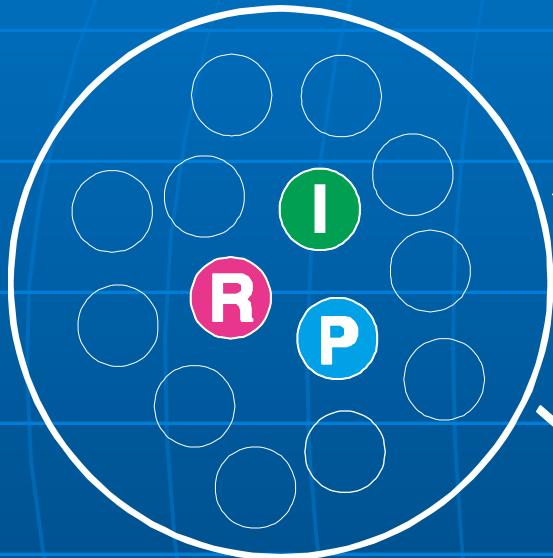
Spontaneous mutations
develop as bacilli
proliferate to

$\rightarrow 10^8$



Drug	Mutation Rate
Rifampin	10^{-8}
Isoniazid	10^{-6}
Pyrazinamide	10^{-6}

Drug-resistant mutants in large bacterial population



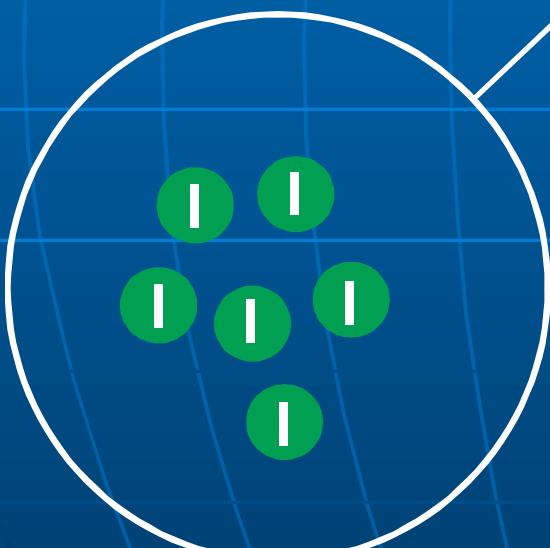
Multidrug therapy:
No bacteria resistant to all 3
drugs
INH
RIF
PZA

Monotherapy: INH-resistant
bacteria proliferate

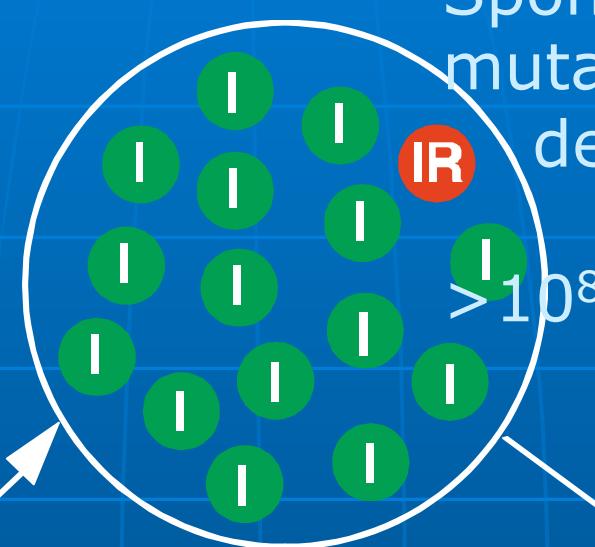
INH



INH resistant
bacteria multiply
to large numbers

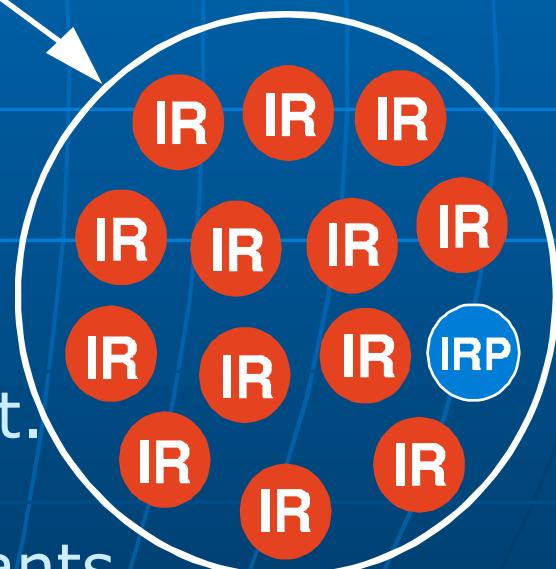


INH



Spontaneous
mutations
develop as bacilli
proliferate to

INH
RIF



INH mono-resist.
mutants killed,
RIF-resist. mutants
proliferate → MDR TB

Epidemiology of anti-tuberculosis drug resistance

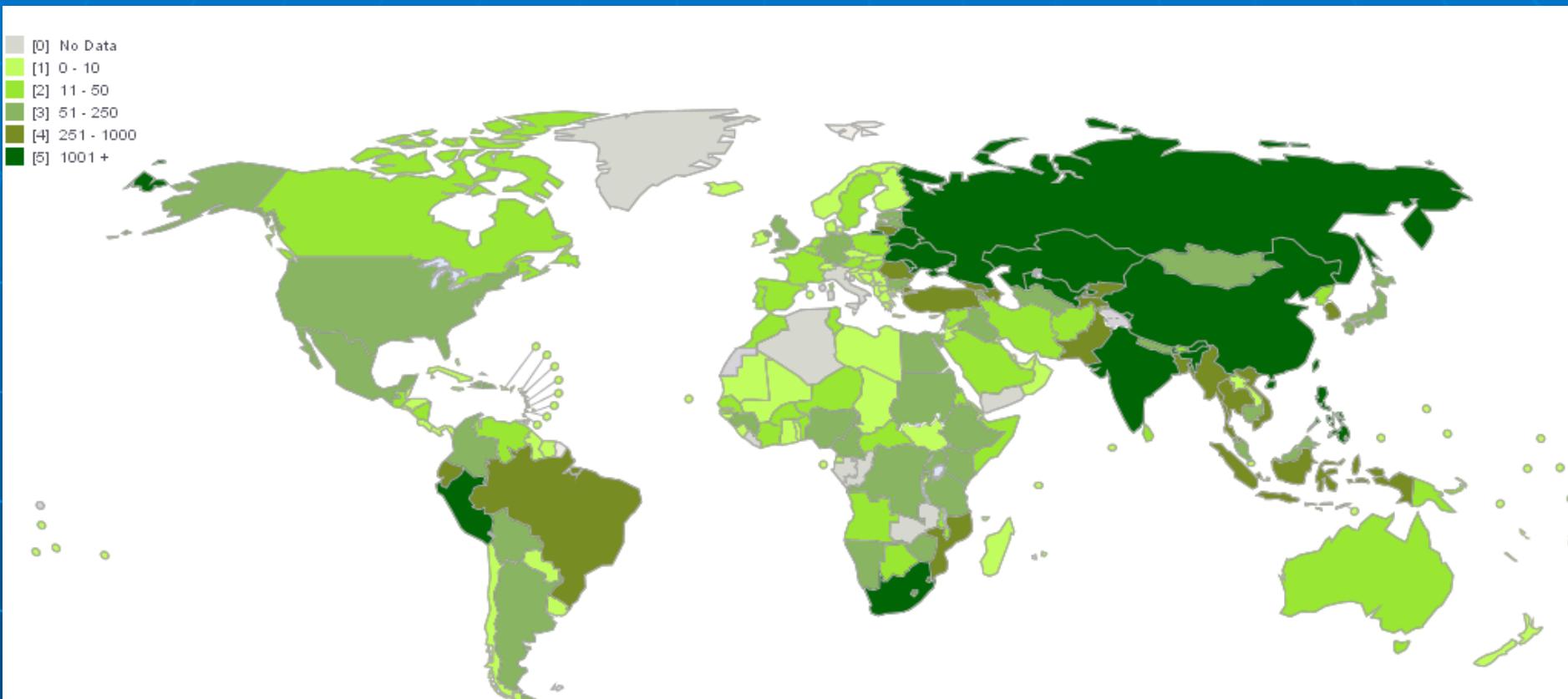
	TB/100 000 inh	MDR (n)	INH R (%)	New cases (n)
Iceland	3,1	0	0	10
Sweden	6,2	13	9,9	515
Norway	5,9	8	10,4	258
Finland	8,8	6	3,5	519
Denmark	6,8	2	4,9	288
Estonia	30	86	20,6	331
Azerbaijan	110	1320	40,8	5872

WHO, 2009

Wright A et al. Lancet 2009: 373:1861

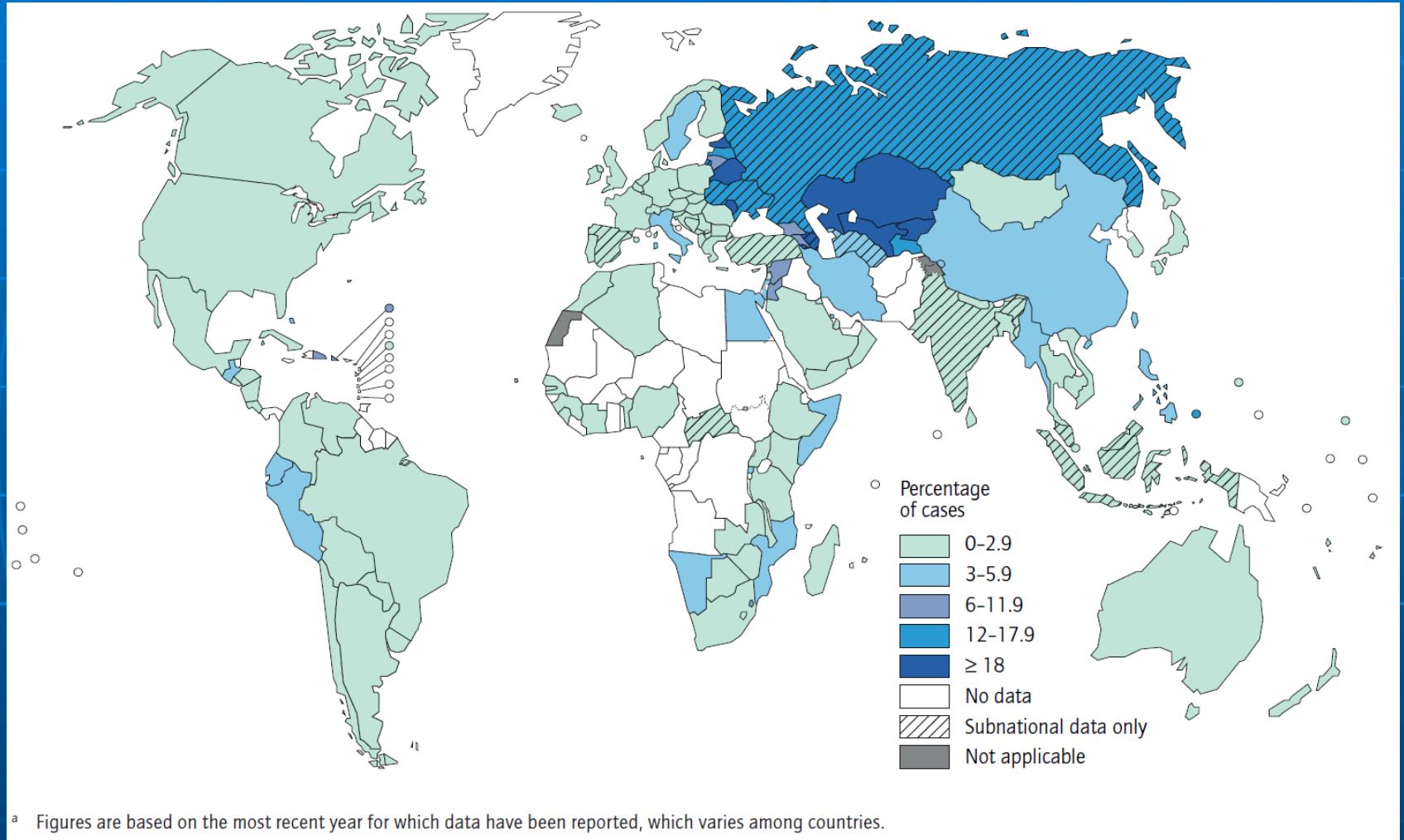
Diagnosis and notification of multidrug-resistant TB

Notified MDR-TB cases (absolute numbers), 2011

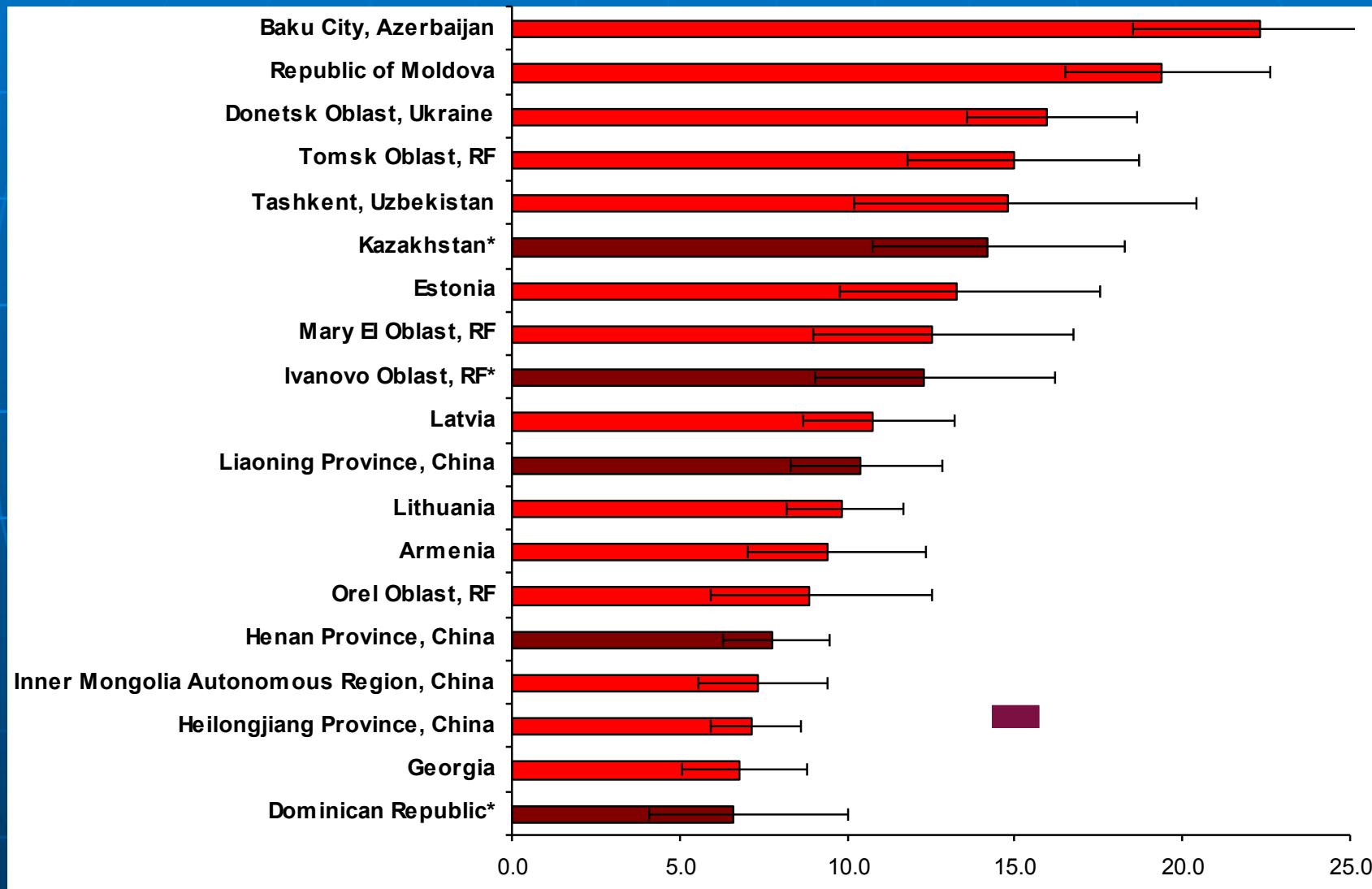


Proportion of MDR among new TB cases

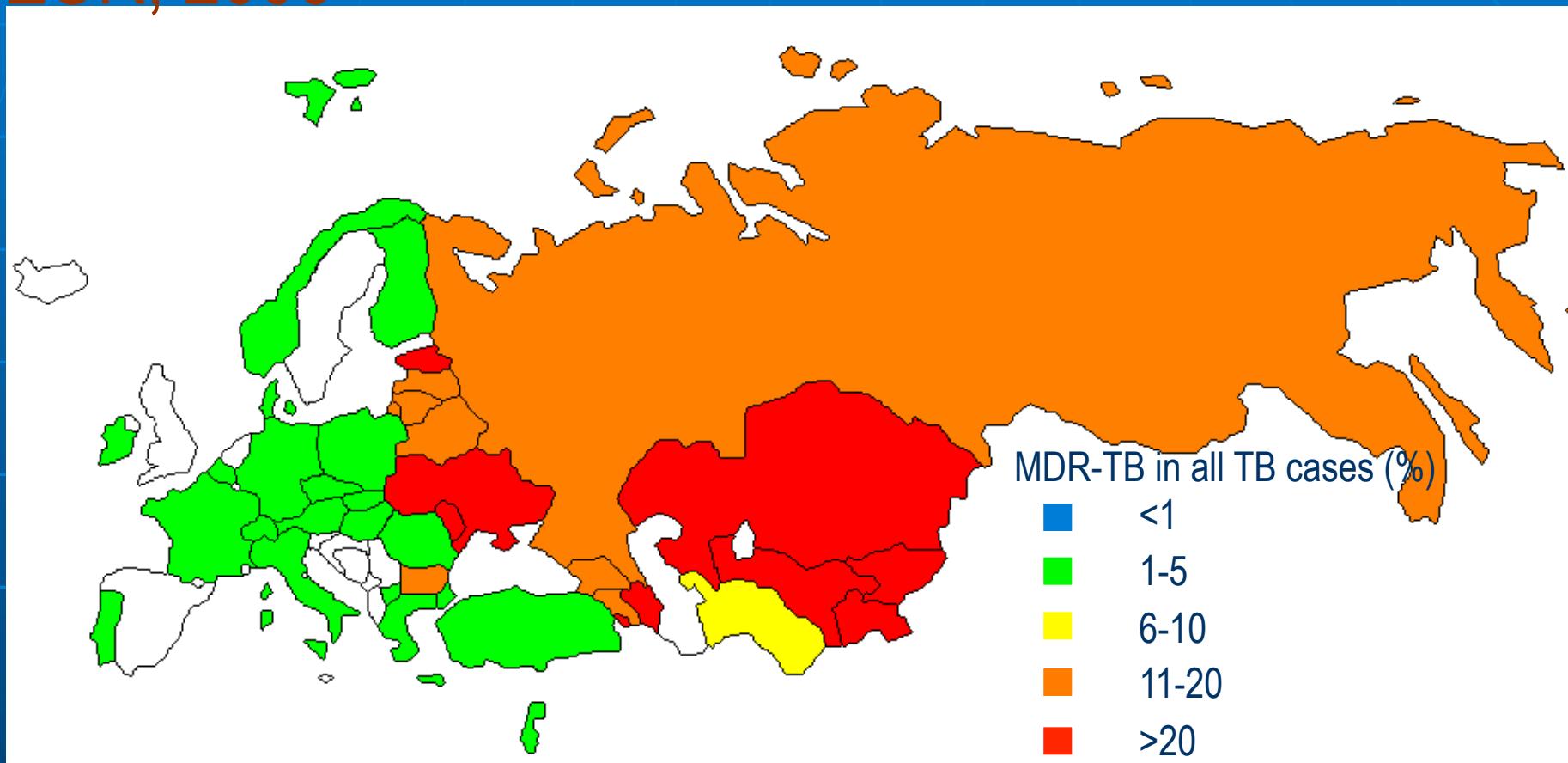
Latest available data, 1994-2011



Top 19 settings with MDR among new cases > 6% (1994-2007), 14 – in EUR



Estimated proportion of MDR-TB in all TB cases: EUR, 2006

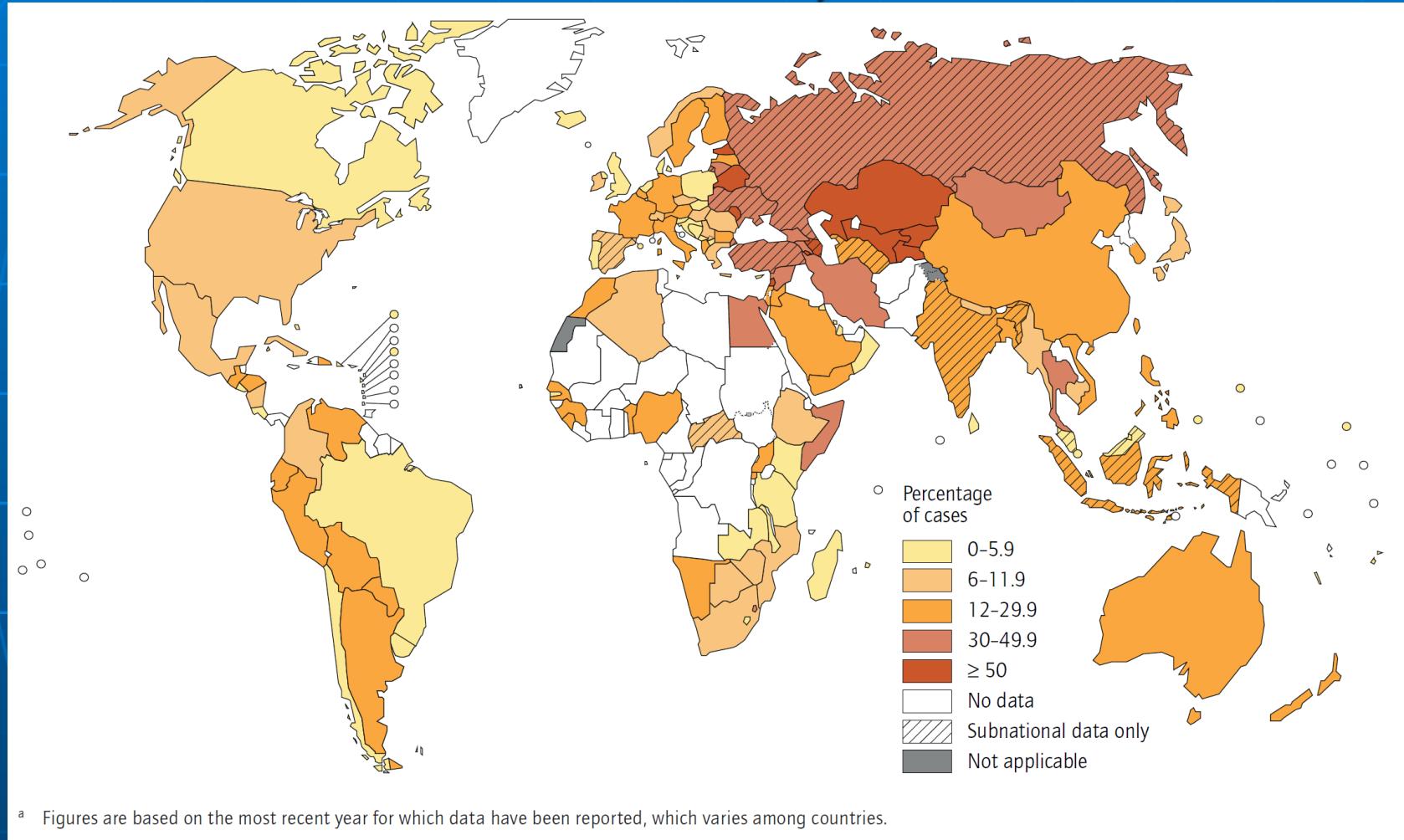


>44,000 new MDR-TB cases in Europe in 2006

*Anti-tuberculosis drug resistance in the world: fourth global report. Pre-publication version.
Geneva: WHO, 2008.*

Proportion of MDR among previously treated TB cases

Latest available data, 1994-2011



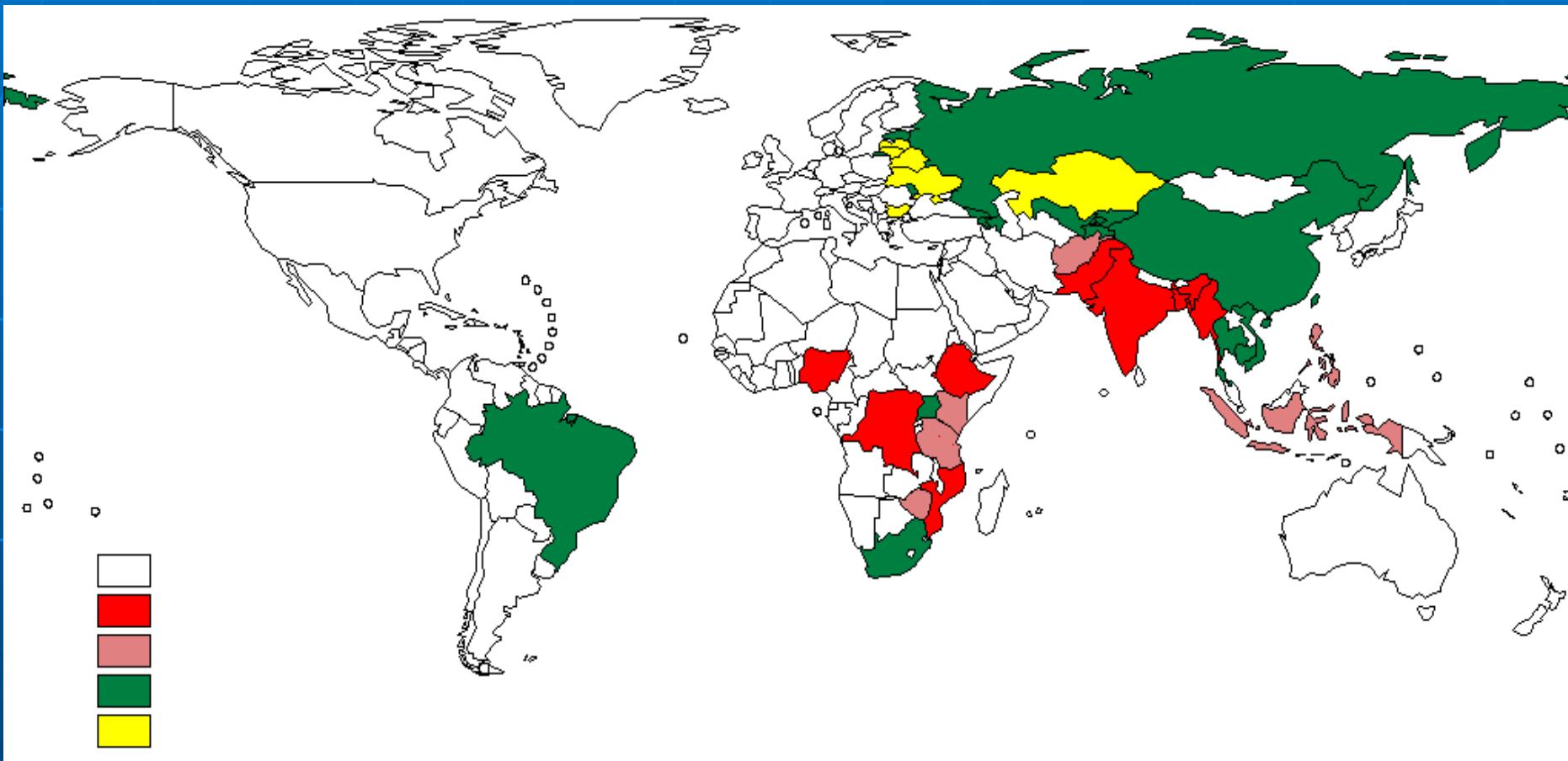
^a Figures are based on the most recent year for which data have been reported, which varies among countries.

The boundaries and names shown and the designations used 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 or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

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Culture laboratories for TB per 5 million population

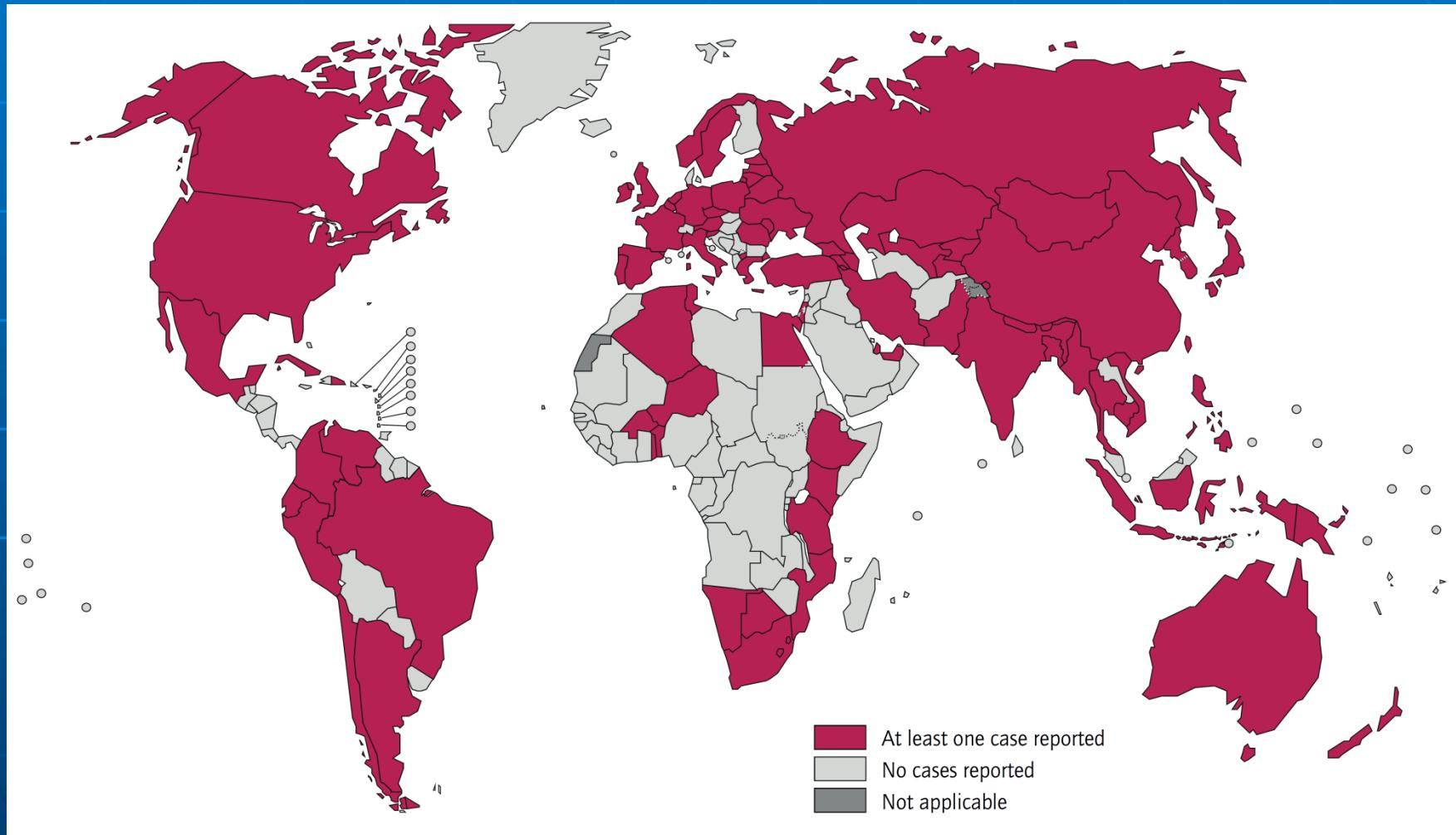
Countries with high burden of TB, MDR-TB or both, 2011



* 2010 data for Azerbaijan, Lithuania,
Rep Moldova, Ukraine

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Lande som har rapporteret mindst én XDR-TB case (2012)

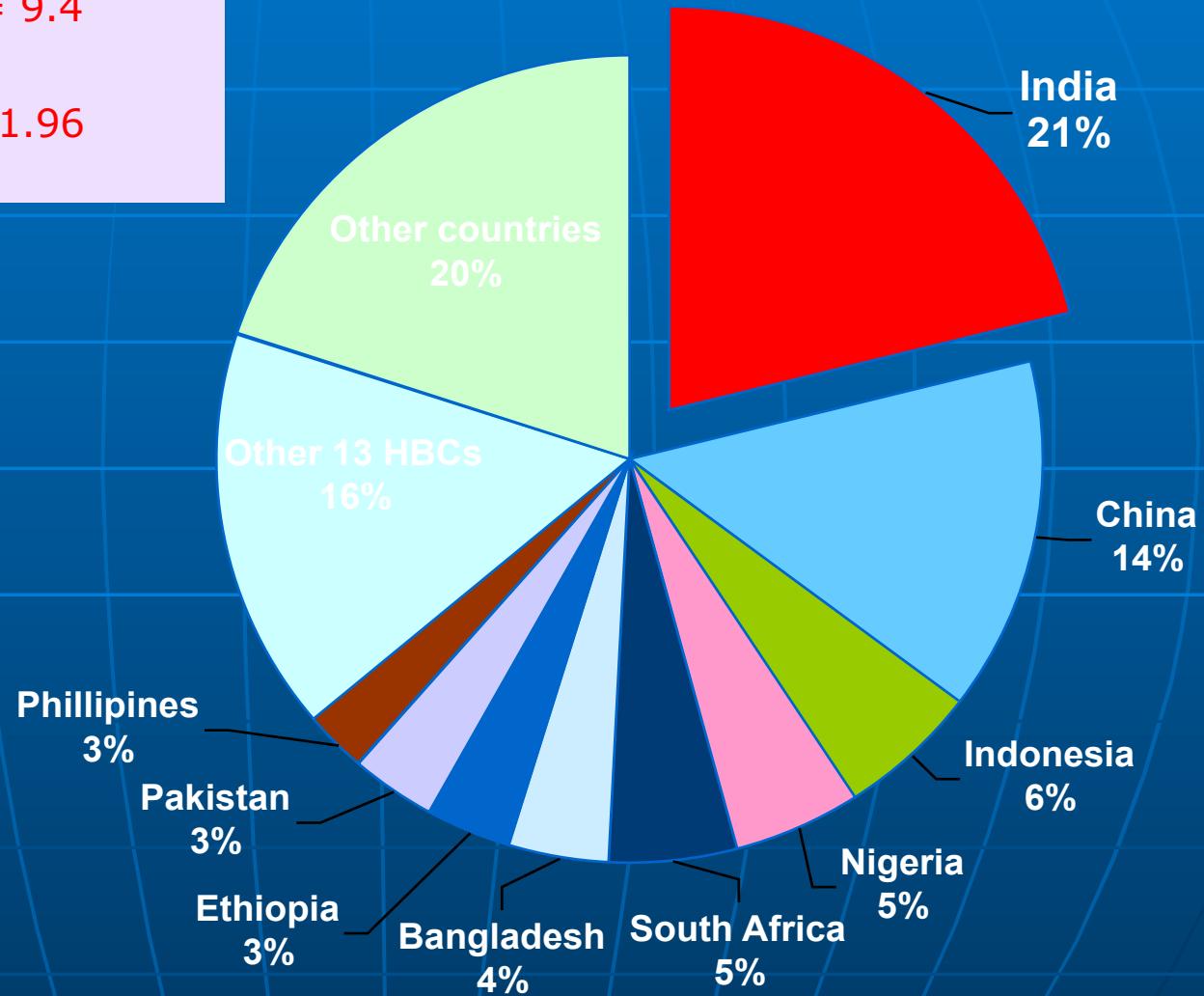


India is the highest TB burden country accounting for more than one-fifth of the global incidence

Global annual incidence = 9.4 million

India annual incidence = 1.96 million

India is 17th among 22 High Burden Countries (in terms of TB incidence rate)



Source: WHO Geneva; WHO Report 2009: Global Tuberculosis Control; Surveillance, Planning and Financing

Case

- 18 årig mand fra Somalia
- Skudt i ryggen, lam i benene.
- Langvarigt problem med liggesår der ikke vil hele
- Lange indlæggelser på sårafsnit i hhv Viborg og Aarhus til sårpleje/revision
- I oktober indlagt på infektionsmed afd, påvist TB

MDR

- Efter en måneds standardbehandling konstateres MDR-TB
- Behandling skiftes til 8 mdr intravenøs behandling med nyre- og hørelsesskadelig medicin
- 5 øvrige medikamenter med svære bivirkninger i 20 måneder

Skudsår, liggesår og fistler



Forløb

- Foreløbig behandlet to måneder
- Sår heller langsomt op
- Ikke længere smittefarlig
- +200 personaler i Viborg og Aarhus er i gang med miljøopsporing

Forskningsagenda

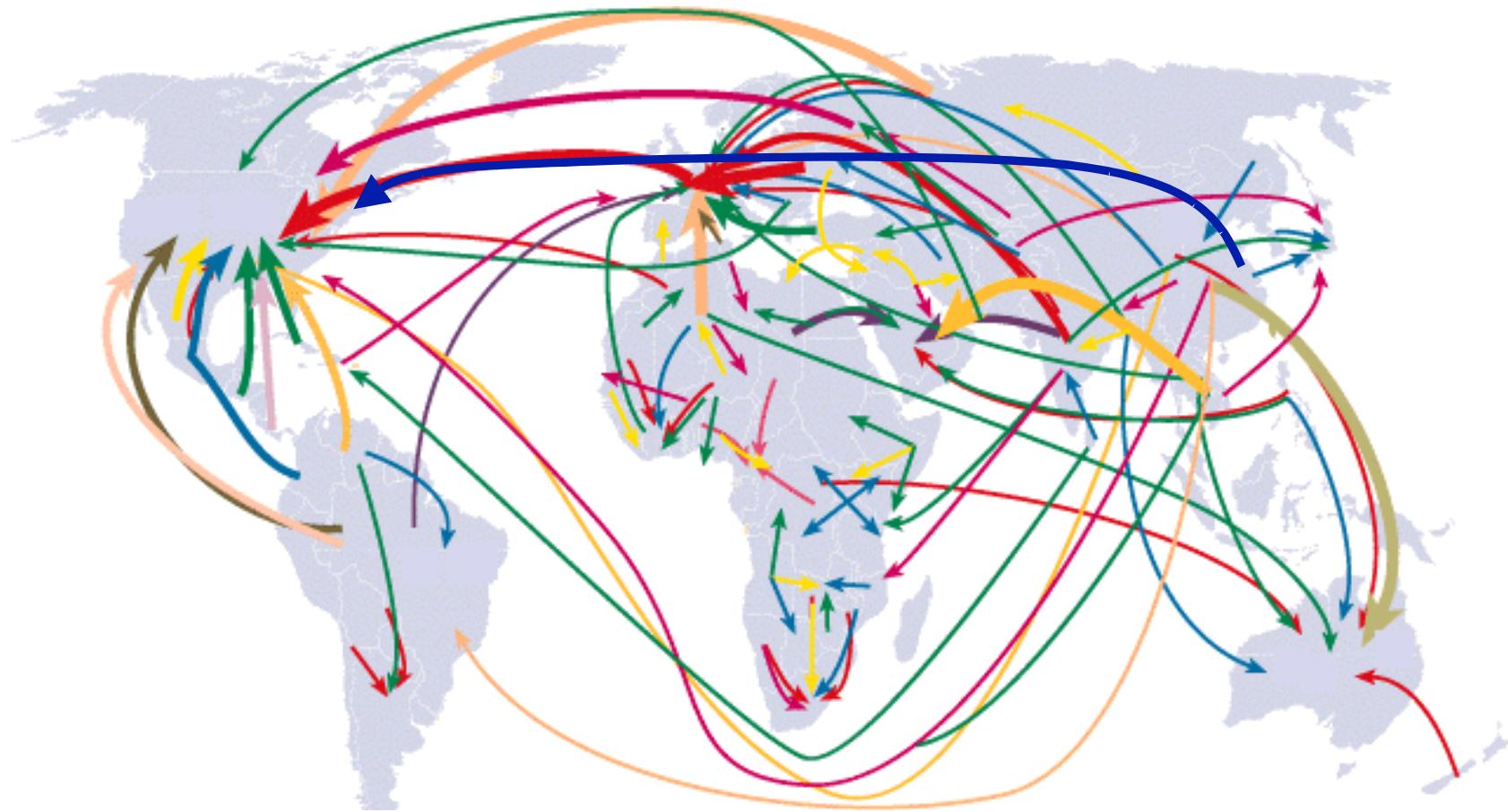
- For få patienter i DK til substantielle studier
- Adgang til større kohorter i TBNET regi (22 EU lande, 49 lande i alt)



Globalt

- Populationsbaserede studier i Guinea Bissau, Vestafrika
- TB kohorte gn 12 år i DSS med 100.000 msk i hovedstaden Bissau
- Dårlige laboratorieforhold, resistensdata usikre
- Formentlig en del resistens (5-10%)

Migrating populations



Source: Population Action International 1994