Epidemiology of antituberculosis drug resistance 2002–07: an updated analysis of the Global Project on Anti-Tuberculosis Drug Resistance Surveillance

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Summary

Background The Global Project on Anti-Tuberculosis Drug Resistance has been gathering data since 1994. This study provides the latest data on the extent of drug resistance worldwide.

Methods Data for drug susceptibility were gathered from 90 726 patients in 83 countries and territories between 2002 and 2007. Standardised collection of results enabled comparison both between and within countries. Where possible, data for HIV status and resistance to second-line drugs were also obtained. Laboratory data were quality assured by the Supranational Tuberculosis Reference Laboratory Network.

Findings The median prevalence of resistance to any drug in new cases of tuberculosis was 11·1% (IQR 7·0–22·3). The prevalence of multidrug resistance in new tuberculosis cases ranged from 0% in eight countries to 7% in two provinces in China, 11·1% in Northern Mariana Islands (although reporting only two cases), and between 6·8% and 22·3% in nine countries of the former Soviet Union, including 19·4% in Moldova and 22·3% in Baku, Azerbaijan (median for countries surveyed 1·6%, IQR 0·6–3·9). Trend analysis showed that between 1994 and 2007, the prevalence of multidrug-resistant (MDR) tuberculosis in new cases increased substantially in South Korea and in Tomsk Oblast and Orel Oblast, Russia, but was stable in Estonia and Latvia. The prevalence of MDR tuberculosis in all tuberculosis cases decreased in Hong Kong and the USA. 37 countries and territories reported representative data on extensively drug-resistant (XDR) tuberculosis. Five countries, all from the former Soviet Union, reported 25 cases or more of XDR tuberculosis each, with prevalence among MDR-tuberculosis cases ranging between 6·6% and 23·7%.

Interpretation MDR tuberculosis remains a threat to tuberculosis control in provinces in China and countries of the former Soviet Union. Data on drug resistance are unavailable in many countries, especially in Africa, emphasising the need to develop easier methods for surveillance of resistance in tuberculosis.

Funding Global Project: United States Agency for International Development and Eli Lilly and Company. Drug resistance surveys: national tuberculosis programmes, the Government of the Netherlands, the Global Fund to Fight AIDS, Tuberculosis and Malaria, Japan International Cooperation Agency, and Kreditanstalt für Wiederaufbau.

Introduction

The Global Project on Anti-Tuberculosis Drug Resistance Surveillance was initiated in 1994 to estimate the burden of drug-resistant tuberculosis worldwide. The project's primary aims are to monitor trends in resistance and estimate the prevalence of multidrug-resistant (MDR) tuberculosis. Countries that participate in the project follow standardised guidelines for data collection to ensure comparability both between and within countries. The report is published approximately every 3 years since most countries need around 18 months to complete a drug resistance survey.

Until 2000, few national tuberculosis programmes were diagnosing and managing drug-resistant tuberculosis cases in the public sector, with the exception of high-income countries and countries of the former Soviet Union. After the successful implementation of pilot projects to manage drug-resistant tuberculosis, the new Stop TB Strategy—which expands on the directly observed treatment, short-course strategy (DOTS)—was launched in 2006. The Stop TB Strategy includes the diagnosis and management of drug-resistant tuberculosis as one of its components and underpins the Second Global Plan to Stop TB 2006–2015, which provides targets and financial estimates for scale-up of the strategy.[1] Nowadays, with the support of the Green Light Committee and other technical and financial partners, many countries are initiating or expanding the diagnosis and management of drug-resistant tuberculosis.

This report provides the latest data on the extent of antituberculosis drug resistance in 83 countries and territories gathered between 2002 and 2007, including the magnitude of extensively drug-resistant (XDR) tuberculosis,[2] and an analysis of the association between HIV and drug-resistant tuberculosis. Data gathered since 1994, from 115 countries, are used to explore trends in resistance. On the basis of such empirical information, new estimates of the global and regional burden of MDR tuberculosis are presented.

Lancet 2009; 373: 1861–73

Published Online
April 16, 2009
DOI:10.1016/S0140-6736(09)60331-7

See Comment page 1822

*For members see webappendix p 6

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For more on **the Green Light Committee** see http://www.who.int/tb/challenges/mdr/greenlightcommittee/en/index.html

Methods

Data collection

A detailed description of the methods of the Global Project can be found in the full report and surveillance guidelines.[3–6] Briefly, the surveys are done on the basis of three main principles: the sample of tuberculosis patients must be representative of all cases of tuberculosis in the geographical setting under assessment; drug resistance must be distinguished according to the treatment history of the patient (ie, never treated or previously treated); and laboratory results must be quality assured by a supranational tuberculosis reference laboratory.[7]

New cases are defined as patients with tuberculosis who have never been treated with antituberculosis drugs or have received them for less than 1 month. Previously treated cases are defined as patients who have been treated for tuberculosis for 1 month or more. All newly registered patients with sputum smear-positive pulmonary tuberculosis were eligible for inclusion; however, in surveillance settings where all tuberculosis cases undergo testing by culture, all culture-positive cases were included irrespective of smear result. In the context of surveys, sample sizes were based on all new smear-positive cases notified in the previous year and the estimated proportion of rifampicin resistance in this population. In most survey settings, previously treated cases were included during the period of intake for new cases, although some countries developed a separate sample size for these cases, and other countries included all cases during the calendar year.

All subcategories of retreatment cases were included: relapse, return after default, and return after failure (ie, patients who were still sputum smear-positive after 5 months of treatment). Countries were encouraged to disaggregate drug resistance data by subcategory of retreatment. Each sample was increased by 15–20% to account for contamination, no culture growth, or loss. One isolate was examined per tuberculosis case. Re-checking of patient treatment history through verification of medical records and patient re-interview was recommended to reduce the possibility of misclassification. Extent and quality rechecking is requested, but not verified by WHO.

Drug susceptibility tests were done by use of the indirect proportion method on Lowenstein-Jensen medium,[8] the absolute concentration method, the resistance ratio method,[9] or the radiometric BACTEC 460 or MGIT 960 methods.[10,11] Species other than *Mycobacterium tuberculosis* were excluded from analysis. Quality assurance was undertaken by the supranational reference laboratories by sending a panel of isolates before the implementation of the survey and later by re-checking a percentage of isolates from patients included in the survey.

Statistical analysis

Aggregate data reported from settings were entered into a database built with Microsoft Access software. All the data were re-checked, and all data files and epidemiological profiles were returned to countries for verification. Summary analyses were done in Stata (version 9.0). For geographical settings that reported more than one data point since the third report, only the latest data point was used for the estimation of point prevalence. All tests of significance were two-tailed and the alpha error was kept at the 0·05 level in all inference procedures. 95% CIs were calculated around the proportions and the means. Trend analysis was done for geographical settings that reported more than two data points since the beginning of the project. Statistical significance of trends was determined through logistic regression. The association between HIV and drug-resistant tuberculosis was assessed by calculation of an odds ratio to compare proportion of drug resistance in HIV-positive patients with tuberculosis with the proportion in HIV-negative patients with tuberculosis. Fisher's exact test was used to determine statistical significance. For analysis of resistance to second-line antituberculosis drugs, the denominator used was MDR isolates tested for resistance to at least one fluoroquinolone and one injectable second-line antituberculosis drug (needed to define XDR tuberculosis[12]); for this analysis, MDR-tuberculosis and XDR-tuberculosis cases were not differentiated by history of previous treatment.

On the basis of drug resistance data reported from 115 countries and territories, we estimated the proportion of MDR tuberculosis in new, previously treated, and combined tuberculosis cases for a further 70 countries and developed a global estimate of incident MDR-tuberculosis cases.[5] The estimated number of new tuberculosis cases by country was used to calculate the number of MDR-tuberculosis cases that occurred in new cases. To estimate the number of previously treated cases, we multiplied the ratio of notified previously treated cases to notified new cases in 2006 by the total number of new cases estimated to have occurred in the same year for each country; therefore, the total number of estimated cases includes estimated re-treatment cases. Estimates were developed by use of a logistic regression model described in detail elsewhere.[13,14]

Role of the funding source

The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had access to all data in the study and had final responsibility for the decision to submit for publication.

Results

The fourth round of the Global Project includes data from 83 countries and territories that provided at least one data point since 2002. Two settings in India completed drug resistance surveys in 2001. We have reported these data in the tables; however, they have been excluded from the analyses. Worldwide, 90726 tuberculosis

cases (consisting of new cases, previously treated cases, and those with an unknown history of previous treatment) were tested for antituberculosis drug resistance. Nine countries provided data that did not differentiate between new and previously treated cases.

The median number of cases tested per setting was 553, ranging from five cases in New Caledonia (all with unknown history of previous treatment) to 4350 in Hong Kong (3271 new cases, 163 previously treated, and 916 with unknown history of previous treatment), 4800 in the UK (3428 new cases, 271 previously treated, and 1101 with unknown history of previous treatment), and 10 584 in the USA (all with unknown history of previous treatment).

75 countries and territories provided data on drug resistance in new cases of tuberculosis (table 1). The proportion of new tuberculosis cases with resistance to any drug ranged from 0% (Iceland) to 56·3% (Baku, Azerbaijan), with a median value of 11·1% (IQR 7·0–22·3). The prevalence of resistance to any drug was higher than 30% in 13 settings. A median of 6·7% (IQR 4·2–11·6) of new tuberculosis cases in the surveyed countries were isoniazid resistant. 17 settings reported a prevalence of resistance to isoniazid higher than 15%, 14 of which were located in the former Soviet Union or China. The median prevalence of MDR tuberculosis in new tuberculosis cases was 1·6% (IQR 0·6–3·9), ranging from 0% in eight countries with low tuberculosis prevalence to 19·4% in Moldova (Republic of Moldova) and 22·3% in Baku, Azerbaijan. The prevalence of multidrug resistance in new cases of tuberculosis was higher than 6% in 15 settings. 12 of these settings were in countries of the former Soviet Union, two were provinces in China, and one was Northern Mariana Islands (however, only two cases of MDR tuberculosis were reported in this country; table 1, figure). The two settings in India with drug resistance surveys completed in 2001 that were excluded from the analysis had a prevalence of multidrug resistance among new tuberculosis cases similar to that reported elsewhere in the country in subsequent years.

68 countries and territories provided data on drug resistance in previously treated cases of tuberculosis (table 2). The median prevalence of resistance to any drug in previously treated cases was 25·1% (IQR 6·0–46·3). No drug resistance was reported in Iceland, Israel, and Norway, where previously treated patients numbered eight or fewer. By contrast, resistance to any drug was reported in 84·4% of previously treated tuberculosis cases in Baku, Azerbaijan, and 85·9% of cases in Tashkent, Uzbekistan. The prevalence of resistance to any drug was 50% or higher in 16 settings. The median prevalence of MDR tuberculosis in previously treated tuberculosis cases was 11·7% (IQR 4·9–20·9). Six countries reported no patients with MDR tuberculosis, whereas 55·8% of patients in Baku, Azerbaijan, and 60·0% in Tashkent, Uzbekistan, had MDR tuberculosis. In 17 settings, more than 25% of previously treated patients had MDR tuberculosis. Nine of these settings were in countries of the former Soviet Union.

The global estimated number of incident MDR-tuberculosis cases in 2006 was 489 139, which was 4·8% of the total number of estimated incident tuberculosis cases in 185 countries (10 192 986; estimates include estimated re-treatment cases; table 3). The prevalence of MDR tuberculosis in all tuberculosis cases ranged from 0% to 28·9%, with a median of 2·4% (IQR 1·4–4·2). Estimates by country can be found in the annexes of the fourth report from the WHO/International Union Against Tuberculosis and Lung Disease Global Project on Anti-Tuberculosis Drug Resistance Surveillance.[5]

Trends in resistance in new tuberculosis cases were analysed for 47 countries and territories that provided at least three data points between 1994 and 2007. For countries with low tuberculosis prevalence that undertake continuous surveillance, trends were determined in all cases reported. For countries that undertake surveys, or where the population of previously treated cases tested changed over time, trends were determined in new cases only (webappendix pp 1–4).

See Online for webappendix

The USA and Hong Kong reported substantial reductions in both the prevalence of MDR tuberculosis (in all tuberculosis cases; USA p=0·005, Hong Kong p=0·011) and tuberculosis notification rates between 1994 and 2007 (webappendix pp 1–4). In most high-resource countries with low prevalence of tuberculosis, such as the UK, France, and Germany, trends in MDR tuberculosis were stable, and the absolute numbers of MDR tuberculosis were low. Both Peru and South Korea (Republic of Korea) reported increases in the prevalence of multidrug resistance in new cases, but at the same time showed steady declines in tuberculosis notification rates followed by a recent plateau. In countries of the former Soviet Union, where the prevalence of MDR tuberculosis is the highest, there were two scenarios: in the Baltic region, Estonia and Latvia showed stable trends in the prevalence of MDR tuberculosis in new cases, whereas Lithuania showed a slow but significant increase (p=0·012). All three countries showed a decreasing tuberculosis notification rate (5–8% reduction per year). In Orel Oblast and Tomsk Oblast in Russia (Russian Federation), the prevalence of MDR tuberculosis in new cases increased (p=0·001 and p=0·006, respectively) as did the absolute number of MDR tuberculosis cases. Tuberculosis notification rates fell in both regions but at a slower rate (1–3% reduction per year) than in the Baltic countries. Thailand and Nepal showed stable trends in the prevalence of MDR tuberculosis in both new and all tuberculosis cases.

27 countries or territories and two settings in Spain reported routine surveillance data on XDR tuberculosis and nine countries and one setting in Spain reported data from periodic surveys. Most countries that reported

	Method of data collection	Number of patients tested	Any resistance	Resistance to isoniazid	Resistance to rifampicin	Resistance to rifampicin only	Multidrug resistance*	Resistance to isoniazid, rifampicin, ethambutol, and streptomycin
African region								
Cote d'Ivoire, 2006	SVY	320	76 (23·8%, 19·2–28·8)	39 (12·2%, 8·8–16·3)	10 (3·1%, 1·5–5·7)	0 (0·0%, 0·0–0·9)	8 (2·5%, 1·1–4·9)	0 (0·0%, 0·0–0·9)
Ethiopia, 2005	SVY	804	216 (26·9%, 23·4–30·7)	62 (7·7%, 5·9–9·9)	22 (2·7%, 1·7–4·1)	8 (1·0%, 0·4–2·0)	13 (1·6%, 0·9–2·8)	9 (1·1%, 0·5–2·1)
Madagascar, 2007†	SVY	810	51 (6·3%, 4·7–8·3)	37 (4·6%, 3·2–6·3)	4 (0·5%, 0·1–1·3)	0 (0·0%, 0·0–0·4)	4 (0·5%, 0·1–1·3)	2 (0·2%, 0·0–0·9)
Rwanda, 2005	SVY	616	64 (10·4%, 8·0–13·3)	38 (6·2%, 4·4–8·5)	24 (3·9%, 2·5–5·8)	0 (0·0%, 0·0–0·5)	24 (3·9%, 2·5–5·8)	21 (3·4%, 2·1–5·2)
Senegal, 2006	SVY	237	25 (10·5%, 6·9–15·2)	10 (4·2%, 2·0–7·6)	5 (2·1%, 0·7–4·9)	0 (0·0%, 0·0–1·3)	5 (2·1%, 0·7–4·9)	3 (1·3%, 0·3–3·7)
American region								
Argentina, 2005	SVY	683	68 (10·0%, 7·7–12·6)	39 (5·7%, 4·1–7·8)	16 (2·3%, 1·3–3·8)	1 (0·1%, 0·0–0·8)	15 (2·2%, 1·2–3·6)	2 (0·3%, 0·0–1·1)
Canada, 2006	SNC	1058	81 (7·7%, 6·1–9·5)	67 (6·3%, 4·9–8·0)	12 (1·1%, 0·6–2·0)	4 (0·4%, 0·1–1·0)	8 (0·8%, 0·3–1·5)	2 (0·2%, 0·0–0·7)
Costa Rica, 2006	SVY	263	19 (7·2%, 4·4–11·1)	9 (3·4%, 1·6–6·4)	5 (1·9%, 0·6–4·4)	1 (0·4%, 0·0–2·1)	4 (1·5%, 0·4–3·8)	0 (0·0%, 0·0–1·1)
Cuba, 2005	SEN	169	12 (7·1%, 3·7–12·1)	1 (0·6%, 0·0–3·3)	1 (0·6%, 0·0–3·3)	1 (0·6%, 0·0–3·3)	0 (0·0%, 0·0–1·8)	0 (0·0%, 0·0–1·8)
Guatemala, 2002	SVY	668	233 (34·9%, 30·5–39·7)	72 (10·8%, 8·4–13·6)	28 (4·2%, 2·8–6·1)	5 (0·7%, 0·2–1·7)	20 (3·0%, 1·8–4·6)	10 (1·5%, 0·7–2·8)
Honduras, 2004	SVY	457	55 (12·0%, 9·2–15·4)	27 (5·9%, 3·9–8·5)	10 (2·2%, 1·1–4·0)	2 (0·4%, 0·1–1·6)	8 (1·8%, 0·8–3·4)	5 (1·1%, 0·4–2·5)
Nicaragua, 2006	SVY	320	42 (13·1%, 9·6–17·3)	21 (6·6%, 4·1–9·9)	3 (0·9%, 0·2–2·7)	1 (0·3%, 0·0–1·7)	2 (0·6%, 0·1–2·2)	0 (0·0%, 0·0–0·9)
Paraguay, 2001	SVY	235	26 (11·1%, 7·4–15·8)	15 (6·4%, 3·6–10·3)	8 (3·4%, 1·5–6·6)	3 (1·3%, 0·3–3·7)	5 (2·1%, 0·7–4·9)	1 (0·4%, 0·0–2·3)
Peru, 2006	SVY	1809	420 (23·2%, 21·0–25·5)	209 (11·6%, 10·0–13·2)	105 (5·8%, 4·7–7·0)	9 (0·5%, 0·2–0·9)	95 (5·3%, 4·2–6·4)	27 (1·5%, 1·0–2·2)
Puerto Rico, 2005	SNC	Combined only	..	..	..	..	..	..
Uruguay, 2005	SVY	335	7 (2·1%, 0·8–4·3)	4 (1·2%, 0·3–3·0)	1 (0·3%, 0·0–1·7)	1 (0·3%, 0·0–1·7)	0 (0·0%, 0·0–0·9)	0 (0·0%, 0·0–0·9)
USA, 2005	SNC	Combined only	..	..	..	..	..	..
Eastern Mediterranean region								
Jordan, 2004	SVY	111	36 (32·4%, 23·9–42·0)	10 (9·0%, 4·4–15·9)	13 (11·7%, 6·4–19·2)	4 (3·6%, 1·0–9·0)	6 (5·4%, 2·0–11·4)	3 (2·7%, 0·6–7·7)
Lebanon, 2003	SVY	190	37 (19·5%, 14·1–25·8)	23 (12·1%, 7·8–17·6)	5 (2·6%, 0·9–6·0)	2 (1·1%, 0·1–3·8)	2 (1·1%, 0·1–3·8)	1 (0·5%, 0·0–2·9)
Morocco, 2006	SVY	1049	73 (7·0%, 5·5–8·7)	43 (4·1%, 3·0–5·5)	8 (0·8%, 0·3–1·5)	2 (0·2%, 0·0–0·7)	5 (0·5%, 0·2–1·1)	1 (0·1%, 0·0–0·5)
Oman, 2006	SNC	150	10 (6·7%, 3·2–11·9)	7 (4·7%, 1·9–9·4)	2 (1·3%, 0·2–4·7)	0 (0·0%, 0·0–2·0)	2 (1·3%, 0·2–4·7)	1 (0·7%, 0·0–3·7)
Qatar, 2006	SNC	Combined only	..	..	..	..	..	..
Yemen, 2004	SVY	510	49 (9·6%, 7·1–12·7)	20 (3·9%, 2·4–6·1)	15 (2·9%, 1·6–4·9)	0 (0·0%, 0·0–0·6)	15 (2·9%, 1·6–4·9)	11 (2·2%, 1·1–3·9)
European region								
Andorra, 2005	SNC	9	1 (11·1%, 0·3–48·2)	1 (11·1%, 0·3–48·2)	0 (0·0%, 0·0–28·3)	0 (0·0%, 0·0–28·3)	0 (0·0%, 0·0–28·3)	0 (0·0%, 0·0–28·3)
Armenia, 2007	SVY	552	207 (37·5%, 32·6–43·0)	150 (27·2%, 23·0–31·9)	60 (10·9%, 8·3–14·0)	7 (1·3%, 0·5–2·6)	52 (9·4%, 7·0–12·4)	11 (2·0%, 1·0–3·6)
Austria, 2005	SNC	570	69 (12·1%, 9·4–15·3)	54 (9·5%, 7·1–12·4)	14 (2·5%, 1·3–4·1)	2 (0·4%, 0·0–1·3)	11 (1·9%, 1·0–3·5)	6 (1·1%, 0·4–2·3)
Azerbaijan, Baku City, 2007	SVY	551	310 (56·3%, 50·2–62·9)	225 (40·8%, 35·7–46·5)	125 (22·7%, 18·9–27·0)	1 (0·2%, 0·0–1·0)	123 (22·3%, 18·5–26·6)	57 (10·3%, 7·8–13·4)
Belgium, 2005	SNC	588	34 (5·8%, 4·0–8·1)	29 (4·9%, 3·3–7·1)	9 (1·5%, 0·7–2·9)	2 (0·3%, 0·0–1·2)	7 (1·2%, 0·5–2·5)	0 (0·0%, 0·0–0·5)
Bosnia and Herzegovina, 2005	SNC	1035	15 (1·4%, 0·8–2·4)	8 (0·8%, 0·3–1·5)	7 (0·7%, 0·3–1·4)	3 (0·3%, 0·1–0·8)	4 (0·4%, 0·1–1·0)	1 (0·1%, 0·0–0·5)
Croatia, 2005	SNC	586	17 (2·9%, 1·7–4·6)	12 (2·0%, 1·1–3·6)	6 (1·0%, 0·4–2·2)	0 (0·0%, 0·0–0·5)	3 (0·5%, 0·1–1·5)	0 (0·0%, 0·0–0·5)
Czech Republic, 2005	SNC	562	43 (7·7%, 5·5–10·3)	21 (3·7%, 2·3–5·7)	8 (1·4%, 0·6–2·8)	0 (0·0%, 0·0–0·5)	7 (1·2%, 0·5–2·6)	3 (0·5%, 0·1–1·6)
Denmark, 2005	SNC	307	17 (5·5%, 3·3–8·7)	15 (4·9%, 2·8–7·9)	5 (1·6%, 0·5–3·8)	0 (0·0%, 0·0–1·0)	5 (1·6%, 0·5–3·8)	0 (0·0%, 0·0–1·0)
Estonia, 2005	SNC	316	91 (28·8%, 23·9–34·1)	65 (20·6%, 16·2–25·5)	42 (13·3%, 9·7–17·5)	0 (0·0%, 0·0–0·9)	42 (13·3%, 9·7–17·5)	39 (12·3%, 8·9–16·5)
Finland, 2005	SNC	198	8 (4·0%, 1·8–7·8)	7 (3·5%, 1·4–7·1)	2 (1·0%, 0·1–3·6)	0 (0·0%, 0·0–1·5)	2 (1·0%, 0·1–3·6)	1 (0·5%, 0·0–2·8)
France, 2005	SEN	1291	112 (8·7%, 7·1–10·4)	71 (5·5%, 4·3–6·9)	15 (1·2%, 0·7–1·9)	1 (0·1%, 0·0–0·4)	14 (1·1%, 0·6–1·8)	2 (0·2%, 0·0–0·6)
Georgia, 2006	SVY	799	393 (49·2%, 44·4–54·3)	187 (23·4%, 20·2–27·0)	61 (7·6%, 5·8–9·8)	4 (0·5%, 0·1–1·3)	54 (6·8%, 5·1–8·8)	21 (2·6%, 1·6–4·0)
Germany, 2005	SNC	3094	339 (11·0%, 9·8–12·2)	225 (7·3%, 6·4–8·3)	68 (2·2%, 1·7–2·8)	8 (0·3%, 0·1–0·5)	57 (1·8%, 1·4–2·4)	29 (0·9%, 0·6–1·3)
Iceland, 2005	SNC	7	0 (0·0%, 0·0–34·8)	0 (0·0%, 0·0–34·8)	0 (0·0%, 0·0–34·8)	0 (0·0%, 0·0–34·8)	0 (0·0%, 0·0–34·8)	0 (0·0%, 0·0–34·8)
Ireland, 2005	SNC	200	6 (3·0%, 1·1–6·4)	6 (3·0%, 1·1–6·4)	1 (0·5%, 0·0–2·8)	0 (0·0%, 0·0–1·5)	1 (0·5%, 0·0–2·8)	1 (0·5%, 0·0–2·8)
Israel, 2005	SNC	211	46 (21·8%, 16·4–28·0)	32 (15·2%, 10·6–20·7)	12 (5·7%, 3·0–9·7)	0 (0·0%, 0·0–1·4)	12 (5·7%, 3·0–9·7)	8 (3·8%, 1·7–7·3)

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	Method of data collection	Number of patients tested	Any resistance	Resistance to isoniazid	Resistance to rifampicin	Resistance to rifampicin only	Multidrug resistance*	Resistance to isoniazid, rifampicin, ethambutol, and streptomycin
(Continued from previous page)								
Italy, eight regions, 2005	SNC	485	47 (9·7%, 7·2–12·7)	30 (6·2%, 4·2–8·7)	11 (2·3%, 1·1–4·0)	1 (0·2%, 0·0–1·1)	8 (1·6%, 0·7–3·2)	3 (0·6%, 0·1–1·8)
Latvia, 2005	SNC	873	313 (35·9%, 32·0–40·1)	270 (30·9%, 27·3–34·8)	94 (10·8%, 8·7–13·2)	0 (0·0%, 0·0–0·3)	94 (10·8%, 8·7–13·2)	82 (9·4%, 7·5–11·7)
Lithuania, 2005	SNC	1293	313 (24·2%, 21·6–27·0)	262 (20·3%, 17·9–22·9)	128 (9·9%, 8·3–11·8)	0 (0·0%, 0·0–0·2)	127 (9·8%, 8·2–11·7)	51 (3·9%, 2·9–5·2)
Luxembourg, 2005	SNC	36	4 (11·1%, 3·1–26·1)	3 (8·3%, 1·8–22·5)	0 (0·0%, 0·0–8·0)	0 (0·0%, 0·0–8·0)	0 (0·0%, 0·0–8·0)	0 (0·0%, 0·0–8·0)
Malta, 2005	SNC	11	2 (18·2%, 2·3–51·8)	0 (0·0%, 0·0–23·8)	0 (0·0%, 0·0–23·8)	0 (0·0%, 0·0–23·8)	0 (0·0%, 0·0–23·8)	0 (0·0%, 0·0–23·8)
Moldova, 2006	SNC	825	354 (42·9%, 38·6–47·6)	257 (31·2%, 27·5–35·2)	171 (20·7%, 17·7–24·1)	6 (0·7%, 0·3–1·6)	160 (19·4%, 16·5–22·6)	69 (8·4%, 6·5–10·6)
Netherlands, 2005	SNC	709	59 (8·3%, 6·3–10·7)	46 (6·5%, 4·8–8·7)	10 (1·4%, 0·7–2·6)	5 (0·7%, 0·2–1·6)	5 (0·7%, 0·2–1·6)	2 (0·3%, 0·0–1·0)
Norway, 2005	SNC	193	43 (22·3%, 16·6–28·8)	20 (10·4%, 6·4–15·6)	3 (1·6%, 0·3–4·5)	0 (0·0%, 0·0–1·5)	3 (1·6%, 0·3–4·5)	0 (0·0%, 0·0–1·5)
Poland, 2004	SNC	2716	152 (5·6%, 4·7–6·6)	91 (3·4%, 2·7–4·1)	15 (0·6%, 0·3–0·9)	6 (0·2%, 0·1–0·5)	8 (0·3%, 0·1–0·6)	2 (0·1%, 0·0–0·3)
Portugal, 2005	SNC	1407	203 (14·4%, 12·5–16·6)	91 (6·5%, 5·2–7·9)	14 (1·0%, 0·5–1·7)	1 (0·1%, 0·0–0·4)	12 (0·9%, 0·4–1·5)	3 (0·2%, 0·0–0·6)
Romania, 2004	SNC	849	122 (14·4%, 11·9–17·2)	71 (8·4%, 6·5–10·5)	41 (4·8%, 3·5–6·6)	13 (1·5%, 0·8–2·6)	24 (2·8%, 1·8–4·2)	9 (1·1%, 0·5–2·0)
Russia								
Tomsk Oblast, 2005	SNC	515	182 (35·3%, 30·4–40·9)	136 (26·4%, 22·1–31·2)	86 (16·7%, 13·4–20·6)	1 (0·2%, 0·0–1·1)	77 (15·0%, 11·8–18·7)	30 (5·8%, 3·9–8·3)
Orel Oblast, 2006	SNC	317	87 (27·4%, 22·6–32·7)	64 (20·2%, 15·9–25·0)	30 (9·5%, 6·5–13·2)	1 (0·3%, 0·0–1·7)	28 (8·8%, 5·9–12·5)	10 (3·2%, 1·5–5·7)
Mary El Oblast, 2006	SNC	304	91 (29·9%, 24·8–35·4)	79 (26·0%, 21·1–31·3)	38 (12·5%, 9·0–16·8)	..	38 (12·5%, 9·0–16·8)	..
Serbia, 2005	SNC	1112	33 (3·0%, 2·0–4·2)	9 (0·8%, 0·4–1·5)	9 (0·8%, 0·4–1·5)	3 (0·3%, 0·1–0·8)	4 (0·4%, 0·1–0·9)	1 (0·1%, 0·0–0·5)
Slovakia, 2005	SNC	248	18 (7·3%, 4·4–11·2)	13 (5·2%, 2·8–8·8)	7 (2·8%, 1·1–5·7)	1 (0·4%, 0·0–2·2)	4 (1·6%, 0·4–4·1)	0 (0·0%, 0·0–1·2)
Slovenia, 2005	SNC	217	10 (4·6%, 2·2–8·3)	7 (3·2%, 1·3–6·5)	0 (0·0%, 0·0–1·4)	0 (0·0%, 0·0–1·4)	0 (0·0%, 0·0–1·4)	0 (0·0%, 0·0–1·4)
Spain	SNC							
Galicia, 2005	SNC	566	37 (6·5%, 4·6–9·0)	20 (3·5%, 2·2–5·5)	1 (0·2%, 0·0–1·0)	0 (0·0%, 0·0–0·5)	1 (0·2%, 0·0–1·0)	0 (0·0%, 0·0–0·5)
Aragon, 2005	SNC	200	13 (6·5%, 3·5–10·9)	11 (5·5%, 2·8–9·6)	1 (0·5%, 0·0–2·8)	1 (0·5%, 0·0–2·8)	0 (0·0%, 0·0–1·5)	0 (0·0%, 0·0–1·5)
Barcelona, 2005	SNC	Combined only	..	..	..	..	..	..
Sweden, 2005	SNC	425	52 (12·2%, 9·3–15·7)	42 (9·9%, 7·2–13·1)	3 (0·7%, 0·1–2·0)	1 (0·2%, 0·0–1·3)	2 (0·5%, 0·1–1·7)	1 (0·2%, 0·0–1·3)
Switzerland, 2005	SNC	326	15 (4·6%, 2·6–7·5)	14 (4·3%, 2·4–7·1)	3 (0·9%, 0·2–2·7)	1 (0·3%, 0·0–1·7)	2 (0·6%, 0·1–2·2)	0 (0·0%, 0·0–0·9)
Ukraine, Donetsk Oblast, 2006	SVY	1003	399 (39·8%, 36·0–43·9)	311 (31·0%, 27·7–34·6)	180 (17·9%, 15·4–20·8)	12 (1·2%, 0·6–2·1)	160 (16·0%, 13·6–18·6)	15 (1·5%, 0·8–2·5)
UK, 2005	SNC	3428	245 (7·1%, 6·3–8·1)	230 (6·7%, 5·9–7·6)	34 (1·0%, 0·7–1·4)	11 (0·3%, 0·2–0·6)	23 (0·7%, 0·4–1·0)	0 (0·0%, 0·0–0·1)
Uzbekistan, Tashkent, 2005	SVY	203	104 (51·2%, 44·1–58·3)	86 (42·4%, 35·5–49·5)	32 (15·8%, 11·0–21·5)	1 (0·5%, 0·0–2·7)	30 (14·8%, 10·2–20·4)	19 (9·4%, 5·7–14·2)
Southeast Asian region								
Burma (Myanmar), 2003	SVY	733	73 (10·0%, 7·8–12·5)	48 (6·5%, 4·8–8·7)	34 (4·6%, 3·2–6·5)	0 (0·0%, 0·0–0·4)	29 (4·0%, 2·6–5·7)	4 (0·5%, 0·1–1·4)
India								
Ernakulam District, Kerala State, 2004	SVY	305	85 (27·9%, 22·9–33·3)	27 (8·9%, 5·9–12·6)	11 (3·6%, 1·8–6·4)	3 (1·0%, 0·2–2·8)	6 (2·0%, 0·7–4·2)	3 (1·0%, 0·2–2·8)
Gujarat State, 2006	SVY	1571	335 (21·3%, 19·1–23·7)	173 (11·0%, 9·4–12·8)	40 (2·5%, 1·8–3·5)	3 (0·2%, 0·0–0·6)	37 (2·4%, 1·7–3·2)	13 (0·8%, 0·4–1·4)
Mayhurbhanj District, Orissa State, 2001‡	SVY	282	15 (5·3%, 3·0–8·6)	7 (2·5%, 1·0–5·0)	2 (0·7%, 0·1–2·5)	0 (0·0%, 0·0–1·1)	2 (0·7%, 0·1–2·5)	1 (0·4%, 0·0–2·0)
Hoogli district, West Bengal State, 2001‡	SVY	263	44 (16·7%, 12·4–21·8)	27 (10·3%, 6·9–14·6)	8 (3·0%, 1·3–5·9)	0 (0·0%, 0·0–1·1)	8 (3·0%, 1·3–5·9)	3 (1·1%, 0·2–3·3)
Indonesia, Mimika District, Papua Province, 2004	SVY	101	14 (13·9%, 7·8–22·2)	13 (12·9%, 7·0–21·0)	2 (2·0%, 0·2–7·0)	0 (0·0%, 0·0–2·9)	2 (2·0%, 0·2–7·0)	0 (0·0%, 0·0–2·9)

(Continues on next page)

	Method of data collection	Number of patients tested	Any resistance	Resistance to isoniazid	Resistance to rifampicin	Resistance to rifampicin only	Multidrug resistance*	Resistance to isoniazid, rifampicin, ethambutol, and streptomycin
(Continued from previous page)								
Nepal, 2007	SVY	766	113 (14·8%, 12·2–17·7)	64 (8·4%, 6·4–10·7)	22 (2·9%, 1·8–4·3)	0 (0·0%, 0·0–0·4)	22 (2·9%, 1·8–4·3)	14 (1·8%, 1·0–3·1)
Sri Lanka, 2006	SVY	561	8 (1·4%, 0·6–2·8)	4 (0·7%, 0·2–1·8)	3 (0·5%, 0·1–1·6)	2 (0·4%, 0·0–1·3)	1 (0·2%, 0·0–1·0)	1 (0·2%, 0·0–1·0)
Thailand, 2006	SVY	1150	180 (15·7%, 13·4–18·1)	111 (9·7%, 7·9–11·6)	30 (2·6%, 1·8–3·7)	10 (0·9%, 0·4–1·6)	19 (1·7%, 1·0–2·6)	7 (0·6%, 0·2–1·3)
Western Pacific region								
Australia, 2005	SNC	Combined only	..	..	..	..	..	..
China								
Inner Mongolia Autonomous Region, 2002	SVY	806	282 (35·0%, 31·0–39·3)	164 (20·3%, 17·3–23·7)	79 (9·8%, 7·8–12·2)	13 (1·6%, 0·9–2·8)	59 (7·3%, 5·6–9·4)	13 (1·6%, 0·9–2·8)
Beijing Municipality, 2004	SVY	1043	187 (17·9%, 15·4–20·7)	91 (8·7%, 7·0–10·7)	44 (4·2%, 3·1–5·7)	11 (1·1%, 0·5–1·9)	24 (2·3%, 1·5–3·4)	3 (0·3%, 0·1–0·8)
Heilongjiang Province, 2005	SVY	1574	569 (36·1%, 33·2–39·2)	268 (17·0%, 15·0–19·2)	167 (10·6%, 9·1–12·3)	34 (2·2%, 1·5–3·0)	113 (7·2%, 5·9–8·6)	22 (1·4%, 0·9–2·1)
Shanghai Municipality, 2005	SVY	764	118 (15·4%, 12·8–18·5)	85 (11·1%, 8·9–13·8)	37 (4·8%, 3·4–6·7)	6 (0·8%, 0·3–1·7)	30 (3·9%, 2·6–5·6)	5 (0·7%, 0·2–1·5)
Fiji	SNC	Combined only	..	..	..	..	..	..
Guam, 2002	SVY	Combined only	..	..	..	..	..	..
Hong Kong (Special Administrative Region, China), 2005	SNC	3271	362 (11·1%, 10·0–12·3)	164 (5·0%, 4·3–5·8)	36 (1·1%, 0·8–1·5)	7 (0·2%, 0·1–0·4)	28 (0·9%, 0·6–1·2)	11 (0·3%, 0·2–0·6)
Japan, 2002	SNC	2705	233 (8·6%, 7·5–9·8)	77 (2·8%, 2·2–3·6)	28 (1·0%, 0·7–1·5)	5 (0·2%, 0·1–0·4)	19 (0·7%, 0·4–1·1)	11 (0·4%, 0·2–0·7)
Macao (Special Administrative Region, China), 2005	SNC	265	42 (15·8%, 11·7–20·8)	28 (10·6%, 7·1–14·9)	7 (2·6%, 1·1–5·4)	1 (0·4%, 0·0–2·1)	6 (2·3%, 0·8–4·9)	3 (1·1%, 0·2–3·3)
New Caledonia, 2005	SVY	Combined only	..	..	..	..	..	..
New Zealand, 2006	SNC	250	26 (10·4%, 6·9–14·9)	17 (6·8%, 4·0–10·7)	1 (0·4%, 0·0–2·2)	0 (0·0%, 0·0–1·2)	1 (0·4%, 0·0–2·2)	1 (0·4%, 0·0–2·2)
Northern Mariana Islands, 2006	SNC	18	4 (22·2%, 6·4–47·6)	3 (16·7%, 3·6–41·4)	2 (11·1%, 1·4–34·7)	0 (0·0%, 0·0–15·3)	2 (11·1%, 1·4–34·7)	0 (0·0%, 0·0–15·3)
Philippines, 2004	SVY	965	198 (20·5%, 17·8–23·6)	130 (13·5%, 11·3–16·0)	44 (4·6%, 3·3–6·1)	4 (0·4%, 0·1–1·1)	39 (4·0%, 2·9–5·5)	19 (2·0%, 1·2–3·1)
Singapore, 2005	SNC	895	58 (6·5%, 4·9–8·4)	30 (3·4%, 2·3–4·8)	5 (0·6%, 0·2–1·3)	3 (0·3%, 0·1–1·0)	2 (0·2%, 0·0–0·8)	2 (0·2%, 0·0–0·8)
Solomon Islands, 2004	SVY	Combined only	..	..	..	..	..	..
South Korea, 2004	SVY	2636	321 (12·2%, 10·9–13·6)	261 (9·9%, 8·7–11·2)	98 (3·7%, 3·0–4·5)	25 (0·9%, 0·6–1·4)	71 (2·7%, 2·1–3·4)	10 (0·4%, 0·2–0·7)
Vanuatu, 2006	SNC	29	1 (3·4%, 0·1–17·8)	1 (3·4%, 0·1–17·8)	0 (0·0%, 0·0–9·8)	0 (0·0%, 0·0–9·8)	0 (0·0%, 0·0–9·8)	0 (0·0%, 0·0–9·8)
Vietnam, 2006	SVY	1619	497 (30·7%, 28·1–33·5)	310 (19·1%, 17·1–21·4)	53 (3·3%, 2·5–4·3)	5 (0·3%, 0·1–0·7)	44 (2·7%, 2·0–3·6)	24 (1·5%, 0·9–2·2)

SEN=sentinel. SNC=surveillance. SVY=survey. Data are number of positive cases (%, 95% CI). All data are countrywide testing unless otherwise indicated. The results of drug susceptibility tests for 15 414 tuberculosis cases were not differentiated into new and previously treated cases (combined only). *Resistance to at least isoniazid and rifampicin. †Data from Madagascar are preliminary. ‡The drug resistance surveys in Mayhurbhanj District, Orissa State, and Hoogli district, West Bengal State, India were completed in 2001; these data have therefore been excluded from the analysis.

Table 1: **Notified proportion of drug resistance in new tuberculosis cases tested for resistance to at least isoniazid and rifampicin in 83 countries or territories, by WHO region**

surveillance data were those with low tuberculosis prevalence. Some countries reported data aggregated over a 3-year period, and other countries reported over a 1-year period. In total, data were reported for 3818 MDR-tuberculosis cases, of which 304 (8·0%) were XDR (webappendix p 5). In general, absolute numbers of XDR-tuberculosis cases were low in central and western Europe, the Americas, and in African and Asian countries that reported data. The prevalence of XDR tuberculosis among cases of MDR tuberculosis in these

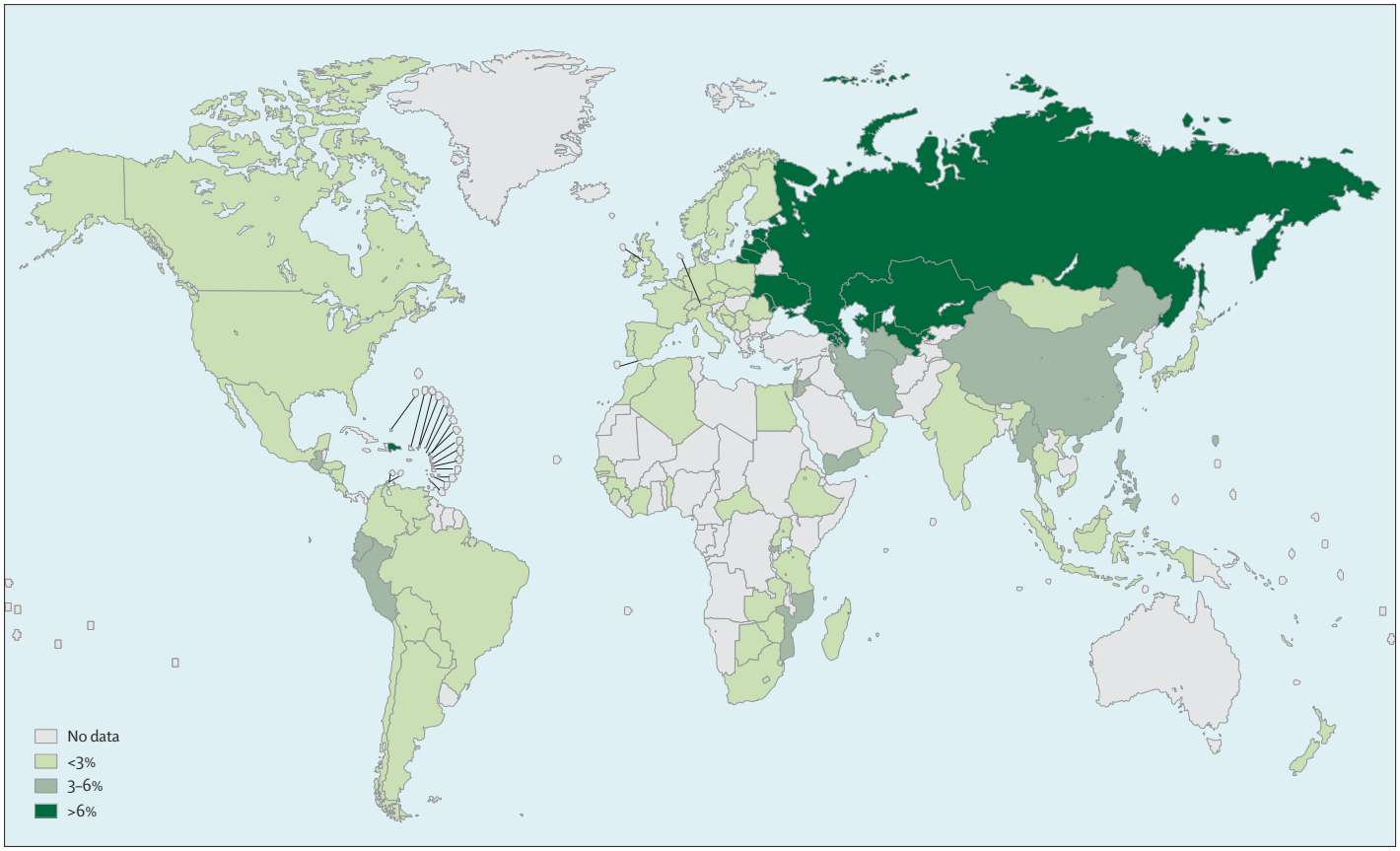

***Figure*: Distribution of multidrug-resistant tuberculosis among new cases, 1994–2007**
Subnational coverage in China, India, Indonesia, and Russia. Source: WHO, 2008.[5] The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city, or area, or of its authorities, or concerning the delimitation of its frontiers or boundaries.

settings ranged from 0% in 13 settings to 33·3% in Ireland and Slovenia (although in these countries very few cases of MDR tuberculosis and only one case of XDR tuberculosis were reported during 4 years and 5 years, respectively). For the eight countries in the former Soviet Union that provided data, approximately 10% of all MDR-tuberculosis cases were XDR, ranging from 4·0% in Armenia to 23·7% in Estonia. Five of these countries reported 25 cases or more of XDR tuberculosis.

Seven settings reported data for drug resistance stratified by HIV status. In five countries (Cuba, Honduras, Russia [Tomsk Oblast], Spain, Uruguay), no significant association between MDR tuberculosis and HIV infection was seen. However, MDR tuberculosis was significantly associated with HIV in Latvia (odds ratio [OR] 2·1, 95% CI 1·4–3·0) and Donetsk Oblast, Ukraine (OR 1·5, 1·1–2·0). In both countries, resistance to any tuberculosis drug was also significantly higher in HIV-positive patients than in HIV-negative patients (Latvia OR 1·5, 1·1–2·1; Donetsk Oblast OR 1·4, 1·1–1·8). However, in Latvia, patients categorised as HIV negative included those with unknown HIV status as well as those who had tested negative. In this country, the proportion of tuberculosis cases that were MDR in patients with HIV was shown to be stable over time.

Discussion

Data from our global survey show regional and national variation in the magnitude and trends in drug-resistant tuberculosis. Countries of the former Soviet Union, followed by some provinces of China, reported the highest prevalence of resistance, while the eastern Mediterranean region and southeast Asia reported prevalence of resistance on par with estimated global averages. The data presented here show that of the half a million MDR-tuberculosis cases estimated to have emerged in 2006, 50% were in India and China alone, and 27 countries account for 86% of the world's MDR-tuberculosis burden. Countries in the Americas, western and central Europe, and Africa reported the lowest prevalences of MDR tuberculosis. Outliers were identified in all regions, suggesting that prevalence of MDR tuberculosis is linked to performance of national tuberculosis control programmes. Although the magnitude and trends in MDR tuberculosis are epidemiologically important to monitor, the estimation of the burden of disease is programmatically relevant in shaping policies for screening and treatment.

	Method of data collection	Number of patients tested	Any resistance	Resistance to isoniazid	Resistance to rifampicin	Resistance to rifampicin only	Multidrug resistance*	Resistance to isoniazid, rifampicin, ethambutol, and streptomycin
African region								
Cote d'Ivoire, 2006	SVY	New only	..	..	..	..	..	..
Ethiopia, 2005	SVY	76	37 (48·7%, 37·0–60·4)	19 (25·0%, 15·8–36·3)	11 (14·5%, 7·5–24·4)	1 (1·3%, 0·0–7·1)	9 (11·8%, 5·6–21·3)	6 (7·9%, 3·0–16·4)
Madagascar, 2007†	SVY	51	6 (11·8%, 4·4–23·9)	5 (9·8%, 3·3–21·4)	3 (5·9%, 1·2–16·2)	0 (0·0%, 0·0–5·7)	2 (3·9%, 0·5–13·5)	0 (0·0%, 0·0–5·7)
Rwanda, 2005	SVY	85	19 (22·4%, 14·0–32·7)	9 (10·6%, 5·0–19·2)	9 (10·6%, 5·0–19·2)	1 (1·2%, 0·0–6·4)	8 (9·4%, 4·2–17·7)	8 (9·4%, 4·2–17·7)
Senegal, 2006	SVY	42	13 (31·0%, 17·6–47·1)	10 (23·8%, 12·1–39·5)	7 (16·7%, 7·0–31·4)	0 (0·0%, 0·0–6·9)	7 (16·7%, 7·0–31·4)	6 (14·3%, 5·4–28·5)
American region								
Argentina, 2005	SVY	136	34 (25·0%, 18·0–33·1)	25 (18·4%, 12·3–25·9)	25 (18·4%, 12·3–25·9)	4 (2·9%, 0·8–7·4)	21 (15·4%, 9·8–22·6)	4 (2·9%, 0·8–7·4)
Canada, 2006	SNC	106	17 (16·0%, 9·6–24·4)	15 (14·2%, 8·1–22·3)	2 (1·9%, 0·2–6·6)	0 (0·0%, 0·0–2·8)	2 (1·9%, 0·2–6·6)	1 (0·9%, 0·0–5·1)
Costa Rica, 2006	SVY	21	1 (4·8%, 0·1–23·8)	1 (4·8%, 0·1–23·8)	1 (4·8%, 0·1–23·8)	0 (0·0%, 0·0–13·3)	1 (4·8%, 0·1–23·8)	0 (0·0%, 0·0–13·3)
Cuba, 2005	SEN	19	7 (36·8%, 16·3–61·6)	2 (10·5%, 1·3–33·1)	1 (5·3%, 0·1–26·0)	0 (0·0%, 0·0–14·6)	1 (5·3%, 0·1–26·0)	0 (0·0%, 0·0–14·6)
Guatemala, 2002	SVY	155	85 (54·8%, 46·7–62·8)	56 (36·1%, 28·6–44·2)	45 (29·0%, 22·0–36·9)	3 (1·9%, 0·4–5·6)	41 (26·5%, 19·7–34·1)	25 (16·1%, 10·7–22·9)
Honduras, 2004	SVY	73	28 (38·4%, 27·2–50·5)	18 (24·7%, 15·3–36·1)	15 (20·5%, 12·0–31·6)	5 (6·8%, 2·3–15·3)	9 (12·3%, 5·8–22·1)	3 (4·1%, 0·9–11·5)
Nicaragua, 2006	SVY	103	37 (35·9%, 26·7–46·0)	30 (29·1%, 20·6–38·9)	9 (8·7%, 4·1–15·9)	1 (1·0%, 0·0–5·3)	8 (7·8%, 3·4–14·7)	5 (4·9%, 1·6–11·0)
Paraguay, 2001	SVY	51	10 (19·6%, 9·8–33·1)	6 (11·8%, 4·4–23·9)	6 (11·8%, 4·4–23·9)	4 (7·8%, 2·2–18·9)	2 (3·9%, 0·5–13·5)	1 (2·0%, 0·0–10·4)
Peru, 2006	SVY	360	150 (41·7%, 36·5–46·9)	109 (30·3%, 25·6–35·3)	95 (26·4%, 21·9–31·3)	8 (2·2%, 1·0–4·3)	85 (23·6%, 19·3–28·3)	26 (7·2%, 4·8–10·4)
Puerto Rico, 2005	SNC	Combined only	..	..	..	..	..	..
Uruguay, 2005	SVY	33	3 (9·1%, 1·9–24·3)	2 (6·1%, 0·7–20·2)	2 (6·1%, 0·7–20·2)	0 (0·0%, 0·0–8·7)	2 (6·1%, 0·7–20·2)	0 (0·0%, 0·0–8·7)
USA, 2005	SNC	Combined only	..	..	..	..	..	..
Eastern Mediterranean region								
Jordan, 2004	SVY	30	25 (83·3%, 65·3–94·4)	17 (56·7%, 37·4–74·5)	14 (46·7%, 28·3–65·7)	0 (0·0%, 0·0–9·5)	12 (40·0%, 22·7–59·4)	7 (23·3%, 9·9–42·3)
Lebanon, 2003	SVY	16	12 (75·0%, 47·6–92·7)	12 (75·0%, 47·6–92·7)	10 (62·5%, 35·4–84·8)	0 (0·0%, 0·0–17·1)	10 (62·5%, 35·4–84·8)	5 (31·3%, 11·0–58·7)
Morocco, 2006	SVY	181	37 (20·4%, 14·8–27·1)	32 (17·7%, 12·4–24·0)	22 (12·2%, 7·8–17·8)	0 (0·0%, 0·0–1·6)	22 (12·2%, 7·8–17·8)	5 (2·8%, 0·9–6·3)
Oman, 2006	SNC	14	6 (42·9%, 17·7–71·1)	5 (35·7%, 12·8–64·9)	5 (35·7%, 12·8–64·9)	0 (0·0%, 0·0–19·3)	5 (35·7%, 12·8–64·9)	5 (35·7%, 12·8–64·9)
Qatar, 2006	SNC	Combined only	..	..	..	..	..	..
Yemen, 2004	SVY	53	11 (20·8%, 10·8–34·1)	7 (13·2%, 5·5–25·3)	6 (11·3%, 4·3–23·0)	0 (0·0%, 0·0–5·5)	6 (11·3%, 4·3–23·0)	4 (7·5%, 2·1–18·2)
European region								
Andorra, 2005	SNC	New only	..	..	..	..	..	..
Armenia, 2007	SVY	340	253 (74·4%, 69·4–79·0)	215 (63·2%, 57·9–68·4)	160 (47·1%, 41·7–52·5)	11 (3·2%, 1·6–5·7)	147 (43·2%, 37·9–48·7)	55 (16·2%, 12·4–20·5)
Austria, 2005	SNC	16	2 (12·5%, 1·6–38·3)	2 (12·5%, 1·6–38·3)	2 (12·5%, 1·6–38·3)	0 (0·0%, 0·0–17·1)	2 (12·5%, 1·6–38·3)	1 (6·3%, 0·2–30·2)
Azerbaijan, Baku City, 2007	SVY	552	466 (84·4%, 76·9–92·4)	440 (79·7%, 72·4–87·5)	309 (56·0%, 49·9–62·6)	0 (0·0%, 0·0–0·5)	308 (55·8%, 49·7–62·4)	153 (27·7%, 23·5–32·5)
Belgium, 2005	SNC	41	4 (9·8%, 2·7–23·1)	4 (9·8%, 2·7–23·1)	3 (7·3%, 1·5–19·9)	0 (0·0%, 0·0–7·0)	3 (7·3%, 1·5–19·9)	0 (0·0%, 0·0–7·0)
Bosnia and Herzegovina, 2005	SNC	106	26 (24·5%, 16·7–33·8)	14 (13·2%, 7·4–21·2)	14 (13·2%, 7·4–21·2)	5 (4·7%, 1·5–10·7)	7 (6·6%, 2·7–13·1)	2 (1·9%, 0·2–6·6)
Croatia, 2005	SNC	61	5 (8·2%, 2·7–18·1)	3 (4·9%, 1·0–13·7)	3 (4·9%, 1·0–13·7)	0 (0·0%, 0·0–4·8)	3 (4·9%, 1·0–13·7)	3 (4·9%, 1·0–13·7)
Czech Republic, 2005	SNC	20	8 (40·0%, 19·1–63·9)	7 (35·0%, 15·4–59·2)	6 (30·0%, 11·9–54·3)	0 (0·0%, 0·0–13·9)	6 (30·0%, 11·9–54·3)	5 (25·0%, 8·7–49·1)
Denmark, 2005	SNC	18	4 (22·2%, 6·4–47·6)	3 (16·7%, 3·6–41·4)	0 (0·0%, 0·0–15·3)	0 (0·0%, 0·0–15·3)	0 (0·0%, 0·0–15·3)	0 (0·0%, 0·0–15·3)
Estonia, 2005	SNC	71	45 (63·4%, 51·1–74·5)	43 (60·6%, 48·3–72·0)	37 (52·1%, 39·9–64·1)	0 (0·0%, 0·0–4·1)	37 (52·1%, 39·9–64·1)	34(47·9%,35·9–60·1)
Finland, 2005	SNC	22	1 (4·5%, 0·1–22·8)	1 (4·5%, 0·1–22·8)	1 (4·5%, 0·1–22·8)	0 (0·0%, 0·0–12·7)	1 (4·5%, 0·1–22·8)	1 (4·5%, 0·1–22·8)
France, 2005	SEN	112	24 (21·4%, 14·2–30·2)	16 (14·3%, 8·4–22·2)	9 (8·0%, 3·7–14·7)	1 (0·9%, 0·0–4·9)	8 (7·1%, 3·1–13·6)	3 (2·7%, 0·6–7·6)

(Continues on next page)

	Method of data collection	Number of patients tested	Any resistance	Resistance to isoniazid	Resistance to rifampicin	Resistance to rifampicin only	Multidrug resistance*	Resistance to isoniazid, rifampicin, ethambutol, and streptomycin
(Continued from previous page)								
Georgia, 2006	SVY	515	340 (66·0%, 59·2–73·4)	243 (47·2%, 41·4–53·5)	147 (28·5%, 24·1–33·5)	4 (0·8%, 0·2–2·0)	141 (27·4%, 23·0–32·3)	50 (9·7%, 7·2–12·8)
Germany, 2005	SNC	251	63 (25·1%, 19·9–30·9)	55 (21·9%, 17·0–27·5)	32 (12·7%, 8·9–17·5)	0 (0·0%, 0·0–1·2)	31 (12·4%, 8·5–17·1)	19 (7·6%, 4·6–11·6)
Iceland, 2005	SNC	1	0 (0·0%, 0·0–95·0)	0 (0·0%, 0·0–95·0)	0 (0·0%, 0·0–95·0)	0 (0·0%, 0·0–95·0)	0 (0·0%, 0·0–95·0)	0 (0·0%, 0·0–95·0)
Ireland, 2005	SNC	10	2 (20·0%, 2·5–55·6)	2 (20·0%, 2·5–55·6)	1 (10·0%, 0·3–44·5)	0 (0·0%, 0·0–25·9)	1 (10·0%, 0·3–44·5)	0 (0·0%, 0·0–25·9)
Israel, 2005	SNC	3	0 (0·0%, 0·0–63·2)	0 (0·0%, 0·0–63·2)	0 (0·0%, 0·0–63·2)	0 (0·0%, 0·0–63·2)	0 (0·0%, 0·0–63·2)	0 (0·0%, 0·0–63·2)
Italy, eight regions 2005	SNC	79	29 (36·7%, 26·1–48·3)	24 (30·4%, 20·5–41·8)	14 (17·7%, 10·0–27·9)	0 (0·0%, 0·0–3·7)	14 (17·7%, 10·0–27·9)	7 (8·9%, 3·6–17·4)
Latvia, 2005	SNC	182	96 (52·7%, 45·2–60·2)	90 (49·5%, 42·0–56·9)	66 (36·3%, 29·3–43·7)	0 (0·0%, 0·0–1·6)	66 (36·3%, 29·3–43·7)	58(31·9%,25·2–39·2)
Lithuania, 2005	SNC	440	264 (60·0%, 55·3–64·6)	250 (56·8%, 52·0–61·5)	212 (48·2%, 43·4–53·0)	2 (0·5%, 0·1–1·6)	209 (47·5%, 42·8–52·3)	134 (30·5%, 26·2–35·0)
Luxembourg, 2005	SNC	New only	..	..	..	..	..	..
Malta, 2005	SNC	New only	..	..	..	..	..	..
Moldova, 2006	SNC	2054	1449 (70·5%, 67·0–74·3)	1259 (61·3%, 58·0–64·8)	1108 (53·9%, 50·8–57·2)	23 (1·1%, 0·7–1·7)	1044 (50·8%, 47·8–54·0)	488 (23·8%, 21·7–26·0)
Netherlands, 2005	SNC	30	5 (16·7%, 5·6–34·7)	3 (10·0%, 2·1–26·5)	2 (6·7%, 0·8–22·1)	1 (3·3%, 0·1–17·2)	1 (3·3%, 0·1–17·2)	0 (0·0%, 0·0–9·5)
Norway, 2005	SNC	8	0 (0·0%, 0·0–31·2)	0 (0·0%, 0·0–31·2)	0 (0·0%, 0·0–31·2)	0 (0·0%, 0·0–31·2)	0 (0·0%, 0·0–31·2)	0 (0·0%, 0·0–31·2)
Poland, 2004	SNC	522	94 (18·0%, 14·6–22·0)	71 (13·6%, 10·6–17·2)	51 (9·8%, 7·3–12·8)	7 (1·3%, 0·5–2·8)	43 (8·2%, 6·0–11·1)	7 (1·3%, 0·5–2·8)
Portugal, 2005	SNC	172	35 (20·3%, 14·6–27·1)	26 (15·1%, 10·1–21·4)	19 (11·0%, 6·8–16·7)	2 (1·2%, 0·1–4·1)	16 (9·3%, 5·4–14·7)	5 (2·9%, 1·0–6·7)
Romania, 2004	SNC	382	125 (32·7%, 28·0–37·7)	108 (28·3%, 23·8–33·1)	49 (12·8%, 9·6–16·6)	7 (1·8%, 0·7–3·7)	42 (11·0%, 8·0–14·6)	30 (7·9%, 5·4–11·0)
Russia								
Tomsk Oblast, 2005	SNC	New only	..	..	..	..	..	..
Orel Oblast, 2006	SNC	30	14 (46·7%, 28·3–65·7)	14 (46·7%, 28·3–65·7)	5 (16·7%, 5·6–34·7)	0 (0·0%, 0·0–9·5)	5 (16·7%, 5·6–34·7)	4 (13·3%, 3·8–30·7)
Mary El Oblast, 2006	SNC	New only	..	..	..	..	..	..
Serbia, 2005	SNC	121	14 (11·6%, 6·5–18·7)	7 (5·8%, 2·4–11·6)	8 (6·6%, 2·9–12·6)	1 (0·8%, 0·0–4·5)	5 (4·1%, 1·4–9·4)	1 (0·8%, 0·0–4·5)
Slovakia, 2005	SNC	56	10 (17·9%, 8·9–30·4)	10 (17·9%, 8·9–30·4)	4 (7·1%, 2·0–17·3)	0 (0·0%, 0·0–5·2)	4 (7·1%, 2·0–17·3)	0 (0·0%, 0·0–5·2)
Slovenia, 2005	SNC	28	4 (14·3%, 4·0–32·7)	3 (10·7%, 2·3–28·2)	1 (3·6%, 0·1–18·3)	0 (0·0%, 0·0–10·1)	1 (3·6%, 0·1–18·3)	0 (0·0%, 0·0–10·1)
Spain	SNC							
Galicia, 2005	SNC	68	9 (13·2%, 6·2–23·6)	5 (7·4%, 2·4–16·3)	1 (1·5%, 0·0–7·9)	0 (0·0%, 0·0–4·3)	1 (1·5%, 0·0–7·9)	0 (0·0%, 0·0–4·3)
Aragon, 2005	SNC	26	5 (19·2%, 6·6–39·4)	5 (19·2%, 6·6–39·4)	4 (15·4%, 4·4–34·9)	0 (0·0%, 0·0–10·9)	4 (15·4%, 4·4–34·9)	2 (7·7%, 0·9–25·1)
Barcelona, 2005	SNC	Combined only	..	..	..	..	..	..
Sweden, 2005	SNC	17	4 (23·5%, 6·8–49·9)	4 (23·5%, 6·8–49·9)	2 (11·8%, 1·5–36·4)	0 (0·0%, 0·0–16·2)	2 (11·8%, 1·5–36·4)	0 (0·0%, 0·0–16·2)
Switzerland, 2005	SNC	30	2 (6·7%, 0·8–22·1)	2 (6·7%, 0·8–22·1)	2 (6·7%, 0·8–22·1)	0 (0·0%, 0·0–9·5)	2 (6·7%, 0·8–22·1)	0 (0·0%, 0·0–9·5)
Ukraine, Donetsk Oblast, 2006	SVY	494	347 (70·2%, 66·0–74·2)	298 (60·3%, 55·9–64·7)	241 (48·8%, 44·3–53·3)	8 (1·6%, 0·7–3·2)	219 (44·3%, 39·9–48·8)	30 (6·1%, 4·1–8·6)
UK, 2005	SNC	271	25 (9·2%, 6·1–13·3)	23 (8·5%, 5·5–12·5)	9 (3·3%, 1·5–6·2)	2 (0·7%, 0·1–2·6)	7 (2·6%, 1·0–5·2)	0 (0·0%, 0·0–1·1)
Uzbekistan, Tashkent, 2005	SVY	85	73 (85·9%, 76·6–92·5)	69 (81·2%, 71·2–88·8)	51 (60·0%, 48·8–70·5)	0 (0·0%, 0·0–3·5)	51 (60·0%, 48·8–70·5)	23(27·1%,18·0–37·8)
Southeast Asian region								
Burma, 2003	SVY	116	35 (30·2%, 22·0–39·4)	31 (26·7%, 18·9–35·7)	18 (15·5%, 9·5–23·4)	0 (0·0%, 0·0–2·5)	18 (15·5%, 9·5–23·4)	1 (0·9%, 0·0–4·7)
India								
Ernakulam District, Kerala State, 2004	SVY	New only	..	..	..	..	..	..

(Continues on next page)

	Method of data collection	Number of patients tested	Any resistance	Resistance to isoniazid	Resistance to rifampicin	Resistance to rifampicin only	Multidrug resistance*	Resistance to isoniazid, rifampicin, ethambutol, and streptomycin
(Continued from previous page)								
Gujarat State, 2006	SVY	1047	485 (46·3%, 42·3–50·6)	385 (36·8%, 33·2–40·6)	190 (18·1%, 15·7–20·9)	10 (1·0%, 0·5–1·8)	182 (17·4%, 14·9–20·1)	69 (6·6%, 5·1–8·3)
Mayhurbhanj District, Orissa State, 2001	SVY	New only	..	..	..	..	..	..
Hoogli district, West Bengal State, 2001	SVY	New only	..	..	..	..	..	..
Indonesia, Mimika District, Papua Province, 2004	SVY	New only	..	..	..	..	..	..
Nepal, 2007	SVY	162	41 (25·3%, 18·8–32·7)	37 (22·8%, 16·6–30·1)	19 (11·7%, 7·2–17·7)	0 (0·0%, 0·0–1·8)	19 (11·7%, 7·2–17·7)	11 (6·8%, 3·4–11·8)
Sri Lanka, 2006	SVY	34	3 (8·8%, 1·9–23·7)	2 (5·9%, 0·7–19·7)	0 (0·0%, 0·0–8·4)	0 (0·0%, 0·0–8·4)	0 (0·0%, 0·0–8·4)	0 (0·0%, 0·0–8·4)
Thailand, 2006	SVY	194	98 (50·5%, 43·3–57·8)	86 (44·3%, 37·2–51·6)	68 (35·1%, 28·4–42·2)	1 (0·5%, 0·0–2·8)	67 (34·5%, 27·9–41·7)	38(19·6%,14·2–25·9)
Western Pacific region								
Australia, 2005	SNC	Combined only	..	..	..	..	..	..
China								
Inner Mongolia Autonomous Region, 2002	SVY	308	216 (70·1%, 64·7–75·2)	174 (56·5%, 50·8–62·1)	157 (51·0%, 45·2–56·7)	16 (5·2%, 3·0–8·3)	129 (41·9%, 36·3–47·6)	41 (13·3%, 9·7–17·6)
Beijing Municipality, 2004	SVY	154	54 (35·1%, 27·6–43·2)	38 (24·7%, 18·1–32·3)	23 (14·9%, 9·7–21·6)	2 (1·3%, 0·2–4·6)	18 (11·7%, 7·1–17·8)	3 (1·9%, 0·4–5·6)
Heilongjiang Province, 2005	SVY	421	284 (67·5%, 62·8–71·9)	202 (48·0%, 43·1–52·9)	170 (40·4%, 35·7–45·2)	24 (5·7%, 3·7–8·4)	128 (30·4%, 26·0–35·0)	39 (9·3%, 6·7–12·4)
Shanghai Municipality, 2005	SVY	200	55 (27·5%, 21·4–34·2)	43 (21·5%, 16·0–27·8)	30 (15·0%, 10·4–20·7)	2 (1·0%, 0·1–3·6)	25 (12·5%, 8·3–17·9)	7 (3·5%, 1·4–7·1)
Fiji, 2006	SNC	Combined only	..	..	..	..	..	..
Guam, 2002	SVY	Combined only	..	..	..	..	..	..
Hong Kong (Special Administrative Region, China), 2005	SNC	163	38 (23·3%, 17·1–30·6)	28 (17·2%, 11·7–23·9)	16 (9·8%, 5·7–15·5)	1 (0·6%, 0·0–3·4)	13 (8·0%, 4·3–13·3)	6 (3·7%, 1·4–7·8)
Japan, 2002	SNC	417	105 (25·2%, 21·1–29·6)	79 (18·9%, 15·3–23·0)	46 (11·0%, 8·2–14·4)	2 (0·5%, 0·1–1·7)	41 (9·8%, 7·1–13·1)	19 (4·6%, 2·8–7·0)
Macao (Special Administrative Region, China), 2005	SNC	19	5 (26·3%, 9·1–51·2)	4 (21·1%, 6·1–45·6)	3 (15·8%, 3·4–39·6)	0 (0·0%, 0·0–14·6)	3 (15·8%, 3·4–39·6)	1 (5·3%, 0·1–26·0)
New Caledonia, 2005	SVY	Combined only	..	..	..	..	..	..
New Zealand, 2006	SNC	16	1 (6·3%, 0·2–30·2)	1 (6·3%, 0·2–30·2)	0 (0·0%, 0·0–17·1)	0 (0·0%, 0·0–17·1)	0 (0·0%, 0·0–17·1)	0 (0·0%, 0·0–17·1)
Northern Mariana Islands, 2006	SNC	New only	..	..	..	..	..	..
Philippines, 2004	SVY	129	48 (37·2%, 28·9–46·2)	40 (31·0%, 23·2–39·7)	33 (25·6%, 18·3–34·0)	5 (3·9%, 1·3–8·8)	27 (20·9%, 14·3–29·0)	8 (6·2%, 2·7–11·9)

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	Method of data collection	Number of patients tested	Any resistance	Resistance to isoniazid	Resistance to rifampicin	Resistance to rifampicin only	Multidrug resistance*	Resistance to isoniazid, rifampicin, ethambutol, and streptomycin
(Continued from previous page)								
Singapore, 2005	SNC	105	11 (10·5%, 5·3–18·0)	4 (3·8%, 1·0–9·5)	3 (2·9%, 0·6–8·1)	2 (1·9%, 0·2–6·7)	1 (1·0%, 0·0–5·2)	1 (1·0%, 0·0–5·2)
Solomon Islands, 2004	SVY	Combined only	..	..	..	..	..	..
South Korea, 2004	SVY	278	77 (27·7%, 22·5–33·4)	67 (24·1%, 19·2–29·6)	47 (16·9%, 12·7–21·8)	7 (2·5%, 1·0–5·1)	39 (14·0%, 10·2–18·7)	5 (1·8%, 0·6–4·1)
Vanuatu, 2006	SNC	New only	..	..	..	..	..	..
Vietnam, 2006	SVY	207	122 (58·9%, 51·9–65·7)	90 (43·5%, 36·6–50·5)	44 (21·3%, 15·9–27·5)	2 (1·0%, 0·1–3·4)	40 (19·3%, 14·2–25·4)	20 (9·7%, 6·0–14·5)

SEN=sentinel. SNC=surveillance. SVY=survey. Data are number of positive cases (%, 95% CI). All data are from countrywide testing unless otherwise indicated. The results of drug susceptibility tests for 15 414 tuberculosis cases were not differentiated into new and previously treated cases (combined only). Some countries only provided data for new cases of tuberculosis (new only). *Resistance to at least isoniazid and rifampicin. †Data from Madagascar are preliminary.

Table 2: **Notified proportion of drug resistance in previously treated tuberculosis cases tested for resistance to at least isoniazid and rifampicin in 83 countries or territories, by WHO region**

Most settings that provided three or more data points between 1994 and 2007 were those with low tuberculosis prevalence and showed stable trends of resistance with low absolute numbers of MDR tuberculosis. Of these settings, however, the USA and Hong Kong—both with strong political and financial commitment to tuberculosis control—reported substantial reductions in the prevalence and case load of MDR tuberculosis, with a faster reduction in MDR tuberculosis than in all forms of tuberculosis.[5] Russia, Peru, and South Korea reported increasing trends in the prevalence and estimated incidence of MDR tuberculosis. The specific reasons behind these trends, particularly in South Korea and Peru—two countries with long-term implementation of DOTS—need to be further explored.

The countries of the former Soviet Union are facing a serious and widespread epidemic with the highest prevalence of MDR tuberculosis ever reported in 13 years of global data collection. Almost half of all tuberculosis cases in countries of the former Soviet Union are resistant to at least one drug and one in five cases are MDR. In this region, MDR-tuberculosis cases have more extensive resistance patterns and the highest prevalence of XDR tuberculosis. Trend data from the Baltic countries probably represent the best scenario for this region, with the prevalence of MDR tuberculosis in new cases remaining stable and tuberculosis notification rates declining. These findings are possibly a result of political commitment and long-term investment in tuberculosis control, optimum management of susceptible and drug-resistant tuberculosis cases, and an improving socioeconomic situation. By contrast, the data reported from two Russian oblasts with well-performing tuberculosis control programmes (implementing the WHO recommended strategy to control tuberculosis and with decreasing tuberculosis notification rates) show an alarming situation with increases in both absolute number and prevalence of MDR tuberculosis in new cases and a slowly declining tuberculosis notification rate.

Although the trend data are based on only two of 89 oblasts in Russia, national data—not included in this analysis because of non-conforming methodology—accord with the finding of a nationwide increase in MDR tuberculosis.[15] Tuberculosis control in Russia has been enhanced by new legislation to bring policies in line with the Stop TB Strategy, the expansion of MDR-tuberculosis case management in accordance with international guidelines, and the upgrading of diagnostic services.[16] Nevertheless, efforts will have to be substantially accelerated and backed by strong political commitment if they are to have an effect on the growing epidemic of drug-resistant tuberculosis.

Surveys in eight of 31 provinces and two municipalities in China over a 10-year period show proportions of resistance only second to countries of the former Soviet Union, highlighting a serious drug resistance problem in this region. Trend data are not yet available from provinces in China; however, a nationwide survey currently underway will help to develop a national estimate of MDR tuberculosis.

The widespread reporting of XDR-tuberculosis cases show that they will emerge where second-line drugs are used and cure rates of MDR tuberculosis remain low. The prevalence and distribution of XDR tuberculosis is not well established because of a shortage in laboratory capacity to test for second-line drug resistance, but the data available in this survey show that XDR tuberculosis is currently most severe in countries of the former Soviet Union. With continued use of second-line drugs outside national tuberculosis programmes, the problem of XDR tuberculosis is likely to increase and without appropriate laboratory capacity or new drugs, the world is ill-equipped to manage this emerging crisis. It is important to note that in settings where only one fluoroquinolone and one injectable drug were tested, XDR-tuberculosis rates might be underestimated.

Although results from five of the countries that provided data for drug resistance stratified by HIV status

	Number of tuberculosis cases	Number of MDR-tuberculosis cases (95% CI)	Proportion of MDR-tuberculosis cases (% [95% CI])
New tuberculosis cases			
Established market economies	85 729	724 (573–942)	0·8% (0·7–1·1)
Central Europe	42 464	416 (166–2170)	1·0% (0·4–5·0)
Eastern Europe	336 842	43 878 (35 881–54 877)	13·0% (11·8–15·3)
Latin America	315 216	7196 (5850–10 360)	2·3% (1·9–3·3)
Eastern Mediterranean region	569 446	16 430 (8137–64 077)	2·9% (1·5–11·1)
Africa, low HIV incidence	350 671	5311 (3705–14 948)	1·5% (1·1–4·3)
Africa, high HIV incidence	2 440 270	43 767 (33 907–102 418)	1·8% (1·4–4·2)
Southeast Asia	3 100 354	85 908 (58 085–148 884)	2·8% (2·1–4·7)
Western Pacific region	1 882 930	82 087 (57 531–107 804)	4·4% (3·9–4·8)
Surveyed countries (n=105)	7 029 716	228 367 (190 128–267 943)	3·2% (2·9–3·6)
Non-surveyed countries (n=70)	2 094 206	57 351 (45 599–164 828)	2·7% (2·2–7·7)
All countries (n=175)	9 123 922	285 718 (256 072–399 224)	3·1% (2·9–4·3)
Previously treated tuberculosis cases			
Established market economies	5036	413 (330–528)	8·2% (6·8–10·2)
Central Europe	8038	785 (303–2625)	9·8% (3·9–31·3)
Eastern Europe	79 474	36 179 (29 216–43 769)	45·5% (41·8–49·4)
Latin America	33 856	4873 (4001–5937)	14·4% (12·4–16·9)
Eastern Mediterranean region	31 286	9040 (4733–15 901)	28·9% (15·5–48·9)
Africa, low HIV incidence	25 130	3105 (2169–5527)	12·4% (8·9–21·4)
Africa, high HIV incidence	216 152	14 528 (11 004–24 886)	6·7% (5·4–11·4)
Southeast Asia	363 959	63 707 (43 416–87 495)	17·5% (15·4–20·2)
Western Pacific region	289 214	70 601 (47 134–94 543)	24·4% (22·7–26·1)
Surveyed countries (n=96)	906 968	179 767 (146 915–212 012)	19·8% (18·4–21·3)
Non-surveyed countries (n=79)	145 177	23 463 (19 117–39 326)	16·2% (13·1–26·3)
All countries (n=175)	1 052 145	203 230 (172 935–242 177)	19·3% (18·2–21·3)
All tuberculosis cases			
Established market economies	105 795	1317 (1147–1557)	1·2% (1·1–1·5)
Central Europe	50 502	1201 (623–3694)	2·4% (1·3–7·2)
Eastern Europe	416 316	80 057 (71 893–97 623)	19·2% (18·0–22·2)
Latin America	349 278	12 070 (10 523–15 526)	3·5% (3·0–4·4)
Eastern Mediterranean region	601 225	25 475 (15 737–73 132)	4·2% (2·6–11·9)
Africa, low HIV incidence	375 801	8415 (6889–18 758)	2·2% (1·9–5·0)
Africa, high HIV incidence	2 656 422	58 296 (48 718–118 506)	2·2% (1·9–4·5)
Southeast Asia	3 464 313	149 615 (114 780–217 921)	4·3% (3·5–6·2)
Western Pacific region	2 173 333	152 694 (119 886–188 014)	7·0% (6·1–8·1)
Surveyed countries (n=115)	7 953 603	408 325 (361 264–464 069)	5·1% (4·7–5·7)
Non-surveyed countries (n=70)	2 239 383	80 814 (71 684–188 605)	3·6% (3·2–8·4)
All countries (n=185)	10 192 986	489 139 (455 093–614 215)	4·8% (4·6–6·0)

The total number of estimated cases includes estimated re-treatment cases; see Methods section for details of calculations.

Table 3: **Estimates of multidrug-resistant (MDR) tuberculosis in 2006 by epidemiological region**

showed no association between prevalence of MDR tuberculosis and HIV, data from Latvia and Ukraine supported such an association. The data do not allow for determination as to whether the association is related to acquisition or transmission. Nevertheless, the findings have great implications for health-care systems—for example, addressing clinical management of HIV/MDR tuberculosis co-infected patients, as discussed in a recent review paper.[17] Few population-level data for this association exist, which prevents measurement of the global magnitude. To gain a better understanding of the association and to provide best possible clinical management, health systems should expand diagnostic testing and counselling for both diseases.

Some sources of bias could exist in this study. First, there is potential for bias in estimation of drug resistance in previously treated cases where either the sample is small or where cluster-sampling based on new cases has been used, although the direction of this bias is impossible to predict. Second, although extent and quality rechecking is requested, but not verified by WHO, misclassification of treatment history can lead to bias. The direction of this bias is unpredictable.

Over the past decade, standardised tuberculosis patient management has been widely implemented and new policies to address HIV/tuberculosis co-infection, MDR tuberculosis, improved laboratory diagnosis, and the engagement of all health-care providers and civil society have been developed, tested, and endorsed. However, the Global Project on Anti-Tuberculosis Drug Resistance has not met some of its initial goals. For example, there are still major geographical areas for which there is no information on the burden of drug-resistant tuberculosis, mainly as a result of inadequate laboratory capacity. In the WHO African Region in particular, only 18 of 46 countries had nationwide drug resistance data and only five reported data since 2002. Furthermore, few trend data from countries with a high burden of tuberculosis are available, and thus the possibility of estimating global trends is limited. If trends are to be determined in high tuberculosis burden countries, surveys need to be easier to implement. Molecular diagnostics hold the greatest promise for scaling up surveillance rapidly, with a substantial advantage over conventional culture and drug susceptibility testing because of the reduced laboratory capacity needed and the transportation of non-infectious material.[18] The understanding of mutations that cause resistance to second-line drugs is currently incomplete; therefore, use of molecular methods alone would only provide information for the two most crucial antituberculosis drugs—ie, isoniazid and rifampicin. However, this disadvantage would be offset by the shortened time needed for screening out the most critical cases (MDR tuberculosis) and phenotypic drug susceptibility testing could be undertaken for all other second-line drugs.

Following an expert review of the Global Project, the existing international guidelines will be revised with new recommendations for laboratory and survey methods.[3,19] Knowledge of transmission dynamics and acquisition of resistance is crucial for the prioritisation of interventions, but these factors are difficult to address in the context of routine surveillance in most settings. Thus, more work is needed in the area of coordinated protocol development.

DOTS is now implemented in 184 countries, 52 resource-limited countries are treating MDR tuberculosis according to WHO guidelines, and most

countries are beginning to implement components of the new Stop TB Strategy. The next decade will require accelerated scale-up of the strategy to strengthen basic DOTS activities to ensure quality of treatment to prevent acquisition of resistance, rapid diagnosis of resistant cases, initiation of treatment in accordance with international guidelines to prevent further transmission, and broad application of infection control measures, especially in hospitals and prisons to prevent outbreaks.[20] Currently, the world is far behind reaching the targets for MDR-tuberculosis diagnosis and management set out in the second Global Plan to Stop TB 2006–2015.[1,16] Until drug susceptibility testing is implemented routinely for tuberculosis cases as the standard for diagnosis and surveillance, survey mechanisms will continue to be crucial for the determination of trends and the documentation of emergence of further resistance to second-line drugs.

Contributors

AW participated in data collection and data analysis. AVD organised proficiency testing for the Network of Supranational TB Reference Laboratories. DF contributed drug resistance surveillance data from western and central European countries. AVD, SRG, KF, SH, FD, LB, DvS, FB, CNP, KMK, and SM oversaw quality assurance of laboratory testing in several countries. PN supervised the work of the drug resistance team and Global Project on Anti-Tuberculosis Drug Resistance Surveillance. All authors participated in the writing of the manuscript.

Conflicts of interest

We declare that we have no conflicts of interest.

Acknowledgments

We thank Brian Williams for reviewing the manuscript. The Global Project on Anti-Tuberculosis Drug Resistance is carried out with funding from United States Agency for International Development (USAID) and Eli Lilly and Company as part of the Lilly MDR-TB Partnership. Drug resistance surveys were supported financially by national tuberculosis programmes, the Government of the Netherlands, the Global Fund to Fight AIDS, Tuberculosis and Malaria, Japan International Cooperation Agency, and Kreditanstalt für Wiederaufbau (KfW Entwicklungsbank). The laboratories that form the Network of Supranational TB Reference Laboratories are funded principally by their host institutions. AW, MZ, PN, MR are staff members of WHO. The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the decisions or policies of WHO. *The Lancet* takes responsibility for all country names used in the manuscript.

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