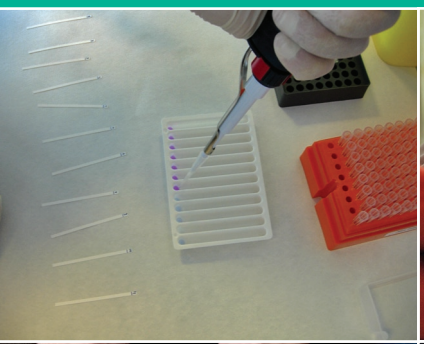
Multidrug and extensively drug-resistant TB (M/XDR-TB)

2010 GLOBAL REPORT ON SURVEILLANCE AND RESPONSE





World Health Organization

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Contents

In memoriam

Sir John Crofton (1912–2009), whose pioneering work in the use of combination drug therapy for the treatment of tuberculosis has resulted in countless lives saved

> "The greatest disaster that can happen to a patient with tuberculosis is that his organisms become resistant to two or more of the standard drugs. Fortunately we can prevent the emergence of drug resistance in virtually all cases if we take enough trouble to ensure that the best drug combinations are prescribed and that the patient takes them as directed. It is often not realized how venial a sin can result in ultimate disaster. It might be suggested that giving a risky combination of drugs, or even giving a drug alone, will not matter if it is only for a short time. It is true that it may not matter in a number of patients, but in some it can matter very much and may make all the difference between survival and death.
>
> The development of drug resistance may be a tragedy not only for the patient himself but for others. For he can infect other people with his drug-resistant organisms. In such patients the disease would not be sensitive to the drug in question. A recent survey by the Medical Research Council (Fox et al., 1957) in various clinics all over the country has shown that no less than 5% of newly diagnosed patients were infected with organisms resistant to at least one of the three main drugs. If physicians come to apply thoroughly the present knowledge about preventing drug resistance, this percentage should steadily diminish".

From *Chemotherapy of pulmonary tuberculosis*, by John Crofton, read to a plenary session at the Annual Meeting of the British Medical Association, Birmingham, England, 1958 (*British Medical Journal*, 1959, 5138(1):1610–1614).

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All members of the core team contributed to the writing of the report. Dennis Falzon, Wayne van Gemert and Matteo Zignol managed data. Dennis Falzon, Philippe Glaziou, Charalambos Sismanidis, Wayne van Gemert and Matteo Zignol reviewed and analysed data and prepared the figures and tables. Philippe Glaziou and Charalambos Sismanidis led the revision of estimates of MDR-TB incidence and mortality.

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Glossary

The definitions given below apply to the terms as used in this document. They may have different meanings in other contexts.

Class A continuous drug resistance surveillance data Data on drug susceptibility from routine testing of all TB patients, when the following conditions indicating a high degree of representativeness and accuracy are met: new case detection rate or new smear-positive case detection rate of at least 50%; positive culture available in at least 50% of all notified cases; DST results available in at least 75% of all cases with positive culture; accuracy of at least 95% for isoniazid and rifampicin in the most recent DST proficiency testing exercise with a supranational reference laboratory.

Class B continuous drug resistance surveillance data Data on drug susceptibility from routine testing of all TB patients, which do not meet the conditions for Class A data, but do meet the following conditions indicating a moderately high degree of representativeness: positive culture available in at least 35% of all notified cases; DST results available in at least 50% of all cases with positive culture.

Clustering effect When individuals (observations) are sampled from the same geographical region (for example the same country), applying standard statistical approaches, which assume independence of observations, in order to make inferences, can result in biased estimates. This inherent interrelated nature of individuals drawn from the same cluster means these individuals may be correlated, hence do not contain as much information as independent ones. The clustering effect is the extent to which inferences, properly accounting for this clustering of individuals, on both point estimates and their standard errors are influenced.

Cohort A group of TB cases.

Combined cases New and previously treated TB cases.

Countries WHO Member States.

Drug resistance survey A discrete study measuring the proportion of drug resistance among a sample of patients representative of an entire patient population in a country or geographical area.

DST drug susceptibility testing (defined as the testing of a strain of *Mycobacterium tuberculosis* for its susceptibility or resistance to one or more anti-TB drugs).

Geographical areas or settings Part of a country or territory.

GLC Green Light Committee Initiative. The GLC Initiative helps countries gain access to high-quality second-line anti-TB drugs so they can provide treatment for people with multidrug-resistant tuberculosis (MDR-TB) in line with the WHO guidelines, the latest scientific evidence and country experiences.

MDR-TB multidrug-resistant tuberculosis (defined as TB caused by strains of *Mycobacterium tuberculosis* that are resistant to at least isoniazid and rifampicin).

M/XDR-TB multidrug-resistant tuberculosis (see MDR-TB) and extensively drug-resistant tuberculosis (see XDR-TB).

New case A newly registered episode of TB in a patient who, in response to direct questioning, denies having had any prior anti-TB treatment (for less than one month), and in countries where adequate documentation is available, for whom there is no evidence of such history.

Previously treated case A newly registered episode of TB in a patient who, in response to direct questioning admits having been treated for TB for one month or more, or, in countries where adequate documentation is available, there is evidence of such history. Chemoprophylaxis should not be considered treatment for TB.

Relapse case A patient previously treated for TB who had been declared cured or treatment completed, and is again diagnosed with bacteriologically positive (smear or culture) TB.

Territory A legally administered territory, which is a non-sovereign geographical area that has come under the authority of another government.

UNITAID International facility for the purchase of diagnostics and medicines for diagnosis and treatment of HIV/AIDS, malaria and TB.

XDR-TB extensively drug-resistant tuberculosis (defined as MDR-TB plus resistance to a fluoroquinolone and at least one second-line injectable agent: amikacin, kanamycin and/or capreomycin).

Summary

Introduction

This new report on anti-tuberculosis (TB) drug resistance by the World Health Organization (WHO) updates "Anti-tuberculosis drug resistance in the world: Report No. 4" published by WHO in 2008. It summarizes the latest data and provides latest estimates of the global epidemic of multidrug and extensively drug-resistant tuberculosis (M/XDR-TB). For the first time, this report includes an assessment of the progress countries are making to diagnose and treat MDR-TB cases.

Surveillance

In 2008, an estimated 390 000–510 000 cases of MDR-TB emerged globally (best estimate, 440 000 cases). Among all incident TB cases globally, 3.6% (95% confidence interval (CI): 3.0–4.4) are estimated to have MDR-TB. These estimates, which lie in the same range as the previous ones, are based on more data and a revised methodology. Almost 50% of MDR-TB cases worldwide are estimated to occur in China and India. In 2008, MDR-TB caused an estimated 150 000 deaths.

Since 1994, 114 countries have reported surveillance data on MDR-TB:[1] 42 perform continuous surveillance of anti-TB drug resistance based on routine testing of all TB patients; 72 rely on periodic surveys of representative samples of TB patients. This report provides updated information from 35 of these 114 countries.

The highest proportions of MDR-TB ever documented in a subnational area are presented. The Russian Federation, which was able to provide high-quality continuous surveillance data from 12 of its oblasts and republics, reported proportions of 23.8–28.3% MDR-TB among new TB cases in three of its oblasts in the northwest part of the country. Other Russian oblasts were found to have proportions of MDR-TB as low as 5.4% among new TB cases. Tajikistan, in its first ever survey, found proportions of 16.5% MDR-TB among new TB cases and 61.6% MDR-TB among previously treated TB patients in Dushanbe city and Rudaki district, the highest proportion ever reported among previously treated TB patients. To date, 12 countries have reported nationwide or subnational proportions of MDR-TB of 6% or more among new TB cases. Five of these countries also report MDR-TB proportions of 50% or more among previously treated cases. All of these settings are located in the eastern part of Europe or in Central Asia.

- Multidrug-resistant TB (MDR-TB) is caused by bacteria that are resistant to at least isoniazid and rifampicin, the most effective anti-TB drugs. MDR-TB results from either primary infection with resistant bacteria or may develop in the course of a patient's treatment.
- Extensively drug-resistant TB (XDR-TB) is a form of TB caused by bacteria that are resistant to isoniazid and rifampicin (i.e. MDR-TB) as well as any fluoroquinolone and any of the second-line anti-TB injectable drugs (amikacin, kanamycin or capreomycin).

These forms of TB do not respond to the standard six-month treatment with first-line anti-TB drugs and can take up to two years or more to treat with drugs that are less potent, more toxic and much more expensive.

China has reported the results of its first ever nationwide drug resistance survey, with documented proportions of MDR-TB of 5.7% among new cases and 25.6% among those previously treated. This survey confirms previous estimates that about 100 000 MDR-TB cases are emerging in China annually.

Time trend data on the proportion of MDR-TB among TB patients are available from 37 countries. While these data do not permit projections to be made of global trends in drug resistance, they reveal important changes in some settings. The proportion of MDR-TB among new TB cases appears to be in decline after peaking in the two Russian oblasts of Tomsk (in 2004) and Orel (in 2006). This likely reflects the success of TB control efforts and further indicates that the burden of MDR-TB can be curbed even in settings where it presents a serious problem. Similar declines have been documented in Hong Kong Special Administrative Region (China), Estonia, Latvia, Lithuania and the United States of America.

Despite the expansion of HIV testing and treatment globally, only 11 countries and 3 territories were able to

[1] The 114 countries exclude those reporting data on MDR-TB for which representativeness and accuracy are not assured.

provide continuous drug surveillance data stratified by HIV status for this report. Given the large proportion of missing data, it has not been possible to conclude whether an overall association between MDR-TB and HIV epidemics exists. However, TB patients living with HIV in four Eastern European countries – Estonia, Latvia, Lithuania and the Republic of Moldova – appear to be more at risk of harbouring MDR-TB strains. This finding concurs with the results contained in "Anti-tuberculosis drug resistance in the world: Report No. 4" of the survey conducted in another Eastern European country, Ukraine. Preliminary results of a survey conducted in Mozambique in 2007 have also documented a significant association; if confirmed, such a finding could have significant implications for control of the dual TB and HIV epidemics in Sub-Saharan Africa.

This report includes data on testing for XDR-TB from 46 countries that have reported continuous surveillance or representative surveys of second-line drug resistance among MDR-TB cases. Combining data from these countries, 5.4% of MDR-TB cases were found to have XDR-TB. Eight countries reported XDR-TB in more than 10% of MDR-TB cases; six of these countries were located in Eastern Europe and Central Asia. To date, a cumulative total of 58 countries have confirmed at least one case of XDR-TB.

Response

In May 2009, the World Health Assembly resolution WHA 62.15 (**Annex 1**) urged Member States "to achieve universal access to diagnosis and treatment of multidrug-resistant and extensively drug-resistant tuberculosis". As of October 2009, 20 of the 27 high MDR-TB burden countries[1] were updating their national TB control plans to include a MDR-TB component, in compliance with the WHA resolution. By the time of publication of this report, seven of these countries (Armenia, Azerbaijan, Georgia, Kazakhstan, the Republic of Moldova, Tajikistan and Ukraine) had shared their plans with WHO.

Although the cost of drugs alone for treating the average MDR-TB patient is 50 to 200 times higher than for treating a drug-susceptible TB patient and the overall costs for care have been found to be 10 times higher or more, treatment of MDR-TB has been shown to be a cost-effective intervention. According to the Stop TB Partnership's Global Plan to Stop TB, 2006–2015, 1.3 million MDR-TB cases will need to be treated in the 27 high MDR-TB burden countries between 2010 and 2015 at an estimated total cost of US$ 16.2 billion. The current level of funding in 2010 – including grants and other loans – in these countries is US$ 0.4 billion. Mobilization of both national and international resources is urgently required to meet the current and future need. The funding required in 2015 will be 16 times higher than the funding that is available in 2010. The Global Fund to Fight AIDS, Tuberculosis and Malaria is the single biggest source of external funding for TB control. Between 2002 and 2009, it supported the treatment of nearly 30 000 MDR-TB patients. In its ninth round, the Fund approved over US$ 400 million for the management of MDR-TB in 28 countries over 5 years.

The building of laboratory capacity to diagnose MDR-TB and undertake anti-TB drug resistance surveillance is one of the most important challenges that countries face in scaling-up care. In 24 of the 27 high MDR-TB burden countries, at least one laboratory could perform culture for *M. tuberculosis* and drug susceptibility testing (DST) to first-line drugs. Nevertheless, in many settings, diagnostic capacity cannot match the current needs. Due to lack of resources for building laboratory infrastructure, contemporary diagnostics for MDR-TB are available in less than a half of the high MDR-TB burden countries. The EXPAND-TB Project was created in response to this need. This multi-country initiative aims to scale-up and accelerate access to MDR-TB diagnostics in 27 countries through a network of partners, which include WHO, the Global Laboratory Initiative, the Foundation for Innovative New Diagnostics (FIND), the Stop TB Partnership's Global Drug Facility and UNITAID. The Project is funded by UNITAID and has a budget of US$ 87 million over 5 years.

In 2008, there were 29 423 MDR-TB cases reported throughout the world by 127 countries. These cases only represent about 7% of the MDR-TB cases estimated to have emerged that year. This reflects in part the limited use or availability of DST in countries due to lack of laboratory capacity. In the 27 high MDR-TB burden countries, only 1% of new TB cases and 3% of previously treated TB cases underwent DST.

Standards for treatment of MDR-TB patients are known to differ widely between countries. Apart from high-income countries that can allocate sufficient resources for MDR-TB care, lower income countries also have the opportunity to provide high-quality treatment meeting international standards for their patients through the Green Light Committee (GLC) Initiative. Since starting its work in 2000, the GLC has now approved treatment for over 63 000 MDR-TB patients in 111 programmes spanning 70 countries and territories. By the end of 2009, more than 19 000 patients with MDR-TB were reported to have been enrolled in

[1] In this report, the 27 high MDR-TB burden countries refer to those Member States estimated by WHO in 2008 to have had at least 4000 MDR-TB cases arising annually and/or at least 10% of newly registered TB cases with MDR-TB. The countries are: Armenia, Azerbaijan, Bangladesh, Belarus, Bulgaria, China, Democratic Republic of the Congo, Estonia, Ethiopia, Georgia, India, Indonesia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Myanmar, Nigeria, Pakistan, Philippines, Republic of Moldova, Russian Federation, South Africa, Tajikistan, Ukraine, Uzbekistan and Viet Nam.

44 GLC programmes. However, only about 1% of the estimated cases of MDR-TB emerging in 2008 were enrolled on treatment by the GLC programmes.

This report presents for the first time the treatment outcomes from all sites providing complete data for new and previously treated MDR-TB patients. Ten of the 27 high MDR-TB burden countries reported treatment outcomes. A total of 71 countries and territories provided complete data for treatment outcomes for 4 500 MDR-TB patients. In 48 sites documenting outcomes, patient management and drug quality conform to international standards, 26 being GLC-approved programmes and the rest high-income settings. Treatment success was documented in 60% of patients overall. Treatment success in MDR-TB patients overall remains low even in well-resourced settings because of a high frequency of death, default and treatment failure, as well as many cases reported without definitive outcomes.

Conclusion

More data on drug resistance have become available and estimates of the global MDR-TB burden have been improved. The recent experience in two oblasts of the Russian Federation has shown that even in settings gravely affected by drug resistance, it is possible to control MDR-TB. New findings presented in this report give reason to be cautiously optimistic that drug-resistant TB can be controlled.

While information available is growing and more and more countries are taking measures to combat MDR-TB, urgent investments in infrastructure, diagnostics, and provision of care are essential if the target established for 2015 – the diagnosis and treatment of 80% of the estimated M/XDR-TB cases – is to be reached.

Introduction

The introduction more than 50 years ago of multidrug therapy to treat tuberculosis (TB) patients was largely the response to the emergence of drug resistance (*1*). This report describes the global progress that has been made to control and prevent drug-resistant TB. It provides an up-to-date description of activities undertaken globally for the surveillance and control of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) – referred to in this report as M/XDR-TB – focusing on the 27 high MDR-TB burden countries.

The outcomes of the Ministerial Meeting of high MDR-TB burden countries held in Beijing (China) in April 2009 (*2*) and the adoption in May 2009 by the 62nd World Health Assembly of Resolution WHA62.15 on MDR-TB and XDR-TB (**Annex 1**) are encouraging signs of the proactive environment in which countries are committed to addressing the M/XDR-TB epidemic. Resolution WHA62.15 urges countries "to achieve universal access to diagnosis and treatment of multidrug-resistant and extensively drug-resistant tuberculosis", including by "strengthening health information and surveillance systems to ensure detection and monitoring of the epidemiological profile of multidrug-resistant and extensively drug-resistant tuberculosis and monitor achievement in its prevention and control".

Part I of this report provides a comprehensive and up-to-date assessment of the status of the M/XDR-TB epidemic at global, regional and country levels, following up on the series of reports on anti-TB drug resistance in the world published by the World Health Organization (WHO) in 1997 (*3*), 2000 (*4*), 2004 (*5*) and 2008 (*6*). Since 1994, WHO – within the framework of the Global Project on Anti-Tuberculosis Drug Resistance Surveillance – has collected data on drug-resistant TB from countries worldwide. The accumulated database includes information from 114 countries and 6 territories and serves as a common platform for the evaluation at country, regional and global levels of the size of the epidemic and its trends. From 2006 to 2009, data on XDR-TB have been included. Data are collected from countries with continuous surveillance systems based on routine testing of all TB patients for drug resistance and from surveys of representative samples of patients in countries or territories that do not routinely test all patients for drug resistance. This information is critical for planning purposes and for monitoring the scale-up of MDR-TB treatment programmes.

This report highlights the importance of establishing or strengthening continuous national surveillance systems for drug resistance, as articulated in Resolution WHA62.15 (**Annex 1**) and emphasized in guidelines published by WHO for surveillance of drug resistance in TB (*7*).

Part II describes global efforts to diagnose and treat patients with drug-resistant TB, the status of political momentum and country plans to control the M/XDR-TB epidemic and the funding situation of high MDR-TB burden countries. Programmatic management of M/XDR-TB is complex and requires political commitment, strategic planning, careful implementation and monitoring of activities, and adequate human and financial resources.

Countries face enormous hurdles in accelerating access to diagnostic and treatment services for drug-resistant TB, and previous efforts to address this epidemic have clearly been insufficient. Data from selected countries suggest that epidemiological impact is possible when certain conditions are met, namely political commitment and sound use of available tools. Greater political commitment by national health authorities in addressing M/XDR-TB has emerged, giving reason to be optimistic. However, while pledges have been made and plans have been drawn, translating these commitments into actual treatment of patients with M/XDR-TB remains limited to a few thousand patients worldwide.

The aim of this report is to present the latest status of the global burden of drug resistance and the global response. Its goal is to foster urgent action of the need to save lives and prevent further transmission of this lethal condition.

PART I

Surveillance of M/XDR-TB

1.1 Geographical coverage of anti-TB drug resistance data

Since the establishment in 1994 of the Global Project on Anti-Tuberculosis Drug Resistance Surveillance, data on drug resistance have been systematically collected and analysed from 114 countries worldwide (59% of all countries of the world). These data have been generated following three main principles:

- reported data are representative of TB cases in the country or geographical setting under study;
- drug resistance among new TB cases is clearly distinguished from drug resistance among previously treated TB cases; and
- laboratory methods for anti-TB drug susceptibility testing (DST) are selected from among those that are recommended by WHO and all laboratory processes are quality-assured in cooperation with a partner supranational reference laboratory.

The Supranational Reference Laboratory Network[1] expanded to include three additional laboratories in 2007–2009 and now comprises 28 laboratories worldwide (**Map 1**). This network acts as a global mechanism to ensure the quality of laboratory data through a system of proficiency testing.

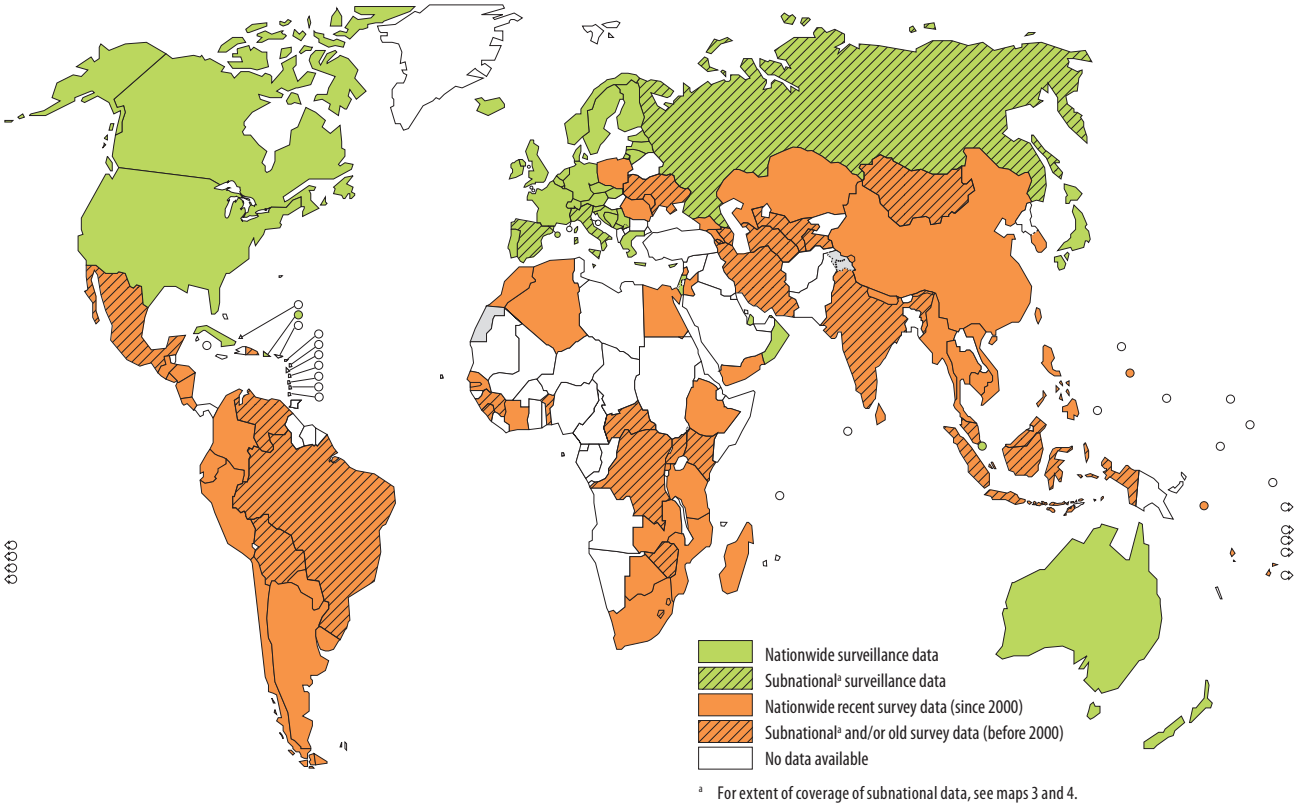
In 42 countries (37% of all countries), continuous surveillance systems based on routine diagnostic DST of all patients are in place; 3 of these countries produce data only at subnational level (**Map 2**). The remaining 72 countries (63% of all countries assessed so far) rely on periodic surveys[2] of representative samples of pa-

MAP 1 Distribution of supranational reference laboratory network, 2009

[1] For the list of supranational reference laboratories, visit the WHO web site at: http://www.who.int/tb/challenges/mdr/srl_network_mar10.pdf.

[2] Surveys are discrete studies measuring drug resistance among a specially-designed sample of TB cases representative of an entire population of TB cases.

MAP 2 Characteristics of available data on drug resistance



[a] For extent of coverage of subnational data, see maps 3 and 4.

tients. Of these 72 countries, 47 have conducted a nationwide survey since 2000 and 25 have conducted a survey only at the subnational level (state, province, or district) or have not repeated a survey in the past decade, or both.

No reliable and representative information on proportions and patterns of drug-resistant TB is yet available in 79 countries (41% of all countries of the world).

New data contained in this report

The understanding of the magnitude of and trends in drug-resistant TB continues to grow. Compared with the 4th report on anti-tuberculosis drug resistance published by WHO in 2008 (*6*), this document provides updated information from:

- 30 countries and 3 territories conducting continuous surveillance;
- 5 countries that have conducted surveys.

One country (Tajikistan) reported drug resistance data for the first time. Updated data on trends are available from 37 countries. In addition, more data are available on XDR-TB (see section 1.5 "Resistance to second-line anti-TB drugs, including XDR-TB").

Two high MDR-TB burden countries (China and the Russian Federation) have made remarkable progress in better understanding the epidemiology of drug-resistant TB. In 2007, China conducted its first nationwide drug resistance survey, and the Russian Federation is moving steadily towards high-quality surveillance of drug-resistant TB.

Major gaps remain in geographical areas covered and epidemiological questions to be answered. Since 1994, only 59% of all countries globally have been able to collect data on drug resistance at national or subnational level. There is therefore an urgent need to obtain information, particularly from the African continent and those high MDR-TB burden countries where data have never been reported according to WHO guidelines: Bangladesh, Belarus, Kyrgyzstan, Pakistan and Nigeria. Moreover, countries need to expand the scope of their surveys to cover entire populations, repeat surveys are needed to better understand trends in drug resistance and countries need to move towards adopting systematic continuous surveillance.

1.2 Resistance to first-line anti-TB drugs, including MDR-TB

Of 114 countries that provided information between 1994 and 2009 on resistance to first-line anti-TB drugs, 109 countries reported data on resistance occurring among new TB cases. Of these 109 countries, 102 also provided data among previously treated cases. Five countries (Australia, the Democratic Republic of the Congo, Fiji, Qatar and the Solomon Islands) did not report drug resistance data disaggregated by treatment

TABLE 1 Number of countries reporting data on resistance to first-line anti-TB drugs, by WHO region

WHO region (no. of countries)	No. of countries reporting first-line anti-TB drug resistance (%)
African (46)	22 (48)
Americas (35)	20 (57)
Eastern Mediterranean (21)	8 (38)
European (53)	44 (83)
South-East Asia (11)	6 (55)
Western Pacific (27)	14 (52)
Total (193)	**114 (59)**

history (i.e. for new and previously treated cases) but provided data for all TB cases combined. Countries reporting data on first-line drug resistance are distributed in the 6 WHO regions (**Table 1**).

In addition to the 114 countries reporting first-line drug resistance data, 4 territories reported data disaggregated by new and previously treated cases: Hong Kong Special Administration Region of China (China, Hong Kong SAR), Macao Special Administrative Region of China (China, Macao SAR), the Northern Mariana Islands and Puerto Rico. Guam and New Caledonia reported these data only for all TB cases combined.

The proportion of MDR-TB among new TB cases reported globally ranges from 0% to 28.3% (**Map 3**). Since 2000, no country outside Eastern Europe and Central Asia has reported proportions of MDR-TB among new cases exceeding 6% (for countries reporting more than 10 MDR-TB cases). While the TB case populations of China and India may have proportions of MDR-TB lower than Eastern European and Central Asian countries, the sheer sizes of the two countries' TB case populations result in the highest estimated numbers of MDR-TB cases emerging annually in these two countries: approximately 100 000 cases each.

The Russian Federation, which was able to report high-quality continuous surveillance data from 12 of its oblasts and republics, reported proportions of 23.8–28.3% MDR-TB among new TB cases in three of its oblasts in the north-western part of the country. Other Russian oblasts reported proportions of MDR-TB as low as 5.4% among new TB cases.

Proportions of MDR-TB exceeding 12% among new TB cases (in countries reporting more than 10 MDR-TB cases) have been documented in the following countries or subnational areas:

- Azerbaijan (Baku city, 22.3%; 95% confidence interval (CI): 18.5–26.6) in 2007
- Estonia (15.4%) in 2008
- Kazakhstan (14.2%; 95% CI: 10.8–18.3) in 2001
- Latvia (12.1%) in 2008
- Republic of Moldova (19.4%; 95% CI: 16.5–22.6) in 2006
- Russian Federation (Bryansk Oblast, 12.9%, Tomsk Oblast, 13.0%, Vladimir Oblast, 14.0%, Republic of Chuvashia, 14.2%, Mary El Republic, 16.1%, Belgorod Oblast, 19.2%, Kaliningrad Oblast, 19.3%, Ivanovo Oblast, 20.0%, Arkhangelsk Oblast, 23.8%, Pskov Oblast, 27.3% and Murmansk Oblast, 28.3%) in 2008
- Tajikistan (Dushanbe city and Rudaki district, 16.5%) in 2009
- Ukraine (Donetsk Oblast, 16.0%; 95% CI: 13.6–18.6) in 2006
- Uzbekistan (Karakalpakstan, 13.2%; 95% CI: 10.8–18.3) in 2002 and (Tashkent, 14.8%; 95% CI: 10.2–20.4) in 2005.

Estonia, Latvia, the Russian Federation and Tajikistan have reported these data to WHO since 2008, the year of publication of the 4th report on anti-tuberculosis drug resistance surveillance (*6*).

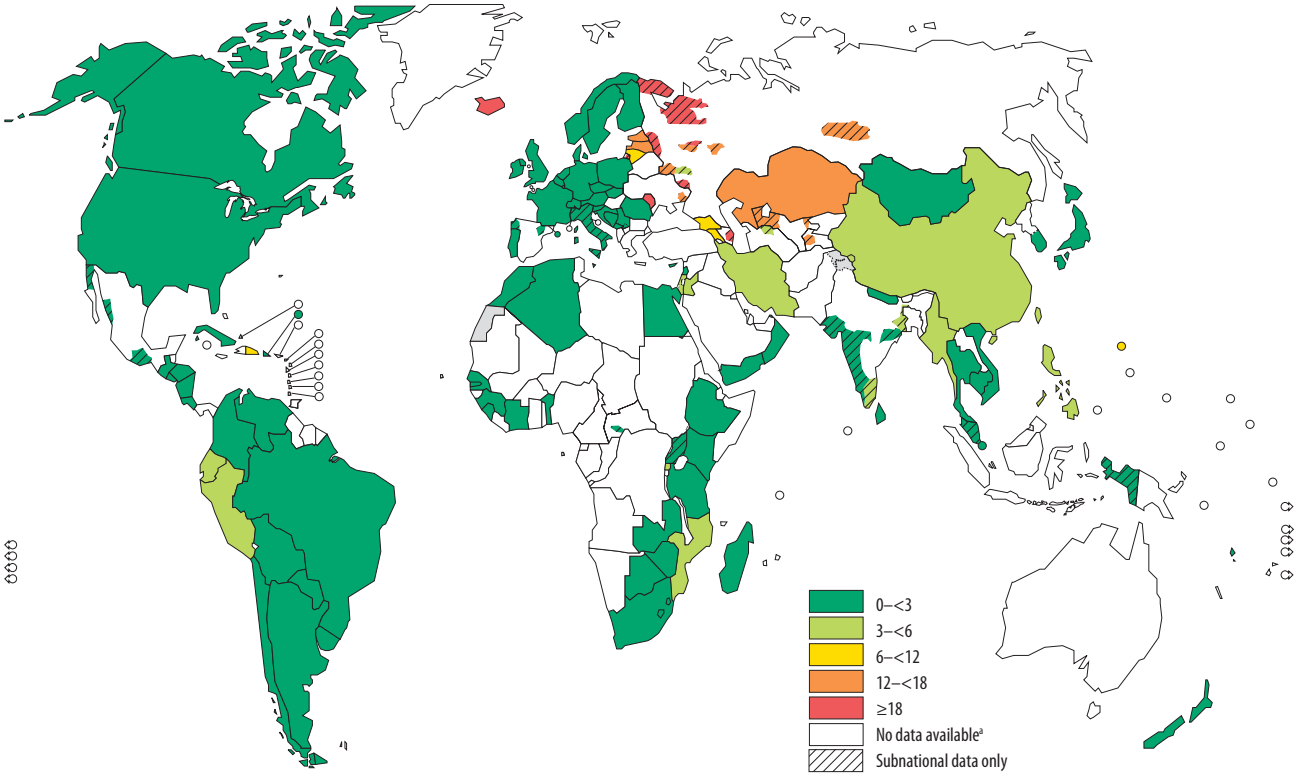
Several countries that reported Class B continuous drug resistance surveillance data in 2008 (see section 1.2.1 "data generated from continuous surveillance") show nationwide or subnational proportions of MDR-TB among new TB cases exceeding 12%. These include Belarus (16.7%), Kazakhstan (24.7%), the Republic of Moldova (24.8% in 2008) and the Russian Federation (countrywide, 14.0%, plus Ryazan Oblast, 12.4%, Tyumen Oblast, 12.7%, Vologda Oblast, 13.4%, Altai Republic, 18.9%, Novosibirsk Oblast, 22.2%, Yamalo-Nenets Autonomous Okrug 26.3%, and Republic of Karelia, 29.9%). The representativeness and accuracy of these sets of data are not assured, and are therefore not included in **Map 3**; however, they provide a basis for an approximation of the MDR-TB proportion.

The proportion of MDR-TB among previously treated TB cases reported globally ranges from 0% to 61.6% (**Map 4**). The countries or subnational areas with proportions of MDR-TB equal to or exceeding 50% include (for countries reporting more than 10 MDR-TB cases):

- Azerbaijan (Baku city, 55.8%; 95% CI: 49.7–62.4) in 2007
- Kazakhstan (56.4%; 95% CI: 50.8–61.9) in 2001
- Republic of Moldova (50.8%; 95% CI: 48.6–53.0) in 2006
- Russian Federation (Arkhangelsk Oblast, 58.8%; Belgorod Oblast, 51.6%; Ivanovo Oblast, 57.7%; Pskov Oblast, 50.0%; Tomsk Oblast, 53.8%) in 2008
- Tajikistan (Dushanbe city and Rudaki district, 61.6%) in 2009
- Uzbekistan (Tashkent, 60.0%; 95% CI: 48.8–70.5) in 2005.

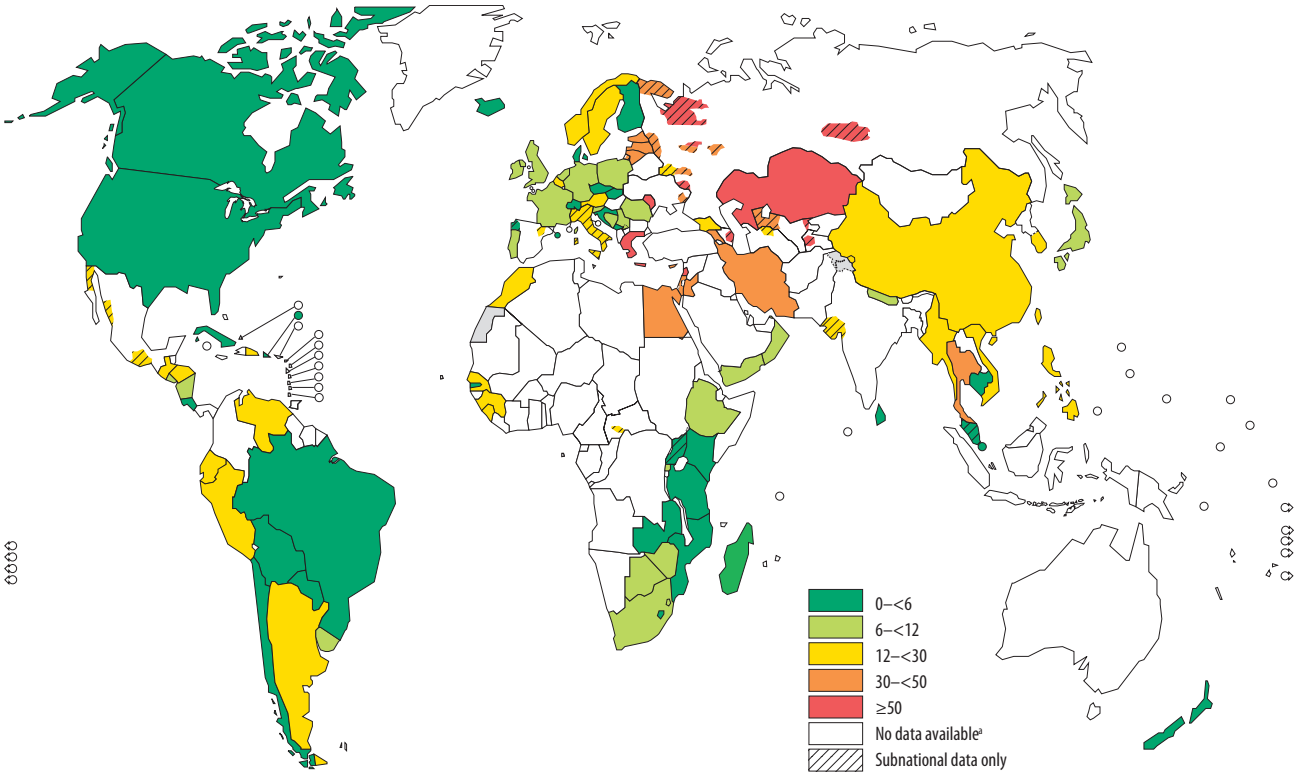
The Russian Federation and Tajikistan have reported these data to WHO since 2008, the year of publication

MAP 3 Distribution of proportion of MDR-TB among new TB cases, 1994–2009



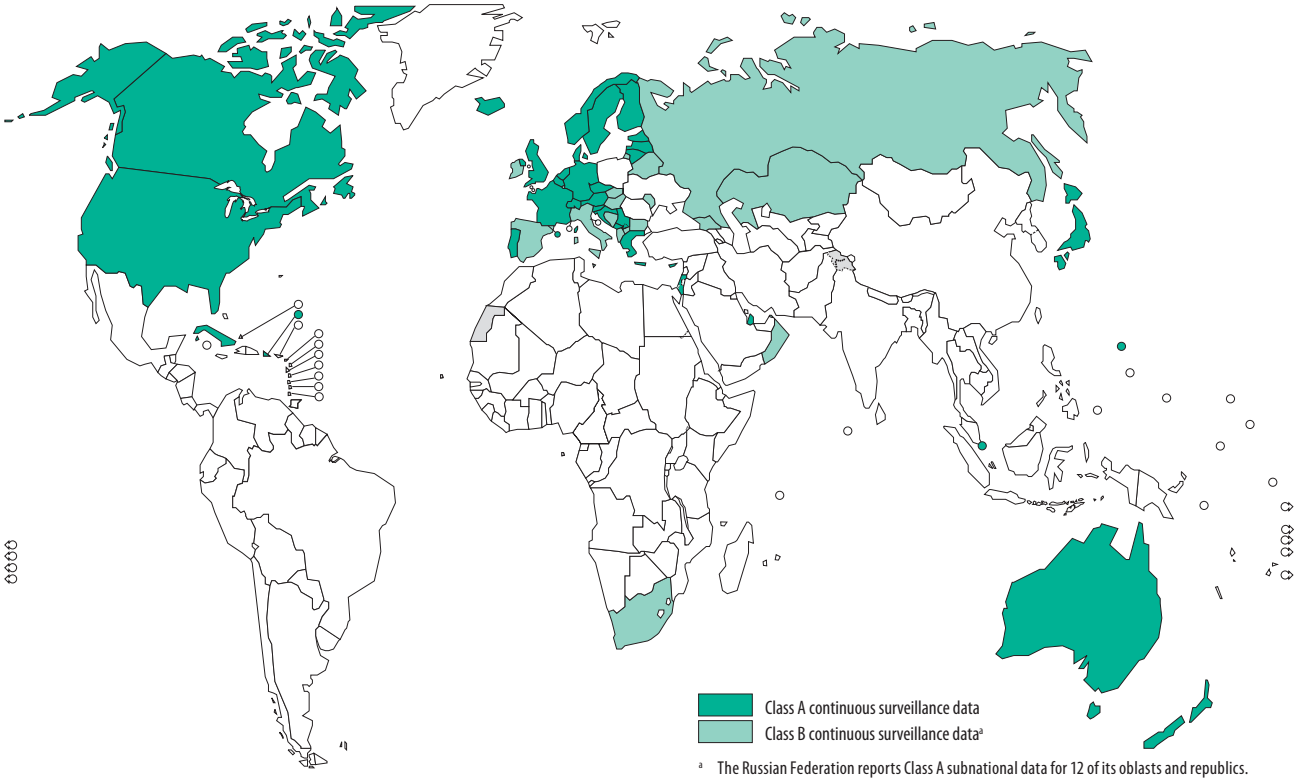
[a] Australia, Democratic Republic of the Congo, Fiji, Guam, New Caledonia, Solomon Islands and Qatar reported data on combined new and previously treated cases.

MAP 4 Distribution of proportion of MDR-TB among previously treated TB cases, 1994–2009



[a] Australia, Democratic Republic of the Congo, Fiji, Guam, New Caledonia, Solomon Islands and Qatar reported data on combined new and previously treated cases.

MAP 5 Distribution of countries with Class A and Class B continuous drug resistance surveillance data



[a] The Russian Federation reports Class A subnational data for 12 of its oblasts and republics.

of the 4th report on anti-tuberculosis drug resistance surveillance (*6*). The proportion of MDR-TB among previously treated TB cases reported in Dushanbe city and the Rudaki district of Tajikistan is the highest proportion ever reported to WHO for a subnational area.

Also in 2008, the Republic of Moldova reported new data showing 61.0% of MDR-TB among previously treated cases. This set of data is considered Class B continuous surveillance data and was therefore not included in **Map 4**.

The data provided in this report confirm that the highest proportions of MDR-TB are found in countries of Eastern Europe and Central Asia. These high proportions explain in part the slow progress made in Eastern European and Central Asian countries in reaching the Millennium Development Goal target of halving TB mortality rates by 2015 compared with their levels of 1990 (*8*).

1.2.1 Data generated from continuous surveillance

Continuous surveillance of drug resistance based on the routine testing of TB patients allows for systematic and ongoing collection of data and analysis for appropriate and timely public health response. Such surveillance allows not only for continuous information on drug resistance patterns among patient groups but also for accurate detection of trends.

Countries performing continuous drug resistance surveillance were classified into two groups based on the representativeness and accuracy of the data reported (**Map 5**). Indicators used to define data as "Class A" or "Class B" are: case detection, culture positivity, DST coverage, and DST accuracy (see Methods section in **Annex 2**). Data quality indicators used to categorize countries among those with Class A and Class B surveillance data are provided in **Annex 3**. The Russian Federation reported both Class A and Class B subnational data, and Class B nationwide data.

Annex 4 presents the most recent data on proportions of TB patients with drug-resistant strains in countries that have conducted continuous surveillance since the time of publication of the 4th report on anti-tuberculosis drug resistance in 2008 (*6*). Data are stratified as Class A or Class B. Countries not meeting the criteria for reporting Class A or Class B data are not included in the table. Within Class categories, countries are stratified by status as high-income countries or non high-income countries, as defined by the World Bank on 1 July 2009.[1]

In Chile and part of Bangladesh (41% of the country in the areas supported by the Damien Foundation), DST is conducted routinely among all previously treated TB cases (**Table 2**). This is because TB cases with a history of previous TB treatment are significantly more likely

[1] World Bank web site on country classifications: http://go.worldbank.org/K2CKM78CC0; accessed March 2010.

TABLE 2 Countries and areas reporting drug resistance surveillance data from previously treated TB cases since 2008

Country or area	WHO region	Year	Previously treated cases				
			Cases with DST results (H+R)	Multidrug resistant		Any isoniazid resistance	
				number	(%)	number	(%)
Bangladesh[a]	South-East Asia	2008	599	168	28.0	225	37.6
Chile	Americas	2008	199	6	3.0	17	8.5

[a] Areas covered by Damien Foundation Bangladesh (41% of the national population).
DST = drug susceptibility testing
H+R = isoniazid plus rifampicin

to have drug resistance than cases without such a history. Therefore, implementation of routine DST of such cases is considered a priority by WHO (*7*) and is a target for all countries by 2015 (*9*). DST of patients with no previous history of TB treatment should also be established for patients of higher risk groups, and for all TB cases when technical and financial capacity allow.

Less than one fourth of all countries (22%), the vast majority being high-income countries, have continuous surveillance systems in place. However, not all high-income countries report Class A continuous surveillance data. At the same time, no low-income country, and no country in the African Region (with the exception of South Africa) and the South-East Asia Region, has continuous drug resistance surveillance in place. However, the work performed by the Damien Foundation in Bangladesh to systematically carry out DST of all previously treated patients can be a model for low-income countries. Four middle-income countries (Latvia, Lithuania, Montenegro and Serbia) and 12 of the 83 federal subjects of the Russian Federation report Class A continuous surveillance data. Several high MDR-TB burden countries – including Belarus, Bulgaria, Kazakhstan, the Russian Federation, Georgia, the Republic of Moldova and South Africa – have surveillance systems in place that with additional efforts could soon provide high-quality nationwide drug resistance data. These countries should serve as models for other countries.

1.2.2 Data generated from surveys of representative samples of TB patients

Given the challenges and costs of establishing continuous surveillance of drug resistance (culture, DST, and associated logistic and human resource costs), many countries have the capacity only for periodic surveys of a representative sample of patients. When properly designed, implemented and with results correctly analysed, surveys can provide a sound estimation of the proportion of MDR-TB among the population under study and, when conducted periodically, the results allow analysis of trends over time.

In order to provide data of value for national planning purposes, surveys should be nationwide in scope and recent. Of the 72 countries that conducted drug resistance surveys between 1994 and 2009, more than one third (25 countries) have data only at the subnational level (state, provincial or district) or data that are older than 10 years (that is, surveys that were conducted before 2000), or both.

Since the publication in 2008 of the 4th report on anti-tuberculosis drug resistance (*6*), five countries have completed drug resistance surveys and reported results to WHO (**Table 3**). Tajikistan's subnational survey of its capital Dushanbe and neighbouring Rudaki district represents the first time the country has provided drug resistance data to WHO. The findings of the first nationwide drug resistance survey conducted in 2007 in China are among those presented in this report (**Table 3** and **Box 1**).

A total of 18 countries are currently conducting surveys: 13 are conducting nationwide surveys (Albania, Benin, Bolivia, Bulgaria, Ecuador, Egypt, Lesotho, Mexico, Nigeria, Poland, Swaziland, Togo and Zambia) and 5 (Belarus, Brazil, India, Indonesia, and Philippines) are conducting surveys at the subnational level (**Map 6**). Five of these countries have never conducted surveys before (Albania, Bulgaria, Belarus, Nigeria and Togo). Results from these surveys will be available in 2010–2011 and will greatly contribute to an understanding of the regional epidemiology of MDR-TB.

1.3 Risk factors for drug resistance: previous treatment, sex and HIV

Several potential demographic and clinical risk factors for MDR-TB were investigated for this report.

1.3.1 MDR-TB among previously treated patients: analysis by sub-categories

Prior exposure to anti-TB drugs is a well-established risk factor for drug resistance, as shown from surveys and surveillance systems worldwide (*6*). Previously treated TB cases, however, are a heterogeneous group composed of relapse cases (that is, patients in whom TB has recurred after successful treatment), cases having failed one or more treatment regimens using first-line and/or second-line drugs, cases returning after treatment default, and others. Accurate categorization of

TABLE 3 Countries and areas reporting data from drug resistance surveys since 2008

Country or area	WHO region	Year	New cases					Previously treated cases				
			Cases with DST results (H+R)	Multidrug resistant		Any isoniazid resistance		Cases with DST results (H+R)	Multidrug resistant		Any isoniazid resistance	
				number	% (95% CI)	number	% (95% CI)		number	% (95% CI)	number	% (95% CI)
Botswana[a]	African	2008	933	32	3.4% (2.4–4.8)	84	9.0% (7.2–11.0)	145	19	13.1% (8.1–19.7)	24	16.6% (10.9–23.6)
China	Western Pacific	2007	3 037	175	5.7% (4.6–7.1)	486	16.0% (14.7–17.4)	892	226	25.6% (21.7–30.0)	344	38.6% (35.4–41.8)
Mozambique[a]	African	2007	1 102	38	3.5% (2.2–4.8)	85	7.8% (6.0–9.6)	25	3	11.2% (0.0–25.2)	4	15.0% (0.0–31.0)
Myanmar	South-East Asia	2008	1 071	45	4.2% (3.1–5.6)	56	5.2% (4.0–6.7)	299	30	10.0% (6.9–14.0)	35	11.7% (8.3–15.9)
Tajikistan[b] (Dushanbe city and Rudaki district)	European	2009	139	23	16.5%	37	26.6%	125	77	61.6%	93	74.4%

[a] Preliminary results
[b] Survey employed a 100% diagnostic centre sampling strategy for 1 year
CI = confidence interval; DST = drug susceptibility testing; H+R = isoniazid plus rifampicin

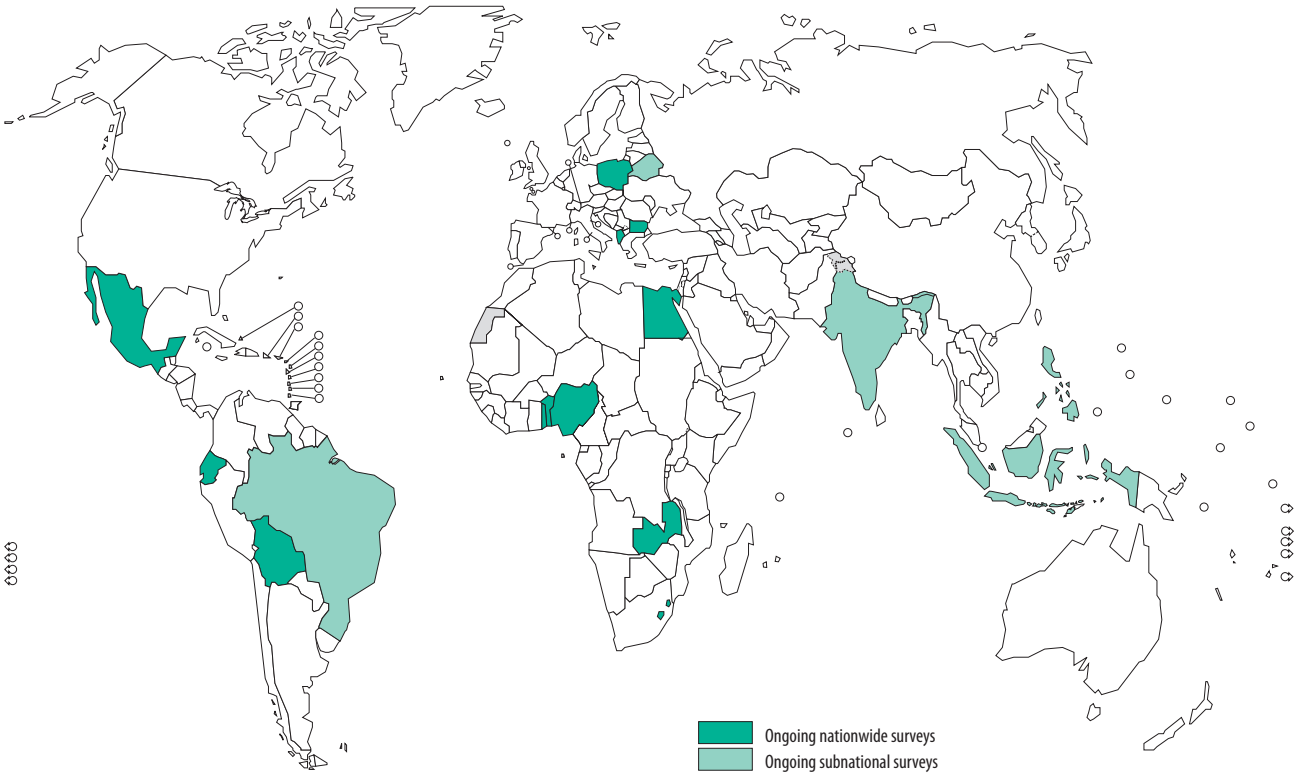
BOX 1

In focus: the 2007 drug resistance survey in China

China – a high MDR-TB burden country estimated to contribute 22% of the global burden of MDR-TB – conducted a nationwide drug resistance survey in 2007. While details about the survey design are not yet available, the values for drug resistance are very close to those estimated by WHO in the past from sub-national studies. The survey revealed a proportion of MDR-TB of 5.7% in new cases (95% CI: 4.6–7.1) and of 25.6% in previously treated cases (95% CI: 21.7–30.0). The overall proportion of MDR-TB among all cases tested was 8.3% (95% CI: 7.1–9.7). Resistance to second-line drugs was tested among all 401 patients whom were diagnosed with MDR-TB during the survey; XDR-TB was detected in 7.2% (95% CI: 4.9–10.2) of them.

This survey has given the country a better understanding of the burden of M/XDR-TB, which will help proper planning of implementation of treatment programmes.

MAP 6 Distribution of ongoing drug resistance surveys as of January 2010



previously treated patients into sub-categories is therefore useful for establishing more adequate treatment algorithms.

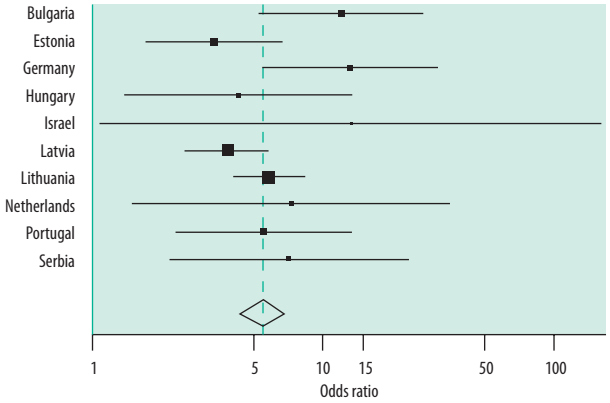
In 2008, a total of 17 countries conducting continuous surveillance reported data on MDR-TB disaggregated by relapse and new TB cases. Among the 10 countries that reported at least one case of MDR-TB among new and relapse cases, the proportion of MDR-TB among new cases was 1.5% (95% CI: 0.5–2.6) and among relapse cases was 7.9% (95% CI: 2.9–12.9). Relapse cases combined from all 10 sites had a 5.5 times higher odds of harbouring MDR-TB strains compared with new cases (95% CI: 4.4–6.8), after adjusting for the clustering effect at the country level (**Figure 1**).

Only a few countries are able to report on patients' MDR-TB status stratified by patients' sub-category of previous treatment, with the exception of relapse TB cases. Bangladesh, however, has reported important data by different retreatment subgroups (**Box 2**).

Based on the data from Bangladesh and from other published studies (*10*), it is clear that routine DST of patients who fail a treatment regimen should be a priority for all countries. This group of patients has the highest risk of MDR-TB, and design of retreatment regimens should as much as possible be based on DST results (*11*).

Patients failing a treatment regimen should be categorized according to whether the failed regimen was an initial regimen using only first-line drugs, a retreatment regimen using only first-line drugs, or a treatment regimen using second-line drugs.

FIGURE 1 Forest plot depicting the association between MDR-TB among relapse vs new TB cases in countries conducting continuous drug resistance surveillance and reporting at least one MDR-TB case among new and relapse TB cases, 2008



Note: Odds ratios are presented together with their corresponding confidence intervals to assess the association between MDR-TB and status as a relapse vs new case for each country separately. An estimated global odds ratio combining all available data is also presented (◊). The vertical **green** line at 1 shows no association between MDR-TB and status as a relapse vs new case. The more data that are available from each country, the bigger the square representing the point estimate of the odds ratio and the shorter the line across the square representing the confidence interval.

1.3.2 Association between sex and MDR-TB

In most countries (95% of those reporting), the majority of TB patients are male. However, differences in access to health-care services or exposure to other risk factors may result in male or female TB patients having different levels of risk for drug resistance.

Among the 38 countries and 3 territories providing drug resistance surveillance data stratified by sex, 27 countries and 2 territories reported at least one case of MDR-TB among male and female cases (**Figure 3**).

BOX 2

In focus: continuous surveillance among previously treated TB cases – a case study from Bangladesh

The Damian Foundation Bangladesh, a nongovernmental organization providing TB care in 26 districts of Bangladesh covering 41% of the national population, routinely conducts DST among all relapse cases, cases returning after default of treatment, and cases failing Category I and Category II treatment regimens. The collection and analysis of data in its surveillance system provide a model to other low-income countries, showing the feasibility and use of such a system.

In this TB treatment programme, 28% of the 599 previously treated cases notified in 2008 had confirmed MDR-TB. The data show a particularly high risk of MDR-TB among cases failing treatment. Among cases that failed an initial treatment regimen, 58% had MDR-TB. Among those that failed a Category II retreatment regimen, 91% had MDR-TB (**Figure 2**).

This type of analysis should be performed routinely by all countries in order to design effective retreatment regimens for each of the different categories of previously treated cases based on the relative risk of MDR-TB.

FIGURE 2 Proportion of MDR-TB among cases of relapse, default and failure of Category I and Category II treatment regimens in 26 districts of Bangladesh, 2008

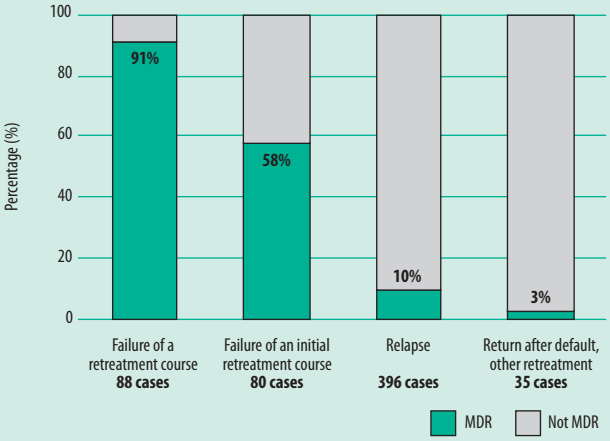
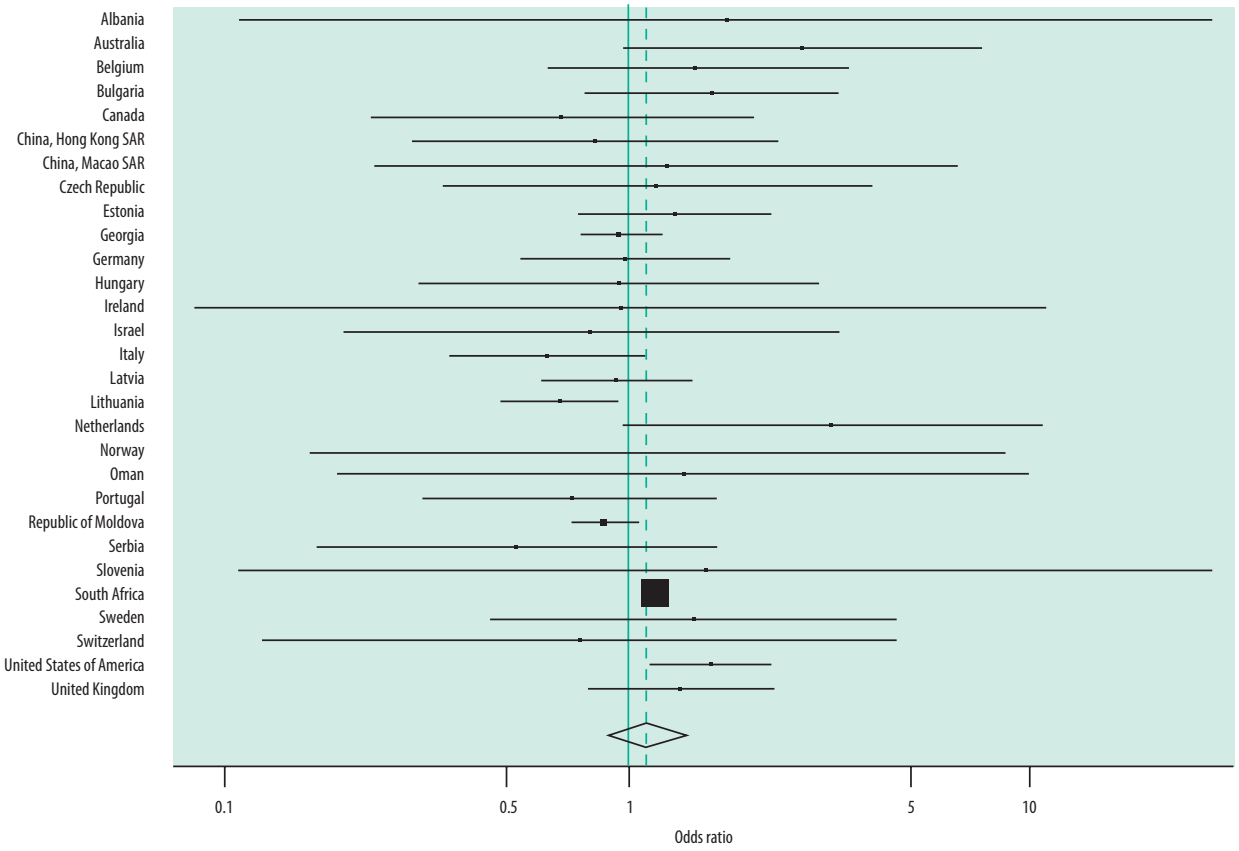


FIGURE 3 Forest plot depicting the association between sex (male vs female) and MDR-TB in countries and territories reporting at least one case of MDR-TB among male and female cases, 2008



Note: Odds ratios are presented together with their corresponding confidence intervals to assess the association between sex and MDR-TB for each country separately. An estimated global odds ratio combining all available data is also presented (◊). The vertical **green** line at 1 shows no association between sex and MDR-TB. The more data that are available from each country, the bigger the square representing the point estimate of the odds ratio and the shorter the line across the square representing the confidence interval.

Overall, combining data from these countries and territories (121 965; 58% males), and using the robust standard errors approach, the odds ratio of harbouring MDR-TB strains for female TB cases compared with male TB cases was 1.1 (95% CI: 0.9–1.4), showing no overall association between MDR-TB and the sex of the patient.

In South Africa, although a higher number of male than female MDR-TB cases were reported (4826 vs 4615 cases, respectively), data from a total of 81 794 TB patients with known sex (95% of all patients) indicate that female TB cases have a 1.2 times higher odds of harbouring MDR-TB strains than male TB cases. Data from Australia, the Netherlands and the United States of America also show a higher risk of MDR-TB in female patients. Conversely, in countries of the former Soviet Union, such as Lithuania, the odds are higher for male TB patients of harbouring MDR-TB strains, which may be associated with alcohol dependency and imprisonment.

While males predominate among TB cases in most countries, this analysis suggests that the overall risk of harbouring MDR-TB strains is not influenced by sex.

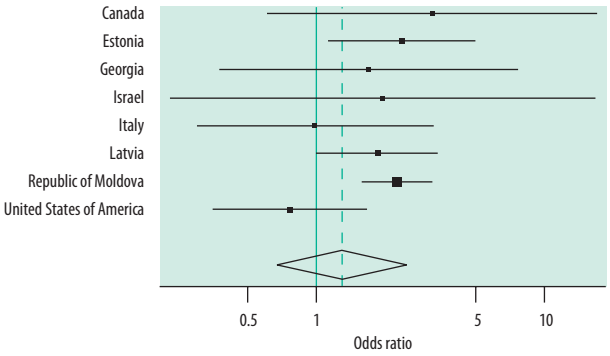
Nevertheless, it is important that countries record the sex of MDR-TB patients for later group analysis. Determining whether females or males in a country or geographical setting are more likely to have MDR-TB provides insight into the epidemiology of the disease, allowing for the development of targeted measures to improve access to care or reduce the risk of acquiring drug-resistant strains.

1.3.3 Association between HIV status and MDR-TB

Drug-resistant TB among people living with HIV have been widely documented in nosocomial and other congregate settings. To date, limited information has been available about the association of HIV and drug-resistant TB at a population level. The 4th report on anti-tuberculosis drug resistance reported a significant association between HIV-positive status and MDR-TB in two settings: Latvia and Donetsk Oblast of Ukraine (*6*).

Among the 11 countries and 3 territories providing continuous drug resistance surveillance data stratified by HIV status for this report, a total of 8 countries reported at least one case of MDR-TB among patients with HIV-positive and HIV-negative status (**Figure 4**).

FIGURE 4 Forest plot depicting the association between cases of HIV (positive vs negative) infection and MDR-TB in countries reporting at least one MDR-TB case among patients with HIV-positive and HIV-negative status



Note: Odds ratios are presented together with their corresponding confidence intervals to assess the association between HIV status and MDR-TB for each country separately. An estimated global odds ratio combining all available data is also presented (◊). The vertical **green** line at 1 shows no association between HIV status and MDR-TB. The more data that are available from each country, the bigger the square representing the point estimate of the odds ratio and the shorter the line across the square representing the confidence interval.

Given the large proportion of missing data, it has not been possible to conclude whether an overall association between MDR-TB and HIV epidemics exists.

However, based on the current data, HIV-positive TB patients in three Eastern European countries (Estonia, Latvia and the Republic of Moldova) appear to be more at risk of harbouring MDR-TB strains. This finding concurs with the results of the earlier reported survey conducted in Ukraine (*6*). Furthermore, in Lithuania – where drug resistance data could not be disaggregated by HIV-negative and unknown HIV status – HIV-positive TB patients had a 8.4 (95% CI: 2.7–28.2) times higher odds of harbouring MDR-TB strains than TB patients for whom HIV status was unknown, indicating a possible association of the two epidemics. In addition, preliminary results of a survey conducted in Mozambique in 2007 have also found a significant association.

Lack of an association between HIV status and MDR-TB in some settings can be due to low numbers of HIV-positive TB patients or patients with MDR-TB and consequent insufficient power in analysis. This may be a result of lack of testing of patients or of incomplete reporting of results.

There are several reasons why drug-resistant TB may be associated with HIV. Firstly, people living with HIV in Eastern Europe – particularly those infected earlier in the epidemic and whose weakened immune systems have since left them vulnerable to TB – frequently come from socially vulnerable populations, including injecting drug users. Socio-behavioural problems and/or lack of access to proper care may make these populations, as TB patients, vulnerable to developing drug resistance as a result of poor adherence to treatment or suboptimal treatment. Furthermore, people living with HIV may also be more likely to be exposed to MDR-TB patients, due either to increased hospitalizations in settings with poor infection control or association with peers who may have MDR-TB, including in penitentiary settings. Secondly, acquisition of rifampicin resistance among people living with HIV under treatment for TB may also be the result of anti-TB drug malabsorption, which has been documented in patient cohorts in settings of high HIV prevalence.

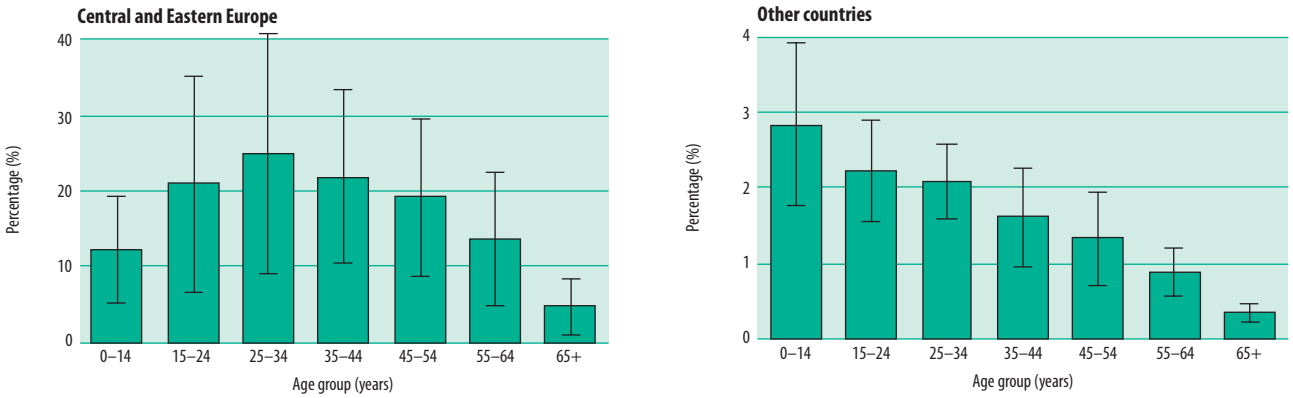
The epidemiological impact of HIV infection on the transmission of MDR-TB is still unclear and may depend on several factors. HIV-positive TB cases are more likely to be sputum smear negative, and therefore less likely to transmit TB. In addition, delayed diagnosis of drug resistance and unavailability of treatment (particularly in previous years) have led to high death rates in people living with HIV, which may also result in a lower rate of TB transmission. On the other hand, people living with HIV progress more rapidly to TB disease, and in settings where MDR-TB is prevalent (either among the general population or in a specific population such as a hospital or a district), this may lead to rapid development of a pool of drug-resistant TB patients.

Although there appears to be an association between drug-resistant TB and HIV infection in some Eastern European countries, the data are still limited to be able to determine whether there is an overlap between the MDR-TB and HIV epidemics worldwide. Unfortunately, the continuous surveillance data in this report come only from two regions, the European Region and the Region of the Americas, and no data are reported from countries with the highest prevalence of HIV infection. It is critical to include HIV testing in drug resistance surveys and in routine surveillance efforts in order to better understand the relationship between the two epidemics, which is key for optimal care of patients.

1.3.4 Association between age and MDR-TB

The number of cases of MDR-TB detected by age group of TB cases was provided by 27 countries/territories providing Class A continuous surveillance data and 7 countries providing Class B continuous surveillance data. In the 13 countries of Central and Eastern Europe (CEEUR), the frequency of MDR-TB was much higher in all age groups compared with the rest of the countries (all high-income) and peaked in young adulthood (**Figure 5**). In the high-income non-CEEUR group, frequency of MDR-TB declined linearly with age-group ($p<0.05$). This pattern suggests that in the countries of the former Soviet Union, where many MDR-TB cases are of local origin, the MDR-TB epidemic is a relatively recent phenomenon and bears the highest toll on young adults.

FIGURE 5 Percentage of MDR-TB cases by age group among all TB cases, by country group



1.4 Trends over time

Several settings conducting continuous surveillance have been reporting high quality data for many years (**Figure 6**).

Recent data from the Russian Federation show that in Orel and Tomsk oblasts absolute numbers and proportions of MDR-TB are decreasing after having reached a peak in 2004 and 2006, respectively. Similar decreasing trends have been documented in Arkhangelsk and Kaliningrad oblasts (*12*). This change of tendency is likely the result of efforts to diagnose and treat MDR-TB put in place in these oblasts since the late 1990s.

These data confirm that, if proper actions are taken, it is possible to substantially reduce the burden of MDR-TB even in settings where drug resistance is a serious problem. The fact that in these oblasts not only absolute numbers but also proportions of MDR-TB are decreasing demonstrates that it is possible to control MDR-TB even faster than TB.

This finding is a confirmation that MDR-TB can be controlled, as demonstrated in other settings such as the Baltic countries, China (Hong Kong SAR) and the USA. Since the late 1990s, three Baltic countries (Estonia, Latvia and Lithuania) have notified decreasing numbers of new and relapse TB cases annually. In Lithuania, the number of new TB cases with MDR-TB notified annually increased until 2005 but has decreased since then. As a result, the proportion of MDR-TB among new TB cases has undergone a slight but significant increase during 1999–2008, which from 2005 is a result of the number of drug-susceptible TB cases decreasing. In Estonia and Latvia, numbers of notified MDR-TB cases have fluctuated since 2005 and trends in the proportion of MDR-TB appear to be flat.

Since the mid-1990s, the number of notified TB and MDR-TB cases in China (Hong Kong SAR) and the USA has decreased. Significant decreases in the proportion of MDR-TB are evident in both settings, although the trend in the USA appears to have flattened since the late 1990s.

Interpreting trends in MDR-TB in most countries of the world faces some important limitations. In many countries that have conducted surveys, the study designs and the size of samples often have insufficient power to detect slight changes that may be important for the programme. Trends are more easily detected in countries or territories conducting routine DST of all TB cases.

The country data reported to WHO make it impossible at this time to conclude whether the MDR-TB epidemic worldwide is growing or shrinking. With an ever increasing number of high-quality surveys being implemented together with countries providing complete continuous surveillance data, the future will allow for a clearer understanding of global trends in drug resistance.

1.5 Resistance to second-line anti-TB drugs, including XDR-TB

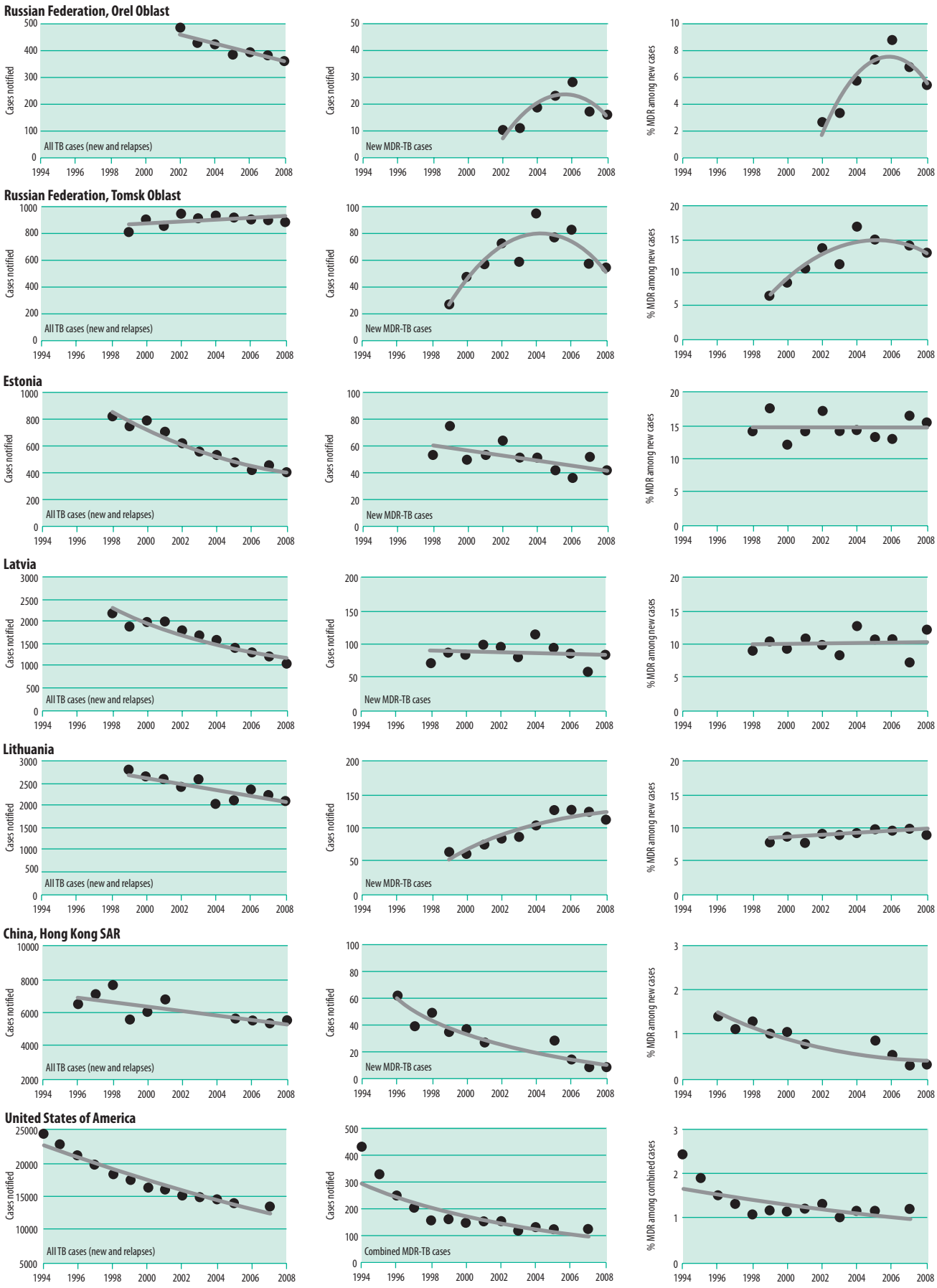
As of January 2010, 58 countries had reported to WHO at least one case of XDR-TB (**Map 7**).

In 2008, 963 cases of XDR-TB were reported to WHO globally from 33 countries compared with 772 cases from 28 countries in 2007. Many XDR-TB cases are believed to be never diagnosed due to weaknesses in laboratory capacity to test for resistance to second-line drugs.

A total of 46 countries, distributed across the six WHO regions (**Table 4**) have reported continuous surveillance or representative survey data on second-line drug resistance among MDR-TB cases. China (Hong Kong SAR) and China (Macao SAR) also reported data. **Annex 5** shows the reported numbers of XDR-TB and fluoroquinolone-resistant strains among MDR-TB cases tested for second-line drug susceptibility in countries conducting continuous surveillance and surveys.

The low numbers of XDR-TB cases reported in most settings (41 countries and areas in **Annex 5** report fewer than 10 cases) make it difficult to establish the proportion of XDR-TB among MDR-TB cases. Combining data from all 31 countries and areas reporting at least

FIGURE 6 Trends in absolute number of all TB cases (new & relapse), in absolute number of new MDR-TB cases, and in proportion of MDR-TB cases among new TB cases in selected countries and territories, 1994–2008



MAP 7 Distribution of countries and territories reporting at least one case of XDR-TB as of January 2010

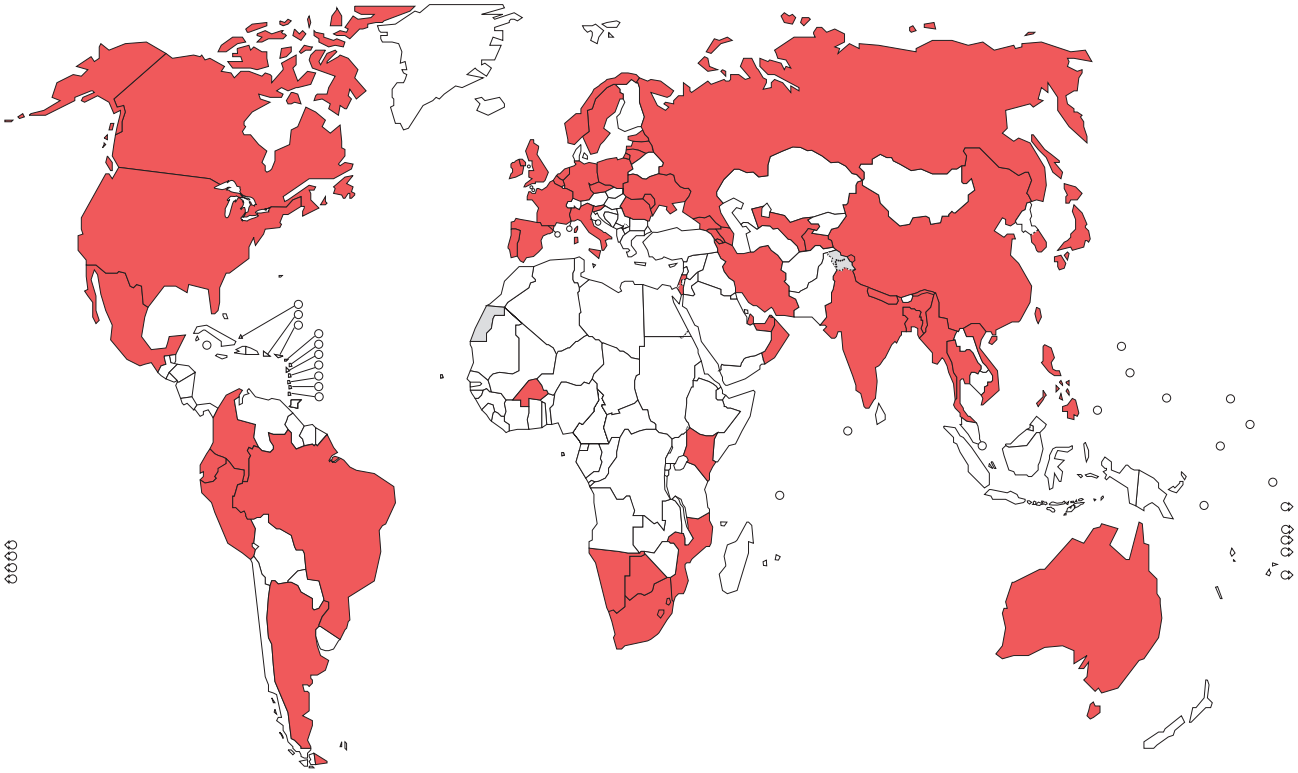


TABLE 4 Number of countries reporting data on resistance to second-line anti-TB drugs, by WHO region

WHO region (no. of countries)	No. of countries reporting second-line anti-TB drug resistance (%)
African (46)	3 (7)
Americas (35)	3 (9)
Eastern Mediterranean (21)	1 (5)
European (53)	31 (58)
South-East Asia (11)	2 (18)
Western Pacific (27)	6 (22)
Total (193)	**46 (24)**

one case of XDR-TB, the overall proportion of MDR-TB cases with XDR-TB, adjusting for the clustering effect at country level, was 5.4% (95% CI: 3.4–7.5). This finding is in line with previous publications (*13*, *14*).

Of the 27 high MDR-TB burden countries, only 2 (Estonia and Latvia) routinely test MDR-TB cases for second-line drug susceptibility; 11 have not yet reported a case of XDR-TB, which is more likely due to the result of lack of laboratory capacity than actual absence of XDR-TB strains.

In certain settings and countries with low burdens of TB and MDR-TB, such as the Czech Republic, Ireland, Israel, Poland, Slovenia and Aragon State in Spain, the high proportion of MDR-TB cases with XDR-TB is the result of detecting a single case of XDR-TB.

A total of 8 countries and settings that have tested more than 10 MDR-TB cases for second-line drug resistance have proportions of XDR-TB among MDR-TB cases higher than 10%: Azerbaijan, Baku city (12.8%), Estonia (12.5%), Japan (30.9%), Latvia (14.8%), Lithuania (14.5%), South Africa (10.5%), Tajikistan, Dushanbe city and Rudaki district (21.0%) and Ukraine, Donetsk Oblast (15.0%).

As more and more patients with MDR-TB are diagnosed and started on treatment using second-line drugs, collection and analysis of data on second-line resistance is of outmost importance for optimal patient care.

1.6 Estimated global burden of MDR-TB

Available drug resistance surveillance data were used to estimate the number of MDR-TB cases occurring each year around the world and, together with case fatality data, were used to estimate MDR-TB mortality.

1.6.1 Estimated annual number of MDR-TB cases emerging globally

The estimated global number of incident MDR-TB episodes among new and relapse TB cases in 2008 was between 310 000 and 430 000 episodes, with the best estimate at 360 000 episodes. The estimated global number of incident acquired MDR-TB episodes was between 83 000 and 110 000 episodes, with the best estimate at 94 000 episodes. Previously treated TB cases

TABLE 5 Estimated number of MDR-TB cases (primary and acquired) in 2008, by WHO region

WHO region	Estimated number of MDR-TB cases (primary and acquired) in 2008 (95% confidence interval)
African	69 000 (53 000–110 000)
Americas	8 200 (7 300–9 300)
Eastern Mediterranean	24 000 (11 000–81 000)
European	81 000 (73 000–90 000)
South-East Asia	130 000 (110 000–170 000)
Western Pacific	120 000 (100 000–140 000)
Total	**440 000 (390 000–510 000)**

may have acquired MDR during the course of treatment (numbers estimated under the term acquired MDR) or may have been infected with an MDR strain in the first place. Primary MDR-TB episodes among retreatment cases are counted among MDR-TB episodes among new and relapse cases but are not counted again among retreatment cases.

Overall, there were an estimated 390 000–510 000 cases of MDR-TB (primary and acquired) arising in 2008, with the best estimate at 440 000 cases. Among all incident TB cases globally, 3.6% (95% CI: 3.0–4.4) are estimated to have MDR-TB.

Annex 2 details the methods used to derive estimates of the global burden of MDR-TB. Methods were updated to incorporate the uncertainty framework used for estimates published by WHO of the burden of TB disease (*8*). The difference between the global estimate of MDR-TB cases published in 2007 and this current estimate reflects the reporting of new drug resistance data, changes in TB incidence and the use of updated methods. It should not, therefore, be considered as the result of a true decline.

Table 5 shows the estimated number of MDR-TB cases (primary and acquired) by WHO region. **Annex 6** gives the estimated proportions of TB cases with MDR-TB and the absolute numbers of MDR-TB cases by country.

China and India account for almost 50% of the esti-

TABLE 6 Estimated proportion and number of MDR-TB cases in the 27 MDR-TB high burden countries, 2008

Country	Source of estimates	% MDR among new TB cases (95% CI)	% MDR among previously treated TB cases (95% CI)	Number of MDR-TB among incident new and relapse TB cases (95% CI)	Number of incident acquired MDR-TB cases (95% CI)	Number of MDR-TB among incident total TB cases (95% CI)
Armenia	DRS, 2007	9.4 (7.3–12.1)	43.2 (38.1–48.5)	260 (180–350)	220 (160–290)	480 (380–580)
Azerbaijan	DRS,[a] 2007	22.3 (19.0–26.0)	55.8 (51.6–59.9)	2 800 (2 200–3 500)	1 200 (940–1 600)	4 000 (3 300–4 700)
Bangladesh	model	2.2 (0.0–5.6)	14.7 (0.0–39.6)	8 900 (1 000–19 000)	940 (0–2 700)	9 800 (1 000–19 000)
Belarus	model	12.5 (0.0–25.3)	42.1 (11.9–72.2)	660 (130–1 200)	140 (12–300)	800 (260–1 300)
Bulgaria	model	12.5 (0.0–25.3)	42.1 (11.9–72.2)	440 (81–810)	18 (2–38)	460 (99–810)
China	DRS, 2007	5.7 (5.0–6.6)	25.6 (22.6–28.3)	84 000 (65 000–106 000)	15 000 (12 000–20 000)	100 000 (79 000–120 000)
Democratic Republic of the Congo	model	1.8 (0.0–4.3)	7.7 (0.0–18.1)	5 100 (470–11 000)	570 (0–1 500)	5 600 (530–11 000)
Estonia	DRS, 2008	15.4 (11.6–20.1)	42.7 (32.1–53.9)	85 (64–110)	9 (5–13)	94 (71–120)
Ethiopia	DRS, 2005	1.6 (0.9–2.7)	11.8 (6.4–21.0)	5 000 (2 600–8 300)	160 (61–310)	5 200 (2 400–8 000)
Georgia	DRS, 2006	6.8 (5.2–8.7)	27.4 (23.7–31.4)	360 (270–460)	310 (240–380)	670 (550–780)
India	DRS,[a] 2005	2.3 (1.8–2.8)	17.2 (14.9–19.5)	55 000 (40 000–74 000)	43 000 (33 000–56 000)	99 000 (79 000–120 000)
Indonesia	DRS,[a] 2004	2.0 (0.5–6.9)	14.7 (0.0–39.6)	8 900 (1 100–25 000)	360 (0–1 000)	9 300 (0–21 000)
Kazakhstan	DRS, 2001	14.2 (11.0–18.2)	56.4 (50.9–61.8)	5 300 (3 900–6 900)	2700 (2 100–3 500)	8 100 (6 400–9 700)
Kyrgyzstan	model	12.5 (0.0–25.3)	42.1 (11.9–72.2)	1 200 (230–2 300)	140 (13–310)	1 400 (350–2 400)
Latvia	DRS, 2008	12.1 (9.9–14.8)	31.9 (24.9–39.9)	160 (130–200)	4 (2–6)	170 (140–200)
Lithuania	DRS, 2008	9.0 (7.5–10.7)	47.5 (42.9–52.2)	270 (210–330)	68 (55–83)	330 (270–390)
Myanmar	DRS, 2007	4.2 (3.2–5.6)	10.0 (7.1–14.0)	8 900 (6 300–12 000)	450 (180–770)	9 300 (6 400–12 000)
Nigeria	model	1.8 (0.0–4.3)	7.7 (0.0–18.1)	9 300 (860–20 000)	1 600 (0–4 300)	11 000 (1 300–20 000)
Pakistan	model	2.9 (0.0–8.0)	35.4 (0.0–75.1)	14 000 (1 200–30 000)	1 700 (0–3 800)	15 000 (1 200–29 000)
Philippines	DRS, 2004	4.0 (3.0–5.5)	20.9 (14.8–28.7)	11 000 (7 300–15 000)	2 000 (1 100–3 000)	13 000 (8 900–17 000)
Republic of Moldova	DRS, 2006	19.4 (16.8–22.2)	50.8 (48.7–53.0)	1 500 (1 200–1 800)	620 (490–770)	2 100 (1 700–2 400)
Russian Federation	DRS,[a] 2008	15.8 (11.9–19.7)	42.4 (38.1–46.7)	26 000 (20 000–34 000)	12 000 (8 700–15 000)	38 000 (30 000–45 000)
South Africa	DRS, 2002	1.8 (1.5–2.3)	6.7 (5.5–8.1)	10 000 (7 500–13 000)	2 800 (1 900–3 900)	13 000 (10 000–16 000)
Tajikistan	DRS,[a] 2008	16.5 (11.3–23.6)	61.6 (52.8–69.7)	2 500 (1 600–3 500)	1 500 (1 100–2 100)	4 000 (2 900–5 100)
Ukraine	DRS,[a] 2002	16.0 (13.8–18.3)	44.3 (40.0–48.7)	8 200 (6 500–10 000)	440 (340–570)	8 700 (6 800–11 000)
Uzbekistan	DRS,[a] 2005	14.2 (10.4–18.1)	49.8 (35.8–63.8)	5 700 (4 000–7 700)	3 000 (1 700–4 400)	8 700 (6 500–11 000)
Viet Nam	DRS, 2006	2.7 (2.0–3.6)	19.3 (14.5–25.2)	5 600 (3 700–8 100)	280 (180–420)	5 900 (3 800–8 100)

[a] Estimates based on subnational drug resistance data.

DRS = drug resistance surveillance or survey data; CI = confidence interval; MDR-TB = multidrug-resistant TB

mated global number of incident MDR-TB cases. **Table 6** lists the 27 countries with a high MDR-TB burden responsible for 85% of the global estimated burden of MDR-TB.

These estimates refer to cases of MDR-TB that arose in 2008 and do not reflect the number of prevalent cases of MDR-TB. The number of prevalent cases of MDR-TB in many parts of the world is estimated to be much higher than the number arising annually.

Using the available data generated from continuous surveillance and surveys as the foundation, mathematical modelling has allowed for the calculation of a global estimate of MDR-TB. By increasing the number of countries providing up-to-date nationally representative data via continuous surveillance and surveys, the global estimates become more accurate and give a better picture of the current state of the epidemic worldwide. This is particularly a priority in Africa (**Box 3**), where large gaps in information remain on the size of the MDR-TB epidemic.

1.6.2 Estimated mortality of MDR-TB

An estimated 150 000 deaths caused by MDR-TB occurred globally in 2008, including those with HIV infection (range: 53 000–270 000). The estimated number of MDR-TB deaths excluding those with HIV infection was 97 000 (range: 6000–220 000). MDR-TB case fatality in HIV-negative cases was estimated at 26% (range: 16–58%). The large uncertainty in mortality and case fatality estimates is partly due to incomplete coverage of global drug resistance surveillance and the lack of direct measurements of MDR-TB case fatality rates.

Estimates of MDR-TB mortality are derived from methods detailed in **Annex 2**, using direct measurements of mortality data from national vital registration systems.

There are very little data providing direct measurements of MDR-TB case fatality. Treatment outcomes for cohorts of MDR-TB patients put under a Category IV treatment regimen capture deaths at 36 months but do not document deaths in cases of treatment default and failure. Furthermore, causes of deaths are not documented and deaths from causes other than TB are included in reported figures. The large majority of MDR-TB cases are undetected and do not receive adequate treatment with second-line drugs. Improvements in DST coverage and in the quality and quantity of MDR-TB surveillance data will allow better understanding of MDR-TB case fatality. Finally, there are hardly any data on MDR-TB treatment outcomes disaggregated by HIV status. Evidence from reports on M/XDR-TB indicates an extremely high rate of case fatality among HIV-infected M/XDR-TB patients.

It remains unclear whether MDR-TB is associated with HIV. We have assumed no association in our estimates, but if conclusive evidence confirms that HIV prevalence among MDR-TB cases is higher than among

BOX 3

In focus: the burden of anti-TB drug resistance in the African Region remains largely unquantified

Of the 46 countries in the African Region, 22 (48%) have provided representative data on drug-resistant TB. Among these countries, 12 have conducted a nationwide survey since 2000; 10 have conducted a survey only at a subnational level (state, province, or district) or have not repeated it in the past decade, or both (**Map 2**). Only one country (South Africa) collects routine surveillance data, although the quality of the data is Class B (**Annex 4** and **Map 5**). Some 34 countries have reported MDR-TB cases and 8 have reported XDR-TB cases. Only 3 countries (Rwanda, the United Republic of Tanzania and South Africa) have examined the proportion of XDR-TB among MDR-TB cases (**Annex 5**). Proportions of MDR-TB among TB patients are generally low in the African Region, with a frequency ranging from 0.5% to 3.9% among new TB cases and 0.0% to 16.7% among previously treated TB patients.

The apparent low general proportion of MDR-TB among TB cases compared with that in regions such as Eastern Europe and Central Asia may be due to outdated studies or surveys in which the scientific rigour is not known or coverage not nationwide. Nevertheless, given that African countries have the highest incidence of TB per population in the world, even at low levels of drug resistance the caseload of MDR-TB patients becomes very high. As a result, the rates of MDR-TB cases arising per 100 000 population in some southern African countries are 5–6 times higher than those of China and India. Latest estimates of WHO put the number of MDR-TB cases emerging in 2008 in Africa at 69 000 (95% CI: 53 000–110 000). The association between MDR-TB and HIV is poorly characterized but is of crucial importance on this continent. Reports of HIV patients suffering from MDR-TB and XDR-TB show very high mortality unless adequate treatment is instituted early on.

The lack of information on drug resistance is a result of inadequate laboratory capacity to perform diagnostic testing among TB patients and barriers to conducting drug resistance surveys. Estimated numbers of MDR-TB cases in many African countries are thus based on mathematical modelling rather than empirical studies. Laboratory surveillance for MDR-TB and XDR-TB should be strengthened and expanded across the region, particularly in large populous countries and where studies have never been done or are now older than five years. Importantly, proper treatment should be available for all MDR-TB cases detected.

non-MDR TB cases, the figures presented here may underestimate the global burden of MDR-TB mortality.

High MDR-TB mortality can be addressed through adequate prevention, diagnosis, treatment and care. Since the vast majority of cases are undetected and do not receive adequate care, we expect a global decline in MDR-TB mortality as the coverage and quality of DST and treatment programmes improve globally. Systematic infection control measures have the potential to greatly reduce transmission in hospitals and other congregate settings, and therefore the mortality of, HIV-associated MDR-TB.

PART II

Progress in the global response to M/XDR-TB

In May 2009, Resolution WHA62.15 of the World Health Assembly, welcoming the Beijing Call for Action on TB control and patient care, urged Member States "to achieve universal access to diagnosis and treatment of multidrug-resistant and extensively drug-resistant tuberculosis" (**Annex 1**). In response, by October 2009, at least 20 of the 27 high MDR-TB burden countries were updating their national TB control plans to include an MDR-TB component. Seven of these countries (Armenia, Azerbaijan, Georgia, Kazakhstan, the Republic of Moldova, Tajikistan and Ukraine) were at an advanced stage of developing their plans at the time of publication of this report. These plans focus mostly on the operational aspects of MDR-TB management and envisage national policy changes of the health systems issues influencing the MDR-TB epidemic.

Part II presents the latest available information on the progress that countries have made in responding to the challenge of MDR-TB, focusing on the 27 high MDR-TB burden countries. For the first time, treatment outcomes from all sites reporting complete data for new and previously treated MDR-TB patients are being presented.

2.1 Scaling up laboratory services for diagnosis of M/XDR-TB

The laboratory plays a central role in patient care and surveillance, and thus provision of quality-assured services is critical. Establishing reference laboratory facilities with adequate capacity to supervise DST and surveillance activities in the country is a critical step in MDR-TB control and care. Country reports to WHO indicate that by 2008, 22 of the 27 high MDR-TB burden countries had an officially recognized national reference laboratory (**Table 7**).

The availability of facilities to conduct culture and DST varied substantially by country. In 24 of these 27 countries, at least one laboratory had capacity to perform culture for *M. tuberculosis* and DST of first-line drugs; 17 countries had in-country facilities to perform DST of second-line drugs and 4 others reported having some access to second-line DST through laboratories outside the country. In many settings, coverage of second-line drug testing is known to be inadequate. Only 15 countries reported that all their DST laboratories participated in external quality assurance; an additional 7 countries reported partial coverage (2–80% of DST laboratories). Overall, the capacity of laboratories to address the huge scaling up of culture and DST services required to meet the diagnostic demand of drug-resistant and HIV-associated TB is still severely limited, as is the absorption of new and rapid technologies (such as liquid culture, rapid *M. tuberculosis* speciation and molecular line probe assays) recently endorsed by WHO. Slow technology transfer, compounded by the need for modern and expensive laboratory infrastructure, meant that contemporary diagnostics for MDR-TB were available in less than half of the high MDR-TB burden countries in 2008.

In response to this need, WHO, the Global Laboratory Initiative and its network of partners are pursuing the EXPAND-TB Project, a multi-country project on scaling up and accelerating access to diagnostic technologies for MDR-TB, which is funded by UNITAID[1] and other partners including the Foundation for Innovative New Diagnostics (FIND)[2] and the Stop TB Partnership's Global Drug Facility.[3] The project is investing a total of US$ 87 million in 15 high MDR-TB burden countries and 12 other countries over a period of 5 years (**Table 7**). It will promote new and rapid diagnostic technologies within appropriate laboratory services through 2013 to ensure that new tools are properly integrated within national TB control programmes. During the first year of EXPAND-TB, activities have started in 12 countries, including needs assessment and preparedness, upgrade of infrastructure and training of staff. Technology transfer has started in five countries, paving the way for accelerated patient diagnosis and continuous surveillance of drug resistance. The progress being made in Ethiopia is described in **Box 4**.

[1] International facility for the purchase of diagnostics and medicines for diagnosis and treatment of HIV/AIDS, malaria and TB (www.unitaid.eu/).
[2] www.finddiagnostics.org/
[3] www.stoptb.org/gdf/

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TABLE 7 Capacity for culture and DST in high MDR-TB burden countries and EXPAND-TB project countries, 2008

Country	NRL	Number of laboratories performing		DST labs for which EQA was carried out	Facilities for second-line DST
		Culture	DST for first-line drugs		
High MDR-TB burden countries[a]					
Armenia	Y	1	1	1	No
Azerbaijan	N	—	—	—	In country
Bangladesh	Y	2	2	2	No
Belarus	Y	91	22	22	In country
Bulgaria	Y	33	22	0	Outside country
China	Y	628	109	87	In country
Democratic Republic of the Congo	Y	1	1	1	No
Estonia	Y	2	2	2	In country
Ethiopia	Y	2	2	2	In country
Georgia	Y	2	1	1	In and outside country
India	Y	12	12	12	In country
Indonesia	N	61	20	5	No
Kazakhstan	Y	21	21	21	In country
Kyrgyzstan	Y	13	1	1	Outside country
Latvia	Y	6	1	1	In country
Lithuania	—	—	—	—	—
Myanmar	Y	2	1	1	Outside country
Nigeria	Y	3	3	1	Outside country
Pakistan	Y	13	11	4	In country
Philippines	Y	3	3	—	In country
Republic of Moldova	Y	4	4	3	In country
Russian Federation	N	397	272	141	In country
South Africa	Y	15	10	10	In country
Tajikistan	Y	—	—	—	In and outside country
Ukraine	N	107	47	1	No
Uzbekistan	Y	2	2	2	In and outside country
Viet Nam	Y	30	2	2	In country
Other EXPAND-TB project countries					
Cameroon	Y	—	—	—	In country
Côte d'Ivoire	Y	1	1	0	No
Djibouti	Y	1	0	—	Outside country
Haiti	Y	1	1	1	In and outside country
Kenya	Y	5	1	1	Outside country
Lesotho	Y	1	1	1	No
Peru	Y	68	7	7	In country
Senegal	Y	3	3	1	In country
Swaziland	Y	1	1	1	Outside country
Uganda	Y	3	2	2	In country
United Republic of Tanzania	Y	3	1	1	No
Zambia	Y	3	3	3	No

[a] High MDR-TB burden countries in *italics* are also included in the list of EXPAND-TB project countries.
DST = drug susceptibility testing
EQA = external quality assurance
MDR-TB = multidrug-resistant TB
NRL = National Reference Laboratory

BOX 4

In focus: experience from Ethiopia in scaling up laboratory diagnostics

Immediately after the 2008 endorsement by WHO of line probe assays (LPAs) for rapid MDR-TB testing, the Ethiopian Health and Nutrition Research Institute (EHNRI) and the Foundation for Innovative New Diagnostics (FIND) accelerated the expansion of TB laboratory capacity in Ethiopia. In 2009 this effort gained momentum when the country was included in the EXPAND-TB project, with two biosafety-level 3 laboratories successfully established in Addis Abeba with support by UNITAID and other partners – the first at the EHNRI to host the National Reference Laboratory for Tuberculosis, and the second in collaboration with Johns Hopkins University at St. Peter's Hospital, a central hospital responsible for the care of TB-HIV co-infected patients experiencing TB treatment failure or relapse. Laboratory technicians were trained at EHNRI and the African Centre for Integrated Laboratory Testing in Johannesburg, South Africa, and at ENHRI, resulting in testing capacity in the two Ethiopian laboratories now including three WHO-endorsed contemporary TB diagnostic technologies: liquid and solid growth detection and drug susceptibility testing for TB, lateral-flow immuno-assay for identification of TB, and rapid detection of MDR-TB by LPA.

Rapid policy reform on the use of these tests in TB control in Ethiopia during 2009 was accompanied by in-country validation of laboratory capability, with LPA introduced in late 2009. In 2010, LPA and liquid culture will be expanded to five regional laboratories that are currently performing HIV-PCR for early infant diagnosis, making Ethiopia one of the first examples of a truly integrated TB-HIV laboratory network while demonstrating that rapid scale-up of laboratory services for MDR-TB diagnosis is feasible even at regional level, in resource-constrained settings.

2.2 Reporting of MDR-TB patients and their treatment outcomes

This section describes the progress made by countries in detecting MDR-TB cases, enrolling them on treatment and reporting the outcomes of their treatment.

2.2.1 Case detection and reporting

In 2008, there were 29 423 MDR-TB cases reported throughout the world, with 127 countries reporting at least one case. This represents only 7% of the number of MDR-TB cases estimated to have emerged in the same year (440 000 cases).

In certain countries DST of TB strains is only performed on a selection of patients based on the availability of resources and local levels of drug-resistance, where these are known. Of the 27 high MDR-TB burden countries, 22 reported routine testing of patients failing one or more treatment courses, while 10 countries – all in Eastern Europe where proportions of MDR-TB are high even in previously untreated patients – reported routine testing even among new cases. However, reporting of DST results to WHO remains low. In 2008, only 1% of new TB cases and 3% of previously treated cases notified by the 27 countries underwent diagnostic DST (**Table 8**). Only countries of Eastern Europe reported testing more than 1% of new cases, 10 of which had a coverage ranging from 28% to 77%. DST coverage exceeding 95% among previously treated TB cases was achieved only in Estonia, Latvia and Lithuania.

2.2.2 Treatment outcomes of MDR-TB patients

This section presents, for the first time, treatment outcomes from all sites reporting complete data for new and previously treated MDR-TB patients to WHO. Globally, 71 countries or territories provided complete, final data on treatment outcomes for new and/or previously treated MDR-TB cases who started treatment in 2006 (**Annex 7**; includes also countries with data only from 2004 or 2005). Forty-eight countries or areas reported outcomes from sites where TB management and drug quality conform to international standards: 26 of these sites are programmes approved by the Green Light Committee (GLC);[1] the remaining 22 are from high-income countries. Three countries reported outcomes from both GLC and non-GLC programmes.

In total, outcomes were reported for 1589 new cases and for 2911 previously treated cases. These outcomes represent 8% of new and 14% of previously treated MDR-TB cases expected to have occurred among the TB cases notified by these countries in the same year. They amounted to 43% of all MDR-TB cases reported by these countries. Only 18 sites had an annual cohort of 50 cases (new cases and previously treated cases combined) or more.

Overall treatment success was 60% (95%CI: 55–66) after adjustment for clustering at country level. Among new cases, treatment success averaged to 64% (95%CI: 55–72), and 8% died (95%CI: 5–11). Treatment success for previously treated cases was 58% (95%CI: 52–64) and 13% died (95%CI: 10–15).

Cohorts from quality-assured sites registered higher treatment success among new cases (69%; 95% CI: 64–75) than cohorts from other sites (51%; 95%CI: 26–76), after adjusting for clustering at country level. For previously treated cases, treatment success was 56% (95%CI: 51–62) for quality-assured sites vs 62% (95%CI: 51–74) for other sites. A direct comparison of the performance of MDR-TB treatment programmes between the two

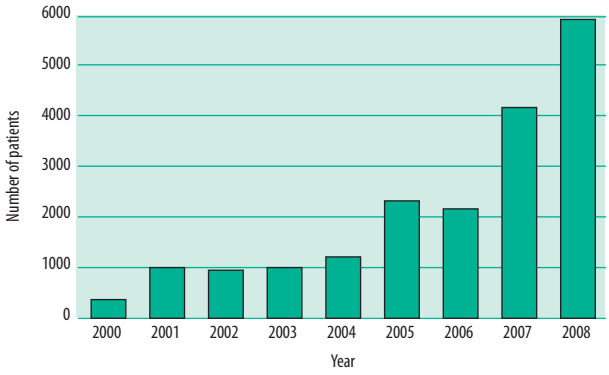
[1] www.who.int/tb/challenges/mdr/greenlightcommittee/

TABLE 8 Estimated number of MDR-TB cases, total notified MDR-TB cases and DST coverage in the 27 high MDR-TB burden countries, 2008

Country	Total number of estimated cases of MDR-TB	Total number of notified MDR-TB cases[a]	DST coverage and notified MDR-TB among new cases		DST coverage and notified MDR-TB among previously treated cases	
			% of notified new TB cases that received diagnostic DST	Notified MDR-TB cases among new cases	% of notified previously treated TB cases that received diagnostic DST	Notified MDR-TB cases among previously treated cases
Armenia	480	128	28	60	31	68
Azerbaijan	4 000	—	—	—	—	—
Bangladesh	9 800	147	—	—	7.3	147
Belarus	800	923	39	301	—	516
Bulgaria	460	32	29	14	66	18
China	100 000	—	—	—	—	—
Democratic Republic of the Congo	5 600	128	0.0	3	2.4	125
Estonia	94	74	77	42	100	32
Ethiopia[b]	5 200	130	—	—	—	—
Georgia	670	481	41	190	43	290
India	99 000	308	—	—	0.5	308
Indonesia[b]	9 300	446	—	—	—	—
Kazakhstan	8 100	3 676	28	1 384	37	1 950
Kyrgyzstan	1 400	269	7.8	97	36	172
Latvia	170	129	75	83	98	46
Lithuania	330	276	67	113	100	162
Myanmar	9 300	508	—	—	7.5	508
Nigeria	11 000	23	0.2	9	0.3	14
Pakistan	15 000	40	0.0	2	0.5	38
Philippines	13 000	929	0.1	14	15	729
Republic of Moldova	2 100	1 048	31	300	65	748
Russian Federation	38 000	6 960	30	5 061	86[c]	1 899
South Africa[b]	13 000	6 219	—	—	—	—
Tajikistan	4 000	—	—	—	—	—
Ukraine	8 700	—	—	—	—	—
Uzbekistan	8 700	342	0.3	52	5.6	290
Viet Nam	5 900	—	—	—	—	—
Total high MDR-TB burden countries	**380 000**	**23 216**	**1.3**	**7 725**	**3.3**	**8 060**

[a] may include cases with unknown previous treatment history
[b] MDR-TB cases not reported separately for new and previously treated cases
[c] only relapses
DST = drug susceptibility testing
MDR-TB = multidrug-resistant TB

FIGURE 7 Annual number of patients enrolled for treatment in programmes approved by the Green Light Committee, 2000–2008



country groups is not always justified. The definitions of outcome may differ, as well as the degree of compliance by projects to recommendations on treatment regimen and duration of treatment. Additionally, most GLC-approved programmes have only started building their capacity in MDR-TB case management in recent years and very few have continuous experience since 2000, when the first projects started recruiting (**Figure 7**). The experiences of GLC-approved programmes in Romania and Nepal are described in **Box 5**.

The GLC has now approved treatment for more than 63 000 MDR-TB patients in 111 programmes spanning 70 countries and territories. By the end of 2009, a cumulative total of more than 19 000 MDR-TB patients were reported to have been enrolled in 44 sites.

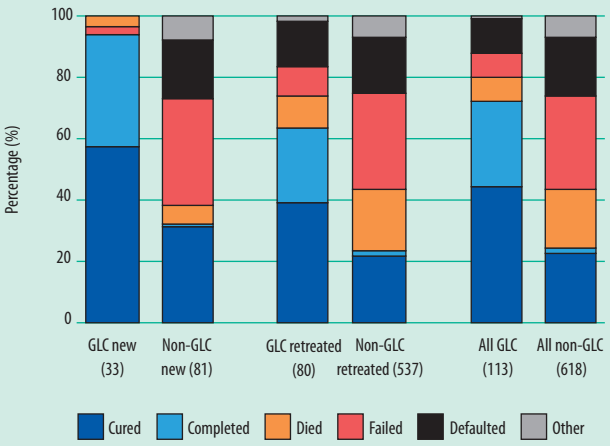
BOX 5

In focus: two case studies from GLC-approved programmes

Romania has two health centres treating patients under GLC-approval. Patient treatment is individualized and hospital-based until sputum converts to culture negative. Enrollment of patients started in 2004, and by the end of 2009 over 500 cases had been started on treatment. Non-GLC treatment is however also provided to many other MDR-TB patients in the country. The outcome of treatment for patients started on treatment in 2006 is compared in the bar chart between GLC patients (N=113) and non-GLC (N=618) (**Figure 8**). The experience in Romania shows that both new and previously treated patients managed following WHO guidelines are doing much better, with lower mortality, failure and interruption of treatment.

Nepal started recruiting MDR-TB patients in a national GLC-approved treatment programme in September 2005. The programme has been entirely ambulatory-based and has used a fully standardized regimen. In the first 12 months of treatment, 175 pulmonary cases were enrolled, most returning after failure of a Category II first-line regimen (87%) or a Category I regimen (6%). Cure was reported among 70% of patients but varied by province. Overall, 8% died, 5% failed treatment, and 17% defaulted (*15*). While this level of default is comparable to that observed in other models of care, it needs to be addressed particularly in certain provinces where it is much higher. Nonetheless this initial experience from Nepal shows clearly that ambulatory-based treatment for MDR-TB patients on a fully standardized regimen can yield high cure rates even in resource-limited settings.

FIGURE 8 Treatment outcomes of MDR-TB patients in Romania in projects approved by the Green Light Committee (GLC) and in non-GLC approved sites, 2006 cohorts



BOX 6

In focus: contribution of MDR-TB to TB patient risk for dying

Case-based surveillance data on over 40 000 TB patients treated in 2005–2006 in 17 European Union countries were collected by the European Centre for Disease Prevention and Control. This dataset provided an opportunity to study the effect of different factors on the outcome of treatment. One half of eligible cases had missing data and were excluded from the analysis. After adjustment for clustering at country level and for other confounders (age, sex, and previous anti-TB treatment), MDR was strongly associated with the risk of dying from any cause (adjusted OR=3.9, 95%CI 3.3–4.6). Incomplete geographical coverage of data, missing information and the absence of variables on important determinants (for example, HIV status and alcohol dependency), preclude a more complete study. Nonetheless it is clear that drug resistance is an important risk for death among TB patients even in developed countries.

In 2008, about 1% of the estimated 440 000 incident cases of MDR-TB were enrolled on treatment through the GLC mechanism. However, annual recruitment has increased in recent years (**Figure 7**).

The number of cases enrolled on treatment by the 10 high MDR-TB burden countries reporting (**Table 9**) represents only 10% of MDR-TB cases notified by these countries. However, the ratio of cases reported with treatment outcomes to total MDR-TB cases notified ranged widely between countries (from 8% to more than 100%). Treatment success among these countries was 61% after adjustment for clustering by country.

2.3 Addressing other health systems considerations for the response to M/XDR-TB

Countries reported on other aspects of their response to the M/XDR-TB challenge and some examples are highlighted in the following five sections.

2.3.1 Information management

By 2008, data for individual TB patients were accessible centrally to the national TB control programmes in 15 of the 27 high MDR-TB burden countries, including China and the Russian Federation. Web-based relational database management systems were reported to be used only in Estonia and the Republic of Moldova, although such systems are known to have become more widely available since then. By the end of 2009, at least 9 high MDR-TB burden countries in Eastern Europe

TABLE 9 Number of MDR-TB cases notified and enrolled for treatment and their treatment outcomes in the 27 high MDR-TB burden countries, 2006 (or 2004–2005)

Country	Year	MDR-TB patients notified that year (a)	Enrolment		MDR-TB patients on treatment (N=1751)[a]			
			Enrolled (b)[b]	Ratio of enrolled to notified (b/a)[b]	% treatment success (cured & completed)	% died	% failed	% other[c]
Armenia	2006	215	27	13	41	11	19	30
Azerbaijan	2006	398	—	—	—	—	—	—
Bangladesh	2006	—	—	—	—	—	—	—
Belarus	2006	651	—	—	—	—	—	—
Bulgaria	2006	53	—	—	—	—	—	—
China	2006	2	—	—	—	—	—	—
DR Congo	2004	—	155	—	60	14	1	26
Estonia	2006	52	53	102	51	23	4	23
Ethiopia	2006	—	—	—	—	—	—	—
Georgia	2005	195	21	11	38	19	10	33
India	2006	33	—	—	—	—	—	—
Indonesia	2006	59	—	—	—	—	—	—
Kazakhstan	2006	4 117	930	23	81	4	4	11
Kyrgyzstan	2006	336	66	20	52	8	14	27
Latvia	2006	143	142	99	68	11	6	15
Lithuania	2006	332	127	38	—	—	—	—
Myanmar	2006	666	—	—	—	—	—	—
Nigeria	2006	—	—	—	—	—	—	—
Pakistan	2006	—	—	—	—	—	—	—
Philippines	2006	403	133	33	63	19	2	17
Republic of Moldova	2006	1 040	88	8	67	5	15	14
Russian Federation	2006	3 949	—	—	—	—	—	—
South Africa	2006	6 065	—	—	—	—	—	—
Tajikistan	2006	—	—	—	—	—	—	—
Ukraine	2006	—	—	—	—	—	—	—
Uzbekistan	2006	83	136	164	62	7	13	19
Viet Nam	2006	—	—	—	—	—	—	—
High MDR-TB burden countries		**19 443**	**1 878**	**10**	**61 (53–69)**	**10 (6–14)**	**6 (3–10)**	**19 (15–23)**

[a] Includes patients enrolled in Green Light Committee-approved sites and others; the bottom row shows the percentage of treatment outcomes and the 95% confidence intervals adjusted for clustering by country.
[b] Enrolled patients may have been detected and notified in a year prior to the year of start of their treatment.
[c] Defaulted, transferred and still on treatment.
MDR-TB = multidrug-resistant TB

handled data on drug-resistant TB by computer and five others planned to computerize their systems in 2010–2011, mostly through support from the Global Fund to Fight AIDS, Tuberculosis and Malaria.

2.3.2 Implementing national airborne infection-control policies

Spurred by the policy gap in TB infection control and increasing demand from countries for guidance on preventing transmission of TB, WHO developed a new, evidence-based TB infection control policy in 2009 (*16*). This new policy emphasizes the needs for implementation at national and subnational levels and provides specific guidance on how to reduce the risk of TB transmission in health-care facilities, congregate settings (such as prisons) and households.

Some countries have started to adapt this policy. Belarus, China, Georgia, Lesotho, South Africa and Viet Nam, for example, have all either produced or are making progress towards producing, national TB infection control guidelines. China and Viet Nam have reported doing training on infection control. In other countries, such as India, the operational feasibility and effectiveness of implementing the national guidelines is being piloted in selected states. Other countries including Papua-New Guinea and Ukraine are conducting infection control assessments of their laboratory and health-care facilities to inform the production of national TB infection control policies.

2.3.3 Strengthening human resources and collaboration with the private sector

To achieve universal access to diagnosis, treatment and care of MDR-TB, a significant amount of additional skilled staff will be needed. Evidence from programme reviews in many high TB and MDR-TB burden coun-

tries has shown that there is often inadequate human resource capacity at central and peripheral levels to ensure the quality of basic TB control services, let alone capacity for expanding services into new interventions such as the diagnosis and management of MDR-TB. However, there has not yet been much progress in addressing the crisis in the workforce that some countries are facing.

Meanwhile, countries are training their workforces. Among the 27 high MDR-TB burden countries, training on different aspects of MDR-TB management has been reported by China, Georgia, India, South Africa and Viet Nam since the implementation of the Resolution WHA62.15 in 2009. Of these 27 countries, 17 reported having developed training material, 11 of them since 2007.

Other countries such as Bangladesh, Nepal, Pakistan and the Philippines have successfully demonstrated how private hospitals, nongovernmental organizations, private chest physicians and informal village doctors can be engaged in MDR-TB management.

2.3.4 Developing a comprehensive framework for management and care of M/XDR-TB, including out-patient and community-based care

The high cost of MDR-TB management is mostly the result of the cost of second-line drugs, the use of hospitalization (up to 50% of the total cost of treatment in middle-income countries) and the workforce necessary to ensure proper care. WHO, the Stop TB Partnership and technical agencies have been assisting countries in creating models of care based on WHO guidelines that meet the needs of patients, and which are feasible and cost-effective in the health system. Decisions on hospitalization, in contrast to out-patient and community-based models, will be governed by patients' needs and preferences, hospital bed capacity, infection control measures in place and geographical barriers to accessing health-care units. South Africa's experience and progress in management and care of M/XDR-TB is described in **Box 7**.

2.3.5 Ensuring an uninterrupted supply of first-line and second-line drugs

Countries need access to sufficient supplies of affordable second-line drugs produced to WHO standards. However, worldwide supply of such quality-assured second-line drugs is small, and volumes are insufficient to treat the increasing numbers of patients being enrolled for care throughout the world.

Uninterrupted supply of anti-TB drugs must also be complemented with measures to minimize misuse of anti-TB drugs by public and private care providers. Countries such as Brazil, Ghana, Malawi and Tanzania have demonstrated ways to promote rational use of anti-TB drugs by restricting their availability and reducing irrational use through collaboration and regulation.

In countries including Ukraine, remarkable progress has been made in initiating registration of quality-assured drugs procured through the GLC Initiative. Bold decisions, such as the one made by the State Pharmacological Center of Ukraine cancelling registration fees for the manufacturers of second-line drugs, will reduce substantially the barriers to access to treatment according to international standards.

To further support country efforts, the Global Drug Facility has created a Strategic Rotating Stockpile, which is used to complete orders in case of late arrival of the ordered drug from the supplier or unavailability of the drug. It has recently increased its reserve to 5800 patient treatments. From January to June 2009, 19 countries have benefited from this facility. It has also been used for emergencies or for avoiding potential stock outs. Lead times for emergency orders have been reduced to less than 30 days.

2.4 Financing the care of drug-resistant TB patients in the 27 high MDR-TB burden countries

The cost of drugs alone for treating the average MDR-TB patient is 50 to 200 times higher than for treating a drug-susceptible TB patient, and the overall costs for care have been found to be 10 times higher or more. However, treatment of MDR-TB can be a cost-effective

BOX 7

In focus: management and care of M/XDR-TB in South Africa

South Africa's policy of hospitalizing all drug resistant TB patients is being reviewed with the aim of introducing community-based management of MDR-TB in order to expand access to care. There have been a number of positive developments. A draft policy on community-based MDR-TB care has been completed, discussions have been held with key TB stakeholders nationally and will be finalized within this year. This policy will ensure decentralization and early treatment of M/XDR-TB care. The Government has announced that from April 2010 all M/XDR-TB patients with HIV infection will qualify for anti-retroviral therapy regardless of CD4 count. TB services in prisons, mines and mobile populations will be coordinated nationally in collaboration with key partners in the Correctional services, Mines and SADC (Southern African Development Community).

FIGURE 9 Costs of second-line anti-TB drugs and treatment as a percentage of gross national income (GNI) per capita in the 27 high MDR-TB burden countries

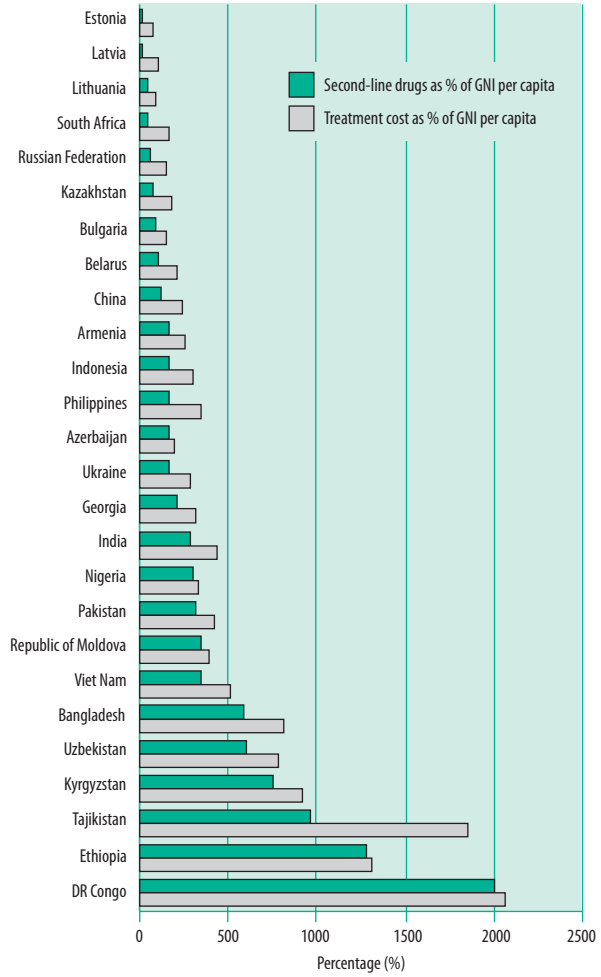
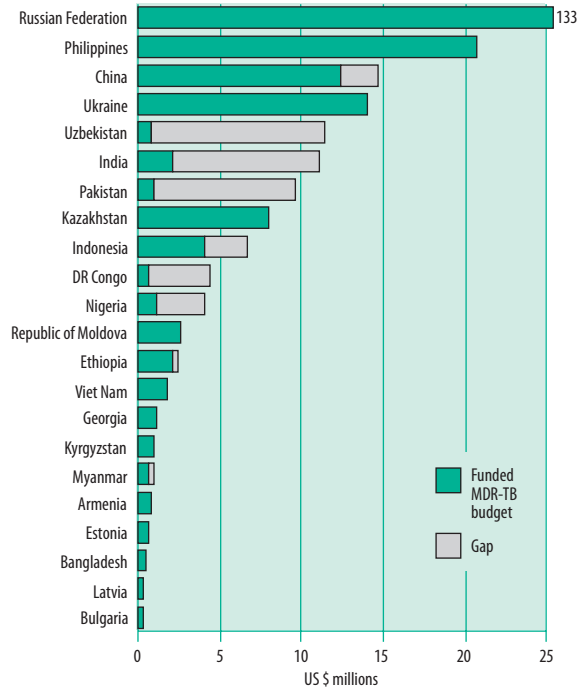


FIGURE 10 Budgets and funding (in US$) for MDR-TB in the 27 high MDR-TB burden countries[a]



[a] No data were available for Azerbaijan, Belarus, Latvia, Lithuania, Tajikistan; incomplete data for South Africa.

intervention in a wide range of situations (*17–19*). Expenditure for MDR-TB treatment exceeds gross national income per capita in all 27 high MDR-TB burden countries (**Figure 9**). Costs of second-line drugs make up a large component of these costs, but studies from Estonia, Peru, the Philippines and the Russian Federation suggest that the variation in treatment costs among countries is mainly due to differences in hospitalization practices. Furthermore, even where drugs are dispensed free of charge, patient costs may be high as a result of losses from gainful employment and travel expenses. To ensure universal access to MDR-TB care, as contemplated by the World Health Assembly (*20*), international as well as domestic resources will need to be mobilized and spent more cost-effectively to reduce the economic burden on patients and health systems.

Achieving the ambitious target of the Stop TB Partnership – to diagnose and treat 80% of the estimated M/XDR-TB cases according to international guidelines by 2015 – comes at a substantial cost (*21*). In the 27 high MDR-TB burden countries alone, approximately 1.3 million M/XDR-TB cases will need to be treated between 2010 and 2015. The associated cost of care

BOX 8

In focus: covering the shortfall in funding for MDR-TB care and control

In 2010, 118 countries territories and areas – accounting for 94% of the world's estimated TB cases – reported that a total of US$ 4.1 billion were available for TB control (including utilization of general health services). Of this total, 86% was from government funding including loans. The Global Fund to Fight AIDS, Tuberculosis and Malaria[1] is the single biggest source of external funding for TB control. Between 2002 and 2009, it supported the treatment of nearly 30 000 MDR-TB patients. In its ninth round, the Global Fund approved over US$ 400 million for the management of MDR-TB in 28 countries. However, external funding is unlikely to be able to finance more than a relatively small share of the costs of MDR-TB diagnosis and treatment. Domestic funding, particularly in middle-income countries, needs to be mobilized and managed cost-effectively to ensure a strong response to the MDR-TB epidemic and to reduce the economic burden on patients and on health systems more broadly.

[1] www.theglobalfund.org

for these patients has been estimated to amount to US$ 16.2 billion over the six years, rising from US$ 1.3 billion in 2010 to US$ 4.4 billion in 2015. Planned budgets for 2010 are far below these figures, amounting to US$ 0.4 billion for all 27 countries combined, including loans. While MDR-TB control in 2010 was estimated to require less than 20% of all TB control programme budgeted costs globally in 2009, by 2015 this proportion is expected to reach 50%.

The funding required for MDR-TB control in 2015 will be 16 times higher than the funding that is available in 2010. In many countries providing information, budgets for MDR-TB care and control in 2010 are vastly inadequate and do not correlate with the estimated MDR-TB burden (**Figure 10**). In five of these countries (the Democratic Republic of the Congo, India, Nigeria, Pakistan and Uzbekistan), more than two-thirds of the planned budget represents a funding gap. Mobilization of both national and international resources is required to meet the current and future need (**Box 8**).

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Annexes

ANNEX 1
Resolution WHA62.15

SIXTY-SECOND WORLD HEALTH ASSEMBLY WHA62.15
Agenda item 12.9 22 May 2009

Prevention and control of multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis

The Sixty-second World Health Assembly,

Having considered the reports on the prevention and control of multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis;[1]

Noting the progress made since 1991 towards achieving the international targets for 2005, the acceleration of efforts following the establishment of the Stop TB Partnership in response to resolution WHA51.13, and more recently following resolution WHA58.14 encouraging Member States to ensure availability of sufficient resources to achieve the internationally agreed goal relevant to tuberculosis contained in the United Nations Millennium Declaration by 2015;

Aware that the development of the Stop TB strategy as a holistic approach to tuberculosis prevention and control and represents a significant expansion in the scale and scope of tuberculosis control activities as a part of strengthening health systems within the context of primary health care and addressing social determinants of health;

Noting that the Stop TB Partnership's Global Plan to Stop TB 2006–2015 sets out the activities oriented towards implementing the Stop TB strategy and achieving the international targets for tuberculosis control set by the Stop TB Partnership – in line with the target of the internationally agreed development goal relevant to tuberculosis contained in the United Nations Millennium Declaration to "have halted by 2015 and begun to reverse the incidence of major diseases" – of halving tuberculosis prevalence and death rates by 2015 compared with 1990 levels;

Noting that the care and control of tuberculosis have progressed significantly during the past decade and the incidence of new cases is estimated to have fallen slightly each year since 2003;

Aware that a significant proportion – an estimated 37% of tuberculosis cases worldwide remain un-notified and receive either no treatment or inappropriate treatment;

Recognizing that the rates of tuberculosis are disproportionately high in high-risk populations including indigenous populations;

Recognizing that emergence and spread of multidrug-resistant and extensively, drug-resistant tuberculosis is facilitated by not detecting sufficient cases of tuberculosis and not treating them appropriately by DOTS-based treatment;

Concerned that the highest levels of multidrug-resistance reported in WHO's fourth global report on anti-tuberculosis drug resistance[2] – an estimated half a million multidrug-resistant cases occurring globally, including 50 000 cases of extensively drug-resistant tuberculosis – pose a threat to global public health security;

Recognizing that there is an urgent need to invest in research for development of new diagnostics, medicines and vaccines and in operational research to prevent and manage tuberculosis, including multidrug-resistant and exten-

[1] Documents A62/20 and A62/20 Add.1.
[2] Document WHO/HTM/TB/2008.394.

sively drug-resistant tuberculosis; while exploring and, where appropriate, promoting a range of incentive schemes for research and development including addressing, where appropriate, the de-linkage of the costs of research and development and the price of health products;

Noting that less than 3% of the estimated total number of multidrug-resistant and extensively drug-resistant cases of tuberculosis receive treatment according to WHO recommended standards;

Concerned that the disease transmission occurs mostly in communities where there is a lack of appropriate infection control;

Concerned that the insufficient demand from countries for internationally quality-assured anti-tuberculosis medicines resulting in an inadequate supply through the Green Light Committee mechanism has been a major bottleneck to treating multidrug-resistant and extensively drug-resistant tuberculosis and that quality-assured fixed-dose drug combinations, developed as a tool to prevent the emergence of resistance, are not widely used;

Aware that the delays in implementing the Global Plan to Stop TB 2006–2015 will result in increasing numbers of tuberculosis cases and deaths, including those due to multidrug-resistant and extensively multidrug-resistant tuberculosis and to the impact of HIV, and therefore in delays in achieving by 2015 the international targets for tuberculosis control and the internationally agreed development goal relevant to tuberculosis contained in the United Nations Millennium Declaration;

Recalling resolution WHA60.19 on tuberculosis control in which the Health Assembly urged Member States to develop and implement long-term plans for tuberculosis including multidrugresistant and extensively drug-resistant tuberculosis prevention and control in line with the Global Plan to Stop TB 2006–2015, within the overall health development plans, and resolution WHA58.33 on achieving universal coverage;

Welcoming the Beijing Call for Action on tuberculosis control and patient care given jointly by representatives of 27 Member States carrying a high burden of multidrug-resistant and extensively drug-resistant tuberculosis, civil society, the private sector and others to address the alarming threat of multidrug-resistant and extensively drug-resistant tuberculosis,[1]

1. URGES all Member States:

(1) to achieve universal access to diagnosis and treatment of multidrug-resistant and extensively drug-resistant tuberculosis as part of the transition to universal health coverage, thereby saving lives and protecting communities, by means of:

(a) developing a comprehensive framework for management and care of multidrugresistant and extensively drug-resistant tuberculosis, that includes directly-observed treatment, community-based and patient-centered care, and which identifies and addresses the needs of persons living with HIV, the poor and other vulnerable groups, such as prisoners, mineworkers, migrants, drug users, and alcohol dependants, as well as the underlying social determinants of tuberculosis and multidrug-resistant and extensively drug-resistant tuberculosis;

(b) strengthening health information and surveillance systems to ensure detection and monitoring of the epidemiological profile of multidrug-resistant and extensively drug resistant tuberculosis and monitor achievement in its prevention and control;

(c) aiming to ensure the removal of financial barriers to allow all tuberculosis patients equitable access to tuberculosis care, that their rights are protected, and that they are treated with respect and dignity in accordance with the local legislation;

(d) making available sufficiently trained and motivated staff in order to enable diagnosis, treatment and care of tuberculosis including multidrug-resistant and extensively drug-resistant tuberculosis, as an integral part of efforts to address the overall health workforce crisis;

(e) strengthening laboratory systems, through increasing capacity and adequate human resources, and accelerating access to faster and quality-assured diagnostic tests;

(f) engaging all relevant public and private health-care providers in managing tuberculosis including multidrug-resistant and extensively drug-resistant tuberculosis and tuberculosis-HIV coinfection according to national policies, and strengthening primary health care in early detection, effective treatment and support to patients;

[2] Document A62/20 Add.1, Annex.

(g) ensuring that national airborne infection-control policies are developed (as part of general infection prevention and control programmes) and implemented in every health-care facility and other high-risk settings and that there is sufficient awareness of tuberculosis infection control in the community;

(h) ensuring uninterrupted supply of first- and second-line medicines for tuberculosis treatment, which meet WHO prequalification standards or strict national regulatory authority standards, and that quality-assured fixed-dose combination medicines of proven bioavailability are prioritized within a system that promotes treatment adherence;

(i) strengthening mechanisms to ensure that tuberculosis medicines are sold on prescription only and that they are prescribed and dispensed by accredited public and private providers;

(j) undertaking effective advocacy, communication and social mobilization, avoiding stigmatization and discrimination, and spreading community awareness about policies and plans for prevention and control of tuberculosis including multidrug-resistant and extensively drug-resistant tuberculosis;

(k) establishing national targets in order to accelerate access to treatment according to WHO guidelines, for multidrug-resistant and extremely drug-resistant tuberculosis patients;

(2) to enhance quality and coverage of DOTS in achieving 70% detection rate and 85% success rate of tuberculosis treatment, thereby preventing secondary multi-drug resistant tuberculosis;

(3) to use all possible financing mechanisms in order to fulfil the commitments made in resolutions WHA58.14 and WHA60.19, including the commitment to ensure sustainable domestic and external financing, thereby filling the funding gaps identified in the Global Plan to Stop TB 2006–2015;

(4) to increase investment by countries and all partners substantially in operational research and research and development for new diagnostics, medicines and vaccines to prevent and manage tuberculosis including multidrug-resistant and extensively drug-resistant tuberculosis;

2. REQUESTS the Director-General:

(1) to provide technical support to Member States in order to develop and implement response plans, based on a comprehensive framework for management of care, for the prevention and control of tuberculosis including multidrug-resistant and extensively drug-resistant tuberculosis;

(2) to provide support to Member States in developing and implementing strategies to engage all relevant public, voluntary, corporate and private health-care providers in the training for and scaling up of prevention and control of tuberculosis including multidrug-resistant and extensively drug-resistant tuberculosis and all aspects of tuberculosis-HIV coinfection;

(3) to advise and support Member States to bring the standards of national drug regulatory agencies in line with international standards, thus enabling national pharmaceutical manufacturers to produce material of assured quality to be sold in the local and international markets;

(4) to provide support to Member States for upgrading laboratory networks to be able to undertake diagnosis and monitoring of multidrug-resistant and extensively drug-resistant tuberculosis and facilitate systematic evaluations of newer and faster diagnostic technology;

(5) to strengthen the Green Light Committee mechanism to help to expand access to concessionally-priced and quality-assured first- and second-line medicines, to encourage and assist the local pharmaceuticals in high-burden countries to get qualification within the Green Light Committee mechanism;

(6) to explore and, where appropriate, promote a range of incentive schemes for research and development including addressing, where appropriate, the de-linkage of the costs of research and development and the price of health products;

(7) to work with countries to develop country indicators and to support monitoring and evaluation of the implementation of the measures outlined in this resolution;

(8) to report through the Executive Board to the Sixty-third and Sixty-fifth World Health Assemblies on overall progress made.

Eighth plenary meeting, 22 May 2009
A62/VR/8

ANNEX 2
Methods

Types of surveillance

Drug resistance data must meet the three aforementioned principles (see page 5) and can be collected via drug resistance surveys or continuous drug resistance surveillance. Drug resistance data are sometimes available from only a subnational geographical area of a country.

Drug resistance surveys are discrete studies measuring drug resistance among a sample of patients representative of an entire patient population. With few exceptions, surveys enroll only smear positive TB cases, as there is no strong evidence to indicate that the proportion of cases that have drug resistance varies substantially according to whether the TB case is smear positive or smear negative. Ongoing surveys were defined as surveys that started enrollment by no later than January 2010, and whose final results were not yet reported to WHO. Countries that have developed protocols but not yet enrolled patients by January 2010 are not considered as having ongoing surveys.

Continuous drug resistance surveillance is a surveillance system based on routine diagnostic DST of patients.

Criteria for classification of countries among those reporting Class A or Class B surveillance data

The representativeness and accuracy of continuous surveillance data was assessed using available indicators measuring case detection, culture positivity, DST coverage, and DST accuracy. Countries with Class A surveillance data were defined as those meeting all four of the following criteria:

- new case detection rate or new smear positive case detection rate over 50%
- positive culture available in at least 50% of all notified cases
- DST results available in at least 75% of all cases with positive culture
- accuracy of at least 95% for isoniazid and rifampicin in the most recent DST proficiency testing exercise with a supranational reference laboratory.

Countries with Class B surveillance data were defined as those not meeting the criteria for Class A data, but meeting the following criteria:

- positive culture available in at least 35% of all notified cases
- DST results available in at least 50% of all cases with positive culture

Note: Case detection and quality assurance of laboratory DST were not criteria for determination of Class B surveillance data.

Definitions

New TB case: a new TB case is defined as a newly registered episode of TB in a patient who, in response to direct questioning denies having had any prior anti-TB treatment (for less than one month), and in countries where adequate documentation is available, for whom there is no evidence of such history.

Previously treated TB case: a previously treated TB case is defined as a newly registered episode of TB in a patient who, in response to direct questioning admits having been treated for TB for one month or more, or, in countries where adequate documentation is available, there is evidence of such history. Chemoprophylaxis is not considered treatment for TB.

Multidrug-resistant TB (MDR-TB) is defined as resistance to at least isoniazid and rifampicin. Extensively drug-resistant TB (XDR-TB) is defined as MDR-TB with additional resistance to a fluoroquinolone and a second-line injectable agent. Resistance to second-line drugs other than fluoroquinolones and second-line injectable agents are not described in the current report. This is because DST to the remaining second-line drugs has not been show to be reproducible (and thus reliable).

The recommended definitions of outcomes for MDR-TB patients are as per the consensus definitions published elsewhere.[1] Cohorts in which 20% of cases or more were classified as "still on treatment" were not included in this report. Likewise cases for whom previous treatment history was not known were not included.

[1] *Guidelines for the programmatic management of drug-resistant tuberculosis: emergency update 2008*. Geneva, World Health Organization, 2008 (WHO/HTM/TB/2008.402; pp23–24).

Countries are defined as WHO Member States (193). Data from other territories are shown when available. The list of High- and Middle-Income countries has been defined by the World Bank as of 1 July, 2009. Country populations used in certain calculations are estimates provided by the United Nations Population Division; these estimates sometimes differ from those available in countries.

High MDR-TB burden countries were selected based on having an estimated absolute number of at least 4,000 MDR-TB cases arising annually and/or at least 10% of all newly registered TB cases estimated with MDR-TB, as of 2008. The 27 high MDR-TB burden countries are Armenia, Azerbaijan, Bangladesh, Belarus, Bulgaria, China, DR Congo, Estonia, Ethiopia, Georgia, India, Indonesia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Myanmar, Nigeria, Pakistan, Philippines, Republic of Moldova, Russian Federation, South Africa, Tajikistan, Ukraine, Uzbekistan, and Viet Nam.

Collection of data

Data shown in this report were officially reported to WHO through January 2010. Completed forms were collected and reviewed at all levels of WHO, by country offices, regional offices and at WHO headquarters.

Countries that conducted a drug resistance survey and had finalized results reported data through a standard data collection form (in Excel format). This included data on first and second-line drug resistance, HIV, and age-group and sex. Countries with continuous surveillance systems submitted data through an adapted version of this form. In the European Region (EUR), this form was incorporated into the CISID, a web-based system for aggregated data reporting. Surveillance data for the EUR region were collected and validated jointly by the WHO Regional Office for Europe and the European Centre for Disease Prevention and Control. Individualized data on TB cases in 2005-2006 as reported by 17 countries to the European Centre for Disease Prevention and Control were used to analyse the risk of dying associated with MDR-TB.

Data from the "WHO global TB data collection system" were the source of the following information:

- first and second-line drug resistance in high MDR-TB burden countries that do not conduct continuous surveillance
- TB notifications and case detection rates
- MDR-TB treatment outcome data, excluding outcome data from sites operating under approval of the GLC
- finance
- laboratory techniques and activity

The 2009 round of TB data collection, coordinated by Stop TB Department in WHO, was for the first time organized via a web-based tool (www.stoptb.org/tme). This system greatly enhanced the collection and validation of data, allowing nearly all countries to report their national data online.

Data on enrollment and outcome of MDR-TB patients in sites operating under GLC approval were collected yearly by the GLC secretariat based at WHO as part of its normal monitoring activities. These data were provided for this analysis as a unified dataset, updated until November 2009.

Statistical analyses

Likelihood ratio tests comparing logistic regression models with and without the risk factor were used to assess the associations between MDR and each of the risk factors separately. In order to address the clustering effect when combining data from all settings, the combined analysis for relapse cases (compared with new cases) and the combined analysis for proportion of MDR-TB cases with XDR-TB used random effects logistic regression models, setting countries as the random effects variable, and the combined analysis for sex used logistic regression with robust standard errors. Confidence limits for proportion of MDR-TB by age-groups were also derived using robust standard errors. Adjusted values for pooled outcomes and their confidence intervals (see **Annex 7**) were derived using random effects models to account for clustering at country level. Likewise, the odds ratio of dying associated with MDR in the analysis of individual data was also adjusted using random effects.

Trends

The proportion of drug resistance among new cases was analysed in survey settings and among new and combined cases in settings conducting routine surveillance. Only countries and settings with three or more data points were included in the exercise. For settings that reported at least three data points, the trend was determined visually as ascending, descending, flat or indeterminate.

Estimates of MDR-TB incidence

The proportion of new and retreatment cases with MDR-TB in 2008 was estimated using the latest data from drug resistance surveys or routine surveillance for 113 (new cases) and 102 (retreatment cases) countries and territories, respectively. These drug resistance surveillance data provide direct measurements of the proportion of MDR-TB among new (previously untreated) patients, noted m_n, and the proportion of MDR-TB among retreatment cases (exposed to one month or more of previous treatment), noted m_r.

Patients with MDR-TB may have acquired *Mycobac-*

terium tuberculosis infection with multidrug resistant strains, and later developed the disease, or may have been infected with susceptible (more precisely, non-multidrug resistant) *Mycobacterium tuberculosis* strains, but their strains subsequently mutated and developed resistance when exposed to anti-TB drugs. To estimate MDR-TB disease burden in terms of incident episodes, it is necessary to separate episodes due to infection with multidrug resistant strains (named primary MDR-TB) from episodes of acquired MDR-TB during the course of anti-TB treatments (named acquired MDR-TB).

Primary MDR-TB is measured from drug resistance surveillance of patients previously untreated. Measurements of MDR-TB in patients previously treated combines cases with primary MDR-TB who failed their treatment and were subsequently registered for retreatment and cases of acquired MDR-TB during the course of treatment of a previous TB episode. We estimate the probability of acquired MDR-TB m_a as the probability of MDR-TB in previously treated patients m_r minus the probability of MDR-TB in previously untreated patients m_n.

For countries with drug resistance surveillance data for only subnational areas, the data were assumed to be nationally representative. For countries with more than one subnational data point, the subnational data were weighted by subnational annual smear-positive population.

From reported drug resistance data we calculated regional estimates for percentages of (i) new (total =new+retreated) TB cases tested; (ii) new/(total =new+retreated) MDR-TB cases and (iii) new/(total= new+retreated) non MDR-TB cases.

Seven countries and territories reported total numbers of TB cases tested and MDR-TB cases found and did not distinguish "new" from "retreated" cases. For these countries, we used the aforementioned regional estimates to re-distribute totals into new and retreated.[1]

When estimating the number of incident episodes of MDR-TB, a complication arises from the fact that TB incidence estimates include relapses. The probability of MDR-TB in relapse cases is typically higher than the probability of MDR-TB in previously untreated cases. However, too few drug-resistance surveillance datasets include data disaggregated by retreatment status (relapse, retreatment after failure, retreatment after default). Therefore, we assumed that the ratio of MDR-TB proportion among relapse cases to MDR-TB proportion among previously untreated cases, denoted α, followed a wide triangular distribution bounded by 1 and 4, with a mode at 2.5. Whenever α times the level of MDR-TB in previously untreated cases was found superior to the level of MDR-TB in retreatment cases, the level of MDR-TB in relapse cases was assumed equal to the level of MDR-TB in retreatment cases.

The number of incident episodes of MDR-TB among incident TB episodes (including relapses) can be estimated as:

$$I_m = [m_n(1 - r)+\alpha m_n r]I \quad (1)$$

where r is the proportion of relapse cases among notified new and relapse cases and I denotes the estimated incidence of TB.

The number of incident episodes of acquired (during treatment) MDR-TB can be estimated as:

$$I_o = (m_o - m_n)\lambda I \quad (2)$$

where m_o is the probability of MDR-TB among retreatment cases excluding relapses and λ is the ratio of non-relapse retreatment cases notified by National TB programmes to WHO to the sum of new and relapse notified cases. To compute m_o, we observe that:

$$m_t = \alpha m_n \rho + m_o(1 - \rho) \quad (3)$$

where m_t denotes the proportion of MDR-TB cases among all retreatment cases and ρ denotes the proportion of relapses among notified retreatment cases. Therefore,

$$m_o = \frac{m_t - \alpha\rho m_n}{1 - \rho}$$

$$I_o = \left(\frac{m_t - \alpha\rho m_n}{1 - \rho} - m_n\right)\lambda I \quad (4)$$

We assumed that all primary MDR-TB cases will fail their treatment and will be later registered for retreatment. Since a number of primary MDR-TB cases may be cured under first-line drugs, or may die during the course of treatment, equation (4) leads to a slight overestimation of the burden of acquired MDR-TB. However, in a few instances, the right hand side of (4) led to negative numbers due to a small difference between measured MDR-TB levels in new and retreatment cases, in which case, we replaced (4) with:

$$I_o = \left(\frac{1}{2}\,\frac{m_t - \alpha\rho m_n}{1 - \rho}\right)\lambda I \quad (5)$$

[1] Percentage of new cases out of all TB cases tested, by WHO region: AFR 86%, AMR 87%, EMR 85%, EUR 79%, SEA 83%, WPR 87%; percentage of retreated cases out of all TB cases tested, by WHO region: AFR 14%, AMR 13%, EMR 15%, EUR 21%, SEA 17%, WPR 13%; percentage of new TB cases out of all MDR-TB cases, by WHO region: AFR 59%, AMR 51%, EMR 33%, EUR 32%, SEA 42%, WPR 49%; percentage of retreated TB cases out of all MDR-TB cases, by WHO region: AFR 41%, AMR 49%, EMR 67%, EUR 68%, SEA 58%, WPR 51%; percentage of new TB cases out of all non-MDR-TB cases, by WHO region: AFR 87%, AMR 88%, EMR 89%, EUR 85%, SEA 85%, WPR 88%; percentage of retreated TB cases out of all non-MDR-TB cases, by WHO region: AFR 13%, AMR 12%, EMR 11%, EUR 15%, SEA 15%, WPR 12%.

A mixed-effects logistic regression model[1] was fitted to the drug-resistance surveillance data with nine epidemiological regions, as defined in the Global TB Report 2009 Update,[2] set as fixed-effects and countries set as random effects. It was felt that predicted standards errors for fixed effects did not reflect the actual uncertainty of predictions for countries where there is no drug resistance surveillance measurement and tended to be too small in our judgment, leading to overly confident predictions. Therefore, we opted for a simpler statistical approach. In countries with no drug resistance surveillance measurement, missing values where imputed using epidemiological-group specific unweighted means and standard deviations of country measurements. No good data on country events leading to high rates of MDR were available to improve predictions, which are very uncertain. For that reason, it is essential that countries with no representative data on drug resistance urgently set-up a national drug-resistance surveillance system or conduct a nationwide survey.

Posterior distributions of MDR probabilities in new and retreatment cases where derived separately in new and retreatment cases from Bayesian beta-binomial models with uninformative priors following a Beta (1,1) distribution. The posterior distribution of ρ was defined as:

$$f(p|y) = \frac{\Gamma(n+2)}{\Gamma(y+1)+\Gamma(n-y+1)}\ p^{y}(1-p)^{n-y} \qquad (6)$$

where y denotes the number of observed MDR cases among n tested individuals, and Γ represents the Gamma function.

Where p is predicted from the mixed-effects logistic regression model and there was no observed event, then $f(p|\theta)$ is assumed to follow a truncated normal distribution bounded by 0 and 1, with parameters θ derived from the model.

Incidence of TB is assumed to follow a log-normal distribution, as described in Global TB Report 2009 Update.[2] Country-specific and aggregated posterior distributions of estimated MDR-TB events were generated from Monte Carlo simulations and then summarized by extracting their expected value, 2.5% and 97.5% quantiles.

Estimated incident cases of MDR-TB and related uncertainty bounds are shown rounded to 2 significant figures.

Estimates of MDR-TB mortality

Estimates of MDR-TB mortality were derived from Vital Registration measurements of TB mortality (excluding HIV) in 3 epidemiological groups of countries including Eastern Europe (EEUR), Latin America (LAC) and High Income countries (EME), as defined in Global TB Report 2009 Update.[2] The ratio of estimated MDR-TB incident episodes to estimated incidence (all forms) in 2006 (a year when the proportion of mortality figures derived from Vital Registration systems was the highest), was 15% (range 13%–17%) in the group EEUR and 2.3% (range 1.9%–2.9%) in the combined group LAC+EME. The ratio of mortality (excluding HIV) to incidence (all forms) was 16% (range 14%–19%) in EEUR and 9% (range 7%–11%) in LAC+EME. We have assumed that the difference in mortality to incidence ratios reflected to some extent differences in ratios of incident MDR-TB to overall TB incidence between EEUR and LAC+EME, with the other contributing factor being differences in the proportion of cases notified to national TB programmes, out of all incident cases.
TB mortality excluding HIV, is defined by the equation:

$$M_i = KI_i^{+} + \Lambda n_i^{-} + T_i\,(I_i^{-} - n_i^{-}) i \in \{1,2\} \qquad (1)$$

where M denotes TB mortality, i denotes the group EEUR (i=1)or LAC+EME (i=2), I^{+} is the combined incidence of primary and acquired MDR-TB (excluding HIV), subscripts + and – denote MDR and non-MDR, respectively, I^{-} is the incidence of non-MDR TB (excluding HIV), K is the case fatality for MDR-TB in HIV-negative cases, assumed similar between the two groups of countries, Λ is the case fatality for estimated non-MDR cases among notified cases (in HIV-negative cases), T is the case fatality for non-notified non-MDR cases (excluding HIV) and n is the number of notified TB cases (excluding HIV). We use in this section capital letters to denote random variables and small letters to denote scalars. The distribution characteristics of T are described in WHO Global TB Report 2009 Update (Annex).[2]

By expansion of (1), we obtain the following system of linear equations with two unknown random variables K and Λ:

$$KI_1^{+} + \Lambda n_1^{-} = M_1 - T_1\,(I_1^{-} - n_1^{-}) \qquad (2)$$
$$KI_2^{+} + \Lambda n_2^{-} = M_2 - T_2\,(I_2^{-} - n_2^{-})$$

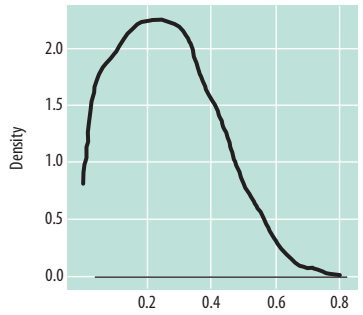
By substitution,

$$K = \frac{n_1^{-}(M_2 - T_2(I_2^{-} - n_2^{-})) - n_2^{-}(M_1 - T_1(I_1^{-} - n_1^{-}))}{I_2^{+}n_1^{-} - I_1^{+}n_2^{-}} \qquad (3)$$

The distribution of K was obtained from Monte Carlo simulations. Its expectation and usual quantiles of interest were extracted. The following plot shows the probability density function of K (**Figure 1**).

[1] Gelman A and Hill J. *Data analysis using regression and multilevel/hierarchical models*. Cambridge, Cambridge University Press, 2006.
[2] *Global tuberculosis control: a short update to the 2009 report*. Geneva, World Health Organization, 2009 (WHO/HTM/TB/2009.426).

FIGURE 1 Probability density function of the estimated case fatality *K* of MDR-TB (excluding HIV)



Global aggregated numbers of MDR-TB deaths were obtained from:

$$M = KI^{+}(1 - H) + XI^{+}H \quad (4)$$

where X denotes MDR-TB case fatality in HIV-positive MDR-TB cases, which was assumed to follow a triangular distribution with bounds 0.5 and 1 and a mode at 0.8. H is the estimated proportion of HIV-infected cases out of incident TB cases (all forms), which was assumed equal to the proportion of HIV-infected cases out of incident MDR-TB cases. The latter assumption is supported by the lack of conclusive evidence of an association between HIV and MDR-TB globally, as discussed in the main text of this report.

Among strong limitations of methods described above is the assumption that MDR-TB case fatality in HIV-negative cases is similar between groups of countries that are very heterogeneous in terms of health systems performance.

Uncertainty ranges presented here are conditional on the underlying data and model specifications and assumptions being correct.

ANNEX 3

Continuous drug resistance surveillance data quality indicators

Country or area	WHO region	Year	Case detection rate among new cases (%)	Culture positivity rate (%)	DST coverage (%)	Satisfactory External Quality Assurance (Yes/No)
Class A surveillance data						
Andorra	EUR	2008	87	75	100	Yes
Australia	WPR	2008	87	72	100	Yes
Austria	EUR	2007	87	59	100	Yes
Bangladesh[a]	SEAR	2008	NA	59	97	Yes
Belgium	EUR	2008	87	81	95	Yes
Canada	AMR	2008	87	81	96	Yes
Chile[a]	AMR	2008	NA	100	100	Yes
China, Hong Kong SAR	WPR	2008	87	61	78	Yes
China, Macao SAR	WPR	2008	87	69	100	Yes
Cyprus	EUR	2008	87	72	100	Yes
Czech Republic	EUR	2008	87	65	93	Yes
Denmark	EUR	2008	87	77	99	Yes
Estonia	EUR	2008	88	78	100	Yes
Finland	EUR	2008	87	71	100	Yes
France	EUR	2007	87	100	99	Yes
Germany	EUR	2008	87	69	78	Yes
Greece	EUR	2007	87	81	100	Yes
Iceland	EUR	2008	87	83	100	Yes
Israel	EUR	2008	87	61	100	Yes
Latvia	EUR	2008	93	78	99	Yes
Lithuania	EUR	2008	89	72	100	Yes
Montenegro	EUR	2008	93	62	101	Yes
Netherlands	EUR	2008	87	73	100	Yes
New Zealand	WPR	2008	87	81	100	Yes
Norway	EUR	2008	87	70	100	Yes
Portugal	EUR	2008	87	67	82	Yes
Puerto Rico	AMR	2008	87	95	100	Yes
Russian Federation, Arkhangelsk Oblast	EUR	2008	85	63	96	Yes
Russian Federation, Belgorod Oblast	EUR	2008	85	58	100	Yes
Russian Federation, Bryansk Oblast	EUR	2008	85	52	100	Yes
Russian Federation, Ivanovo Oblast	EUR	2008	85	72	87	Yes
Russian Federation, Kaliningrad Oblast	EUR	2008	85	52	100	Yes
Russian Federation, Mary El Republic	EUR	2008	85	58	100	Yes
Russian Federation, Murmansk Oblast	EUR	2008	85	55	95	Yes
Russian Federation, Orel Oblast	EUR	2008	85	82	100	Yes
Russian Federation, Pskov Oblast	EUR	2008	85	70	100	Yes
Russian Federation, Republic of Chuvashia	EUR	2008	85	70	98	Yes
Russian Federation, Tomsk Oblast	EUR	2008	85	61	99	Yes
Russian Federation, Vladimir Oblast	EUR	2008	85	51	99	Yes
Serbia	EUR	2008	95	72	80	Yes
Singapore	WPR	2008	87	64	100	Yes
Slovenia	EUR	2008	87	94	97	Yes
Sweden	EUR	2008	87	79	97	Yes
Switzerland	EUR	2008	87	81	99	Yes
United Kingdom	EUR	2007	87	60	93	Yes
United States of America	AMR	2007	87	81	98	Yes

Country or setting	WHO region	Year	Case detection rate among new cases (%)	Culture positivity rate (%)	DST coverage (%)	Satisfactory External Quality Assurance (Yes/No)
Class B surveillance data						
Albania	EUR	2008	87	49	100	Yes
Belarus	EUR	2008	83	59	100	No
Bosnia and Herzegovina	EUR	2008	90	48	100	Yes
Bulgaria	EUR	2008	91	43	69	Yes
Georgia	EUR	2008	96	45	100	Yes
Hungary	EUR	2008	87	48	80	No
Ireland	EUR	2008	87	44	70	Yes
Italy	EUR	2008	87	46	95	Yes
Kazakhstan	EUR	2008	85	36	95	Yes
Luxembourg	EUR	2007	NA	100	67	Yes
Malta	EUR	2008	87	47	100	Yes
Oman	EMR	2008	87	43	100	Yes
Republic of Moldova	EUR	2008	70	44	96	Yes
Russian Federation	EUR	2008	85	41[b]	91[b]	NR
Russian Federation, Altai Republic	EUR	2008	85	49	99	Yes
Russian Federation, Novosibirsk Oblast	EUR	2008	85	43	89	Yes
Russian Federation, Omsk Oblast	EUR	2008	85	40	91	Yes
Russian Federation, Republic of Karelia	EUR	2008	85	46	100	Yes
Russian Federation, Ryazan Oblast	EUR	2008	85	47	100	Yes
Russian Federation, Tyumen Oblast	EUR	2008	85	36	100	Yes
Russian Federation, Vologda Oblast	EUR	2008	85	49	100	Yes
Russian Federation, Yamalo–Nenets Autonomous Okrug	EUR	2008	85	35	89	Yes
Slovakia	EUR	2008	87	61	100	No
South Africa	AFR	2008	72	40	55	NR
The former Yugoslav Republic of Macedonia	EUR	2008	91	45	72	Yes

[a] Data shown for previously treated cases only

[b] Culture positivity rate based on new and relapse cases. DST coverage based on new cases (Ministry of Health and Social Development of the Russian Federation. Indicators from the TB control sector in 2007–2008, Statistical materials, Moscow, 2009)

DST = drug susceptibility testing; NA = not applicable; NR = not reported

AFR = African; AMR = Americas; EMR = Eastern Mediterranean; EUR = European; SEAR = South-East Asia; WPR = Western Pacific

ANNEX 4
Continuous drug resistance surveillance

ANNEX 4A Countries and areas reporting Class A continuous drug resistance surveillance data, 2007–2008

Country income status	Country or area	WHO region	Year	New cases					Previously treated cases					All cases				
				Cases with DST results (H+R)	Multidrug resistant		Any isoniazid resistance		Cases with DST results (H+R)	Multidrug resistant		Any isoniazid resistance		Cases with DST results (H+R)	Multidrug resistant		Any isoniazid resistance	
					number	(%)	number	(%)		number	(%)	number	(%)		number	(%)	number	(%)
MIDDLE-INCOME COUNTRIES	Latvia	EUR	2008	684	83	12.1	193	28.2	144	46	31.9	64	44.4	828	129	15.6	257	31.0
	Lithuania	EUR	2008	1 259	113	9.0	269	21.4	356	162	45.5	199	55.9	1 616	276	17.1	469	29.0
	Montenegro	EUR	2008	75	0	0.0	0	0.0	9	0	0.0	0	0.0	84	0	0.0	0	0.0
	Russian Federation, Arkhangelsk Oblast	EUR	2008	290	69	23.8	—	—	68	40	58.8	—	—	358	109	30.4	—	—
	Russian Federation, Belgorod Oblast	EUR	2008	442	85	19.2	—	—	91	47	51.6	—	—	533	132	24.8	—	—
	Russian Federation, Bryansk Oblast	EUR	2008	549	71	12.9	—	—	54	15	27.8	—	—	603	86	14.3	—	—
	Russian Federation, Ivanovo Oblast	EUR	2008	275	55	20.0	—	—	52	30	57.7	—	—	327	85	26.0	—	—
	Russian Federation, Kaliningrad Oblast	EUR	2008	436	84	19.3	—	—	51	22	43.1	—	—	487	106	21.8	—	—
	Russian Federation, Mary El Republic	EUR	2008	267	43	16.1	—	—	53	20	37.7	—	—	320	63	19.7	—	—
	Russian Federation, Murmansk Oblast	EUR	2008	173	49	28.3	—	—	14	5	35.7	—	—	187	54	28.9	—	—
	Russian Federation, Orel Oblast	EUR	2008	296	16	5.4	—	—	29	14	48.3	—	—	325	30	9.2	—	—
	Russian Federation, Pskov Oblast	EUR	2008	370	101	27.3	—	—	44	22	50.0	—	—	414	123	29.7	—	—
	Russian Federation, Republic of Chuvashia	EUR	2008	613	87	14.2	—	—	92	42	45.7	—	—	705	129	18.3	—	—
	Russian Federation, Tomsk Oblast	EUR	2008	424	55	13.0	—	—	80	43	53.8	—	—	504	98	19.4	—	—
	Russian Federation, Vladimir Oblast	EUR	2008	422	59	14.0	—	—	55	18	32.7	—	—	477	77	16.1	—	—
	Serbia	EUR	2008	923	6	0.7	18	2.0	130	10	7.7	16	12.3	1 058	16	1.5	34	3.2
HIGH-INCOME COUNTRIES	Andorra	EUR	2008	3	0	0.0	0	0.0	0	0	0.0	0	0.0	3	0	0.0	0	0.0
	Australia	WPR	2008	—	—	—	—	—	—	—	—	—	—	887	21	2.4	77	8.7
	Austria	EUR	2007	481	8	1.7	30	6.2	8	1	12.5		0.0	513	9	1.8	34	6.6
	Belgium	EUR	2008	630	15	2.4	42	6.7	48	6	12.5	8	16.7	773	22	2.8	56	7.2
	Canada	AMR	2008	1 098	9	0.8	83	7.6	91	4	4.4	9	9.9	1 249	14	1.1	98	7.8
	China, Hong Kong SAR	WPR	2008	2 443	8	0.3	104	4.3	310	10	3.2	31	10.0	2 753	18	0.7	135	4.9
	China, Macao SAR	WPR	2008	243	5	2.1	6	2.5	25	2	8.0	4	16.0	283	7	2.5	11	3.9
	Cyprus	EUR	2008	29	0	0.0	1	3.4	3	1	33.3	1	33.3	36	1	2.8	4	11.1
	Czech Republic	EUR	2008	483	10	2.1	24	5.0	37	1	2.7	2	5.4	520	11	2.1	26	5.0
	Denmark	EUR	2008	253	0	0.0	11	4.3	28	0	0.0	0	0.0	281	0	0.0	11	3.9
	Estonia	EUR	2008	272	42	15.4	69	25.4	75	32	42.7	34	45.3	347	74	21.3	103	29.7
	Finland	EUR	2008	238	1	0.4	12	5.0	9	0	0.0	0	0.0	247	1	0.4	12	4.9
	France	EUR	2007	1 255	12	1.0	81	6.5	102	7	6.9	13	12.7	1 526	20	1.3	101	6.6

Country income status	Country or area	WHO region	Year	New cases					Previously treated cases					All cases				
				Cases with DST results (H+R)	Multidrug resistant		Any isoniazid resistance		Cases with DST results (H+R)	Multidrug resistant		Any isoniazid resistance		Cases with DST results (H+R)	Multidrug resistant		Any isoniazid resistance	
					number	(%)	number	(%)		number	(%)	number	(%)		number	(%)	number	(%)
HIGH-INCOME COUNTRIES	Germany	EUR	2008	2 360	16	0.7	135	5.7	219	24	11.0	39	17.8	2 854	45	1.6	187	6.6
	Greece	EUR	2007	488	13	2.7	37	7.6	2	1	50.0	1	50.0	533	14	2.6	40	7.5
	Iceland	EUR	2008	5	1	20.0	2	40.0	0	0	0.0	0	0.0	5	1	20.0	2	40.0
	Israel	EUR	2008	222	8	3.6	23	10.4	3	1	33.3	1	33.3	225	9	4.0	24	10.7
	Netherlands	EUR	2008	696	11	1.6	51	7.3	32	2	6.3	4	12.5	728	13	1.8	55	7.6
	New Zealand	WPR	2008	231	0	0.0	10	4.3	6	0	0.0	0	0.0	242	0	0.0	10	4.1
	Norway	EUR	2008	180	1	0.6	25	13.9	14	2	14.3	6	42.9	227	4	1.8	36	15.9
	Portugal	EUR	2008	1 496	19	1.3	104	7.0	145	9	6.2	17	11.7	1 641	28	1.7	121	7.4
	Puerto Rico	AMR	2008	89	1	1.1	5	5.6	1	0	0.0	0	0.0	90	1	1.1	5	5.6
	Singapore	WPR	2008	919	1	0.1	21	2.3	103	3	2.9	10	9.7	1 022	4	0.4	31	3.0
	Slovenia	EUR	2008	182	1	0.5	2	1.1	13	1	7.7	1	7.7	195	2	1.0	3	1.5
	Sweden	EUR	2008	349	7	2.0	36	10.3	30	4	13.3	9	30.0	423	12	2.8	49	11.6
	Switzerland	EUR	2008	258	3	1.2	7	2.7	34	1	2.9	7	20.6	415	5	1.2	17	4.1
	United Kingdom	EUR	2007	3 441	34	1.0	239	6.9	251	14	5.6	25	10.0	4 715	56	1.2	322	6.8
	United States of America	AMR	2007	9 608	104	1.1	717	7.5	496	19	3.8	71	14.3	10 196	125	1.2	796	7.8

DST = drug susceptibility testing
H+R = isoniazid plus rifampicin
AFR = African; AMR = Americas; EMR = Eastern Mediterranean; EUR = European; SEAR = South-East Asia; WPR = Western Pacific

ANNEX 4B Countries and areas reporting Class B continuous drug resistance surveillance data, 2007–2008

Country income status	Country or area	WHO region	Year	New cases					Previously treated cases					All cases				
				Cases with DST results (H+R)	Multidrug resistant		Any isoniazid resistance		Cases with DST results (H+R)	Multidrug resistant		Any isoniazid resistance		Cases with DST results (H+R)	Multidrug resistant		Any isoniazid resistance	
					number	(%)	number	(%)		number	(%)	number	(%)		number	(%)	number	(%)
MIDDLE-INCOME COUNTRIES	Albania	EUR	2008	192	1	0.5	3	1.6	22	1	4.5	—	—	214	2	0.9	—	—
	Belarus	EUR	2008	1 802	301	16.7	382	21.2	1 230	516	42.0	603	49.0	3 237	923	28.5	700	21.6
	Bosnia and Herzegovina	EUR	2008	757	3	0.4	10	1.3	77	9	11.7	22	28.6	834	12	1.4	32	3.8
	Bulgaria	EUR	2008	833	14	1.7	95	11.4	105	18	17.1	27	25.7	938	32	3.4	122	13.0
	Georgia	EUR	2008	1 685	190	11.3	452	26.8	720	290	40.3	392	54.4	2 409	481	20.0	847	35.2
	Kazakhstan	EUR	2008	5 605	1 384	24.7	2 219	39.6	4 474	1 950	43.6	2 571	57.5	10 776	3 676	34.1	5 199	48.2
	Republic of Moldova	EUR	2008	1 212	300	24.8	418	34.5	1 227	748	61.0	851	69.4	2 439	1 048	43.0	1 269	52.0
	Russian Federation	EUR	2008	36 249	5 061	14.0	—	—	6 404	1 899	29.7	—	—	42 653	6 960	16.3	—	—
	Russian Federation, Altai Republic	EUR	2008	95	18	18.9	—	—	21	8	38.1	—	—	116	26	22.4	—	—
	Russian Federation, Novosibirsk Oblast	EUR	2008	1 018	226	22.2	—	—	222	96	43.2	—	—	1 240	322	26.0	—	—
	Russian Federation, Omsk Oblast	EUR	2008	754	111	14.7	—	—	97	30	30.9	—	—	851	141	16.6	—	—
	Russian Federation, Republic of Karelia	EUR	2008	144	43	29.9	—	—	28	13	46.4	—	—	172	56	32.6	—	—
	Russian Federation, Ryazan Oblast	EUR	2008	299	37	12.4	—	—	73	29	39.7	—	—	372	66	17.7	—	—
	Russian Federation, Tyumen Oblast	EUR	2008	458	58	12.7	—	—	111	32	28.8	—	—	569	90	15.8	—	—
	Russian Federation, Vologda Oblast	EUR	2008	232	31	13.4	—	—	37	12	32.4	—	—	269	43	16.0	—	—
	Russian Federation, Yamalo–Nenets Autonomous Okrug	EUR	2008	95	25	26.3	—	—	17	7	41.2	—	—	112	32	28.6	—	—
	South Africa	AFR	2008	—	—	—	—	—	—	—	—	—	—	84 012	8 026	9.6	16 960	20.2
	The former Yugoslav Republic of Macedonia	EUR	2008	130	0	0.0	5	3.8	17	2	11.8	5	29.4	147	2	1.4	10	6.8
HIGH-INCOME COUNTRIES	Hungary	EUR	2008	509	8	1.6	35	6.9	102	8	7.8	13	12.7	611	16	2.6	48	7.9
	Ireland	EUR	2008	114	2	1.8	7	6.1	8	0	0.0	0	0.0	146	3	2.1	9	6.2
	Italy	EUR	2008	1 018	27	2.7	121	11.9	165	24	14.5	46	27.9	1 932	71	3.7	244	12.6
	Luxembourg	EUR	2007	—	—	—	—	—	—	—	—	—	—	26	0	0.0	1	3.8
	Malta	EUR	2008	22	0	0.0	2	9.1	3	0	0.0	0	0.0	25	0	0.0	2	8.0
	Oman	EMR	2008	139	3	2.2	7	5.0	12	1	8.3	4	33.3	151	4	2.6	11	7.3
	Slovakia	EUR	2008	300	1	0.3	7	2.3	62	2	3.2	2	3.2	383	4	1.0	10	2.6

DST = drug susceptibility testing
H+R = isoniazid plus rifampicin
AAFR = African; AMR = Americas; EMR = Eastern Mediterranean; EUR = European; SEAR = South-East Asia; WPR = Western Pacific

ANNEX 5
XDR-TB and resistance to fluoroquinolones, 2002–2009

Country or area	Year	Method	Number of MDR-TB cases	MDR-TB cases tested for second-line drug resistance	Number of fluoro-quinolone-resistant cases	% fluoro-quinolone resistant	Lower CI % fluoro-quinolone resistance	Upper CI % fluoro-quinolone resistance	Number of XDR-TB cases	% XDR	Lower CI % XDR	Upper CI % XDR
Argentina	2005	survey	36	36	3	8.3	1.8	22.5	2	5.6	0.7	18.7
Armenia	2007	survey	199	199	25	12.6	8.3	18.0	10	5.0	2.4	9.0
Australia	2008	surveillance	21	21	—	—	—	—	0	0.0		
Azerbaijan, Baku	2007	survey	431	431	125	29.0	24.8	33.5	55	12.8	9.8	16.3
Bangladesh[a]	2008	surveillance	168	168	15	8.9	—	—	1	0.6	—	—
Belgium	2008	surveillance	22	21	4	19.0	—	—	2	9.5	—	—
Bulgaria	2008	surveillance	32	28	0	0.0	—	—	0	0.0	—	—
Canada	2008	surveillance	14	14	1	7.1	—	—	0	0.0	—	—
China	2007	survey	401	401	110	27.4	23.1	32.1	29	7.2	4.9	10.2
China, Hong Kong SAR	2008	surveillance	18	16	5	31.3	—	—	1	6.3	—	—
China, Macao SAR	2008	surveillance	7	7	1	14.3	—	—	0	0.0	—	—
Croatia	2003–2006	surveillance	5	1	—	—	—	—	0	0.0	—	—
Cyprus	2008	surveillance	1	1	—	—	—	—	0	0.0	—	—
Czech Republic	2008	surveillance	11	10	3	30.0	—	—	1	10.0	—	—
Denmark	2007	surveillance	2	2	—	—	—	—	0	0.0	—	—
Estonia	2008	surveillance	74	72	22	30.6	—	—	9	12.5	—	—
France	2003–2006	surveillance	152	149	—	—	—	—	1	0.7	—	—
Georgia	2006	survey	105	70	3	4.3	0.9	12.0	3	4.3	0.9	12.0
Iceland	2008	surveillance	1	1	1	100.0	—	—	0	0.0	—	—
India, Gujarat State	2006	survey	216	216	52	24.1	18.5	30.3	7	3.2	1.2	6.6
Ireland	2005	surveillance	3	3	—	—	—	—	1	33.3	—	—
Israel	2008	surveillance	9	9	1	11.1	—	—	1	11.1	—	—
Japan	2002	surveillance	60	55	21	38.2	—	—	17	30.9	—	—
Latvia	2008	surveillance	129	128	20	15.6	—	—	19	14.8	—	—
Lithuania	2003–2006	surveillance	656	173	—	—	—	—	25	14.5	—	—
Malta	2007	surveillance	1	1	—	—	—	—	0	0.0	—	—
Netherlands	2003–2006	surveillance	34	33	—	—	—	—	1	3.0	—	—
New Zealand	2008	surveillance	0	—	—	—	—	—	—	—	—	—
Norway	2008	surveillance	4	4	0	0.0	—	—	0	0.0	—	—
Oman	2008	surveillance	4	2	0	0.0	—	—	0	0.0	—	—
Poland	2005	surveillance	46	2	—	—	—	—	1	50.0	—	—
Republic of Korea	2004	survey	110	110	13	11.8	0.1	19.3	2	1.8	0.0	6.4
Republic of Moldova	2006	survey	203	47	11	23.4	12.3	38.0	3	6.4	1.3	17.5
Romania	2003–2006	surveillance	50	44	—	—	—	—	2	4.5	—	—
Russian Federation, Tomsk Oblast	2005	surveillance	201	201	—	—	—	—	11	5.5	—	—
Rwanda	2005	survey	32	32	3	9.4	2.0	25.0	0	0.0	0.0	8.9
Singapore	2008	surveillance	4	4	0	0.0	—	—	0	0.0	—	—
Slovakia	2008	surveillance	4	4	0	0.0	—	—	0	0.0	—	—
Slovenia	2003–2007	surveillance	3	3	—	—	—	—	1	33.3	—	—
South Africa	2008	surveillance	8 026	5 451	776	14.2	—	—	573	10.5	—	—
Spain, Aragon	2005	survey	4	4	1	25.0	0.6	80.6	1	25.0	0.6	80.6
Spain, Barcelona	2005	surveillance	4	4	—	—	—	—	0	0.0	—	—
Spain, Galicia	2006	surveillance	2	2	0	0.0	—	—	0	0.0	—	—
Sweden	2008	surveillance	12	11	1	9.1	—	—	1	9.1	—	—
Switzerland	2008	surveillance	5	5	1	20.0	—	—	0	0.0	—	—
Tajikistan, Dushanbe & Rudaki	2009	survey	100	100	25	25.0	16.9	34.7	21	21.0	13.5	30.3

Country or area	Year	Method	Number of MDR-TB cases	MDR-TB cases tested for second-line drug resistance	Number of fluoro-quinolone-resistant cases	% fluoro-quinolone resistant	Lower CI % fluoro-quinolone resistance	Upper CI % fluoro-quinolone resistance	Number of XDR-TB cases	% XDR	Lower CI % XDR	Upper CI % XDR
Ukraine, Donetsk Oblast	2006	survey	379	20	3	15.0	3.2	37.9	3	15.0	3.2	37.9
United Kingdom	2007	surveillance	53	45	—	—	—	—	1	2.2	—	—
United Republic of Tanzania	2007	survey	6	6	0	0.0	0.0	39.3	0	0.0	0.0	39.3
United States of America	2007	surveillance	125	79	6	7.6	—	—	2	2.5	—	—

[a] Damien Foundation Area, only previously treated cases.
CI = confidence interval
MDR-TB = multidrug-resistant TB
XDR-TB = extensively drug-resistant TB

ANNEX 6
Estimates of MDR-TB, by WHO region, 2008

AFRICAN REGION

Country	Source of estimates	% MDR among new TB cases (95% CI)	% MDR among previously treated TB cases (95% CI)	Number of MDR-TB among incident new and relapse TB cases (95% CI)	Number of incident acquired MDR-TB cases (95% CI)	Number of MDR-TB among incident total TB cases (95% CI)
Algeria	DRS, 2001	1.2 (0.5–2.5)	14.4 (0.0–38.1)	250 (92–500)	20 (0–53)	270 (69–470)
Angola	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	550 (17–1,200)	240 (0–630)	790 (110–1,500)
Benin	DRS, 1997	0.3 (0.0–1.7)	14.4 (0.0–38.1)	26 (1–98)	32 (0–84)	58 (0–120)
Botswana	DRS, 2008	3.4 (2.4–4.8)	13.1 (8.6–19.6)	500 (330–720)	16 (7–28)	520 (330–710)
Burkina Faso	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	350 (14–790)	370 (0–990)	720 (100–1,300)
Burundi	model	1.8 (0.0–4.3)	7.7 (0.0–18.1)	580 (54–1 200)	15 (0–41)	600 (13–1 200)
Cameroon	model	1.8 (0.0–4.3)	7.7 (0.0–18.1)	730 (68–1 600)	46 (0–130)	780 (47–1 500)
Cape Verde	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	8 (0–18)	5 (0–13)	13 (2–23)
Central African Republic	DRSa, 1998	1.1 (0.5–2.5)	18.2 (8.6–34.4)	170 (56–360)	50 (17–98)	220 (70–380)
Chad	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	330 (10–760)	190 (0–520)	530 (80–970)
Comoros	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	3 (0–6)	1 (0–2)	4 (0–7)
Congo	model	1.8 (0.0–4.3)	7.7 (0.0–18.1)	290 (27–620)	17 (0–47)	310 (17–600)
Côte d'Ivoire	DRS, 2006	2.5 (1.3–4.9)	7.7 (0.0–18.1)	2 400 (1 000–4 400)	82 (0–220)	2 500 (820–4 100)
Democratic Republic of the Congo	model	1.8 (0.0–4.3)	7.7 (0.0–18.1)	5 100 (470–11 000)	570 (0–1 500)	5 600 (530–11 000)
Equatorial Guinea	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	36 (2–92)	2 (0–8)	39 (0–83)
Eritrea	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	49 (3–110)	9 (0–23)	58 (3–110)
Ethiopia	DRS, 2005	1.6 (0.9–2.7)	11.8 (6.4–21.0)	5 000 (2 600–8 300)	160 (61–310)	5 200 (2 400–8 000)
Gabon	model	1.8 (0.0–4.3)	7.7 (0.0–18.1)	130 (12–290)	13 (0–34)	150 (12–280)
Gambia	DRS, 2000	0.5 (0.0–2.6)	0.0 (0.0–20.4)	23 (1–85)	19 (0–50)	42 (0–91)
Ghana	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	480 (32–1 100)	160 (0–410)	640 (83–1 200)
Guinea	DRS, 1998	0.6 (0.2–1.6)	28.1 (15.6–45.4)	180 (38–440)	270 (130–460)	460 (200–710)
Guinea-Bissau	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	36 (2–81)	3 (0–7)	39 (0–77)
Kenya	DRS, 1995	0.0 (0.0–0.9)	0.0 (0.0–7.7)	2 500 (230–5 300)	820 (0–2 200)	3 300 (580–6 000)
Lesotho	DRS, 1995	0.9 (0.3–2.6)	5.7 (1.9–15.4)	130 (28–300)	64 (5–170)	200 (38–350)
Liberia	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	110 (8–240)	17 (0–44)	120 (9–240)
Madagascar	DRS, 2007	0.5 (0.2–1.3)	3.9 (1.1–13.2)	270 (76–590)	59 (3–180)	330 (66–600)
Malawi	model	1.8 (0.0–4.3)	7.7 (0.0–18.1)	990 (91–2 100)	220 (0–610)	1 211 (180–2 200)
Mali	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	420 (27–940)	220 (0–580)	640 (110–1 200)
Mauritania	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	110 (2–250)	16 (0–43)	130 (1–250)
Mauritius	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	3 (0–6)	0 (0–1)	3 (0–6)
Mozambique	DRS, 2006	3.5 (2.5–4.7)	11.2 (4.2–30.0)	3 500 (2300–4 900)	100 (7–280)	3 600 (2 300–4 800)
Namibia	model	1.8 (0.0–4.3)	7.7 (0.0–18.1)	350 (30–740)	23 (0–63)	370 (24–720)
Niger	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	270 (10–620)	78 (0–210)	350 (34–670)
Nigeria	model	1.8 (0.0–4.3)	7.7 (0.0–18.1)	9 300 (860–20 000)	1 600 (0–4 300)	11 000 (1 300–20 000)
Rwanda	DRS, 2005	3.9 (2.6–5.7)	9.4 (4.8–17.5)	1 500 (970–2 300)	43 (5–100)	1 600 (950–2 200)
Sao Tome and Principe	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	2 (0–4)	1 (0–3)	3 (0–5)
Senegal	DRS, 2006	2.1 (0.9–4.8)	16.7 (8.3–30.6)	820 (270–1 700)	260 (80–500)	1 100 (360–1 800)
Seychelles	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	0 (0–1)	0 (0–0)	0 (0–1)
Sierra Leone	DRS, 1997	0.9 (0.0–4.7)	23.1 (8.2–50.3)	300 (8–1 100)	170 (32–370)	470 (0–1000)
South Africa	DRS, 2002	1.8 (1.5–2.3)	6.7 (5.5–8.1)	10 000 (7 500–13 000)	2 800 (1 900–3 900)	13 000 (10 000–16 000)
Swaziland	DRS, 1995	0.9 (0.3–2.6)	9.1 (3.6–21.2)	150 (30–350)	120 (22–290)	270 (67–470)
Togo	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	290 (19–650)	140 (0–380)	430 (71–790)
Uganda	DRS,[a] 1997	0.5 (0.1–1.9)	4.4 (1.2–14.8)	570 (72–1 600)	160 (8–480)	730 (0–1 500)
United Republic of Tanzania	DRS, 2007	1.1 (0.4–2.8)	0.0 (0.0–7.3)	940 (260–2 100)	240 (0–640)	1 200 (250–2 100)
Zambia	DRS, 2000	1.8 (0.9–3.5)	2.3 (0.1–11.8)	1 100 (470–2 000)	64 (1–330)	1 100 (400–1 900)
Zimbabwe	DRS, 1995	1.9 (1.1–3.3)	8.3 (2.9–21.8)	1 900 (1 000–3 200)	460 (33–1 300)	2 400 (1 200–3 600)

[a] Estimates based on subnational drug resistance data. DRS = drug resistance surveillance or survey data; CI = confidence interval; MDR-TB = multidrug-resistant TB

REGION OF THE AMERICAS

Country	Source of estimates	% MDR among new TB cases (95% CI)	% MDR among previously treated TB cases (95% CI)	Number of MDR-TB among incident new and relapse TB cases (95% CI)	Number of incident acquired MDR-TB cases (95% CI)	Number of MDR-TB among incident total TB cases (95% CI)
Antigua and Barbuda	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	0 (0–0)	0 (0–0)	0 (0–0)
Argentina	DRS, 2005	2.2 (1.3–3.6)	15.4 (10.3–22.5)	270 (150–440)	220 (120–340)	490 (310–670)
Bahamas	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	2 (0–6)	0 (0–1)	3 (0–6)
Barbados	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	0 (0–0)	0 (0–0)	0 (0–0)
Belize	model	2.0 (0.0–6.0)	12.1 (0.0–28.3)	3 (0–8)	0 (0–1)	4 (0–7)
Bolivia (Plurinational State of)	DRS, 1996	1.2 (0.6–2.6)	4.7 (2.0–10.5)	190 (69–350)	8 (1–21)	190 (54–330)
Brazil	DRS, 1996	0.9 (0.6–1.4)	5.4 (4.1–7.2)	900 (520–1 400)	470 (290–680)	1 400 (900–1 800)
Canada	DRS, 2008	0.8 (0.4–1.6)	4.4 (1.7–10.8)	16 (7–27)	2 (0–4)	17 (7–27)
Chile	DRS, 2001	0.7 (0.3–1.5)	3.8 (2.1–6.6)	15 (6–30)	2 (1–3)	17 (5–29)
Colombia	DRS, 2000	1.5 (0.9–2.4)	12.1 (0.0–28.3)	260 (150–420)	57 (0–150)	320 (170–470)
Costa Rica	DRS, 2006	1.5 (0.6–3.8)	4.8 (0.2–22.7)	8 (2–16)	0 (0–2)	8 (1–15)
Cuba	DRS, 2005	0.0 (0.0–2.2)	5.3 (0.3–24.6)	18 (1–42)	1 (0–3)	19 (0–40)
Dominica	model	2.0 (0.0–6.0)	12.1 (0.0–28.3)	0 (0–1)	0 (0–1)	0 (0–1)
Dominican Republic	DRS, 1995	6.6 (4.3–10.0)	19.7 (13.5–27.8)	550 (340–790)	42 (18–72)	590 (370–810)
Ecuador	DRS, 2002	4.9 (3.6–6.6)	24.3 (18.7–31.0)	590 (400–810)	140 (91–210)	730 (520–950)
El Salvador	DRS, 2001	0.3 (0.1–1.2)	7.0 (3.4–13.7)	7 (1–19)	2 (1–4)	9 (0–18)
Grenada	model	2.0 (0.0–6.0)	12.1 (0.0–28.3)	0 (0–0)	0 (0–0)	0 (0–0)
Guatemala	DRS, 2002	3.0 (1.9–4.6)	26.5 (20.1–33.9)	290 (170–440)	45 (30–63)	330 (200–470)
Guyana	model	2.0 (0.0–6.0)	12.1 (0.0–28.3)	23 (1–54)	12 (0–32)	35 (5–65)
Haiti	model	2.0 (0.0–6.0)	12.1 (0.0–28.3)	630 (40–1 500)	10 (0–27)	640 (0–1300)
Honduras	DRS, 2004	1.8 (0.9–3.4)	12.3 (6.6–21.8)	95 (40–170)	6 (2–11)	100 (35–170)
Jamaica	model	2.0 (0.0–6.0)	12.1 (0.0–28.3)	5 (0–11)	1 (0–2)	5 (0–11)
Mexico	DRS,[a] 1997	2.4 (1.2–4.7)	22.4 (15.6–31.2)	540 (240–980)	130 (79–200)	670 (310–1 000)
Nicaragua	DRS, 2006	0.6 (0.2–2.2)	7.8 (4.0–14.6)	20 (2–53)	7 (2–13)	26 (1–52)
Panama	model	2.0 (0.0–6.0)	12.1 (0.0–28.3)	42 (3–98)	16 (0–40)	58 (7–110)
Paraguay	DRS, 2001	2.1 (0.9–4.9)	3.9 (1.1–13.2)	65 (22–130)	2 (0–9)	68 (14–120)
Peru	DRS, 2006	5.3 (4.3–6.4)	23.6 (19.5–28.3)	2 300 (1 800–2 800)	300 (220–390)	2 600 (2 000–3 100)
Saint Kitts and Nevis	model	2.0 (0.0–6.0)	12.1 (0.0–28.3)	0 (0–0)	0 (0–0)	0 (0–0)
Saint Lucia	model	2.0 (0.0–6.0)	12.1 (0.0–28.3)	1 (0–2)	0 (0–0)	1 (0–1)
Saint Vincent and the Grenadines	model	2.0 (0.0–6.0)	12.1 (0.0–28.3)	1 (0–2)	1 (0–2)	1 (0–3)
Suriname	model	2.0 (0.0–6.0)	12.1 (0.0–28.3)	17 (1–39)	3 (0–8)	20 (1–39)
Trinidad and Tobago	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	14 (1–36)	5 (0–15)	19 (0–37)
United States of America	DRS, 2007	1.1 (0.9–1.3)	3.8 (2.5–5.9)	180 (140–220)	14 (6–24)	190 (150–230)
Uruguay	DRS, 2005	0.0 (0.0–1.1)	6.1 (1.7–19.6)	20 (1–46)	3 (0–7)	23 (1–45)
Venezuela (Bolivarian Republic of)	DRS, 1999	0.5 (0.2–1.3)	13.5 (8.2–21.3)	54 (15–120)	39 (20–63)	93 (37–150)

[a] Estimates based on subnational drug resistance data. DRS = drug resistance surveillance or survey data; CI = confidence interval; MDR-TB = multidrug-resistant TB

EASTERN MEDITERRANEAN REGION

Country	Source of estimates	% MDR among new TB cases (95% CI)	% MDR among previously treated TB cases (95% CI)	Number of MDR-TB among incident new and relapse TB cases (95% CI)	Number of incident acquired MDR-TB cases (95% CI)	Number of MDR-TB among incident total TB cases (95% CI)
Afghanistan	model	2.9 (0.0–8.0)	35.4 (0.0–75.1)	1 800 (160–3 900)	580 (0–1 300)	2 400 (420–4 300)
Bahrain	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	15 (1–39)	1 (0–4)	16 (0–35)
Djibouti	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	55 (2–120)	7 (0–20)	62 (2–120)
Egypt	DRS, 2002	2.2 (1.3–3.7)	38.2 (32.0–44.9)	400 (210–640)	190 (150–250)	590 (370–800)
Iran (Islamic Republic of)	DRS, 1998	5.0 (3.5–6.9)	48.2 (35.7–61.0)	790 (520–1 100)	86 (57–120)	870 (570–1 200)
Iraq	model	2.9 (0.0–8.0)	35.4 (0.0–75.1)	690 (58–1 500)	130 (0–300)	820 (95–1 500)
Jordan	DRS, 2004	5.4 (2.5–11.3)	40.0 (24.6–57.7)	20 (8–39)	4 (2–7)	25 (9–40)
Kuwait	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	43 (2–110)	3 (0–10)	46 (0–99)
Lebanon	DRS, 2003	1.1 (0.3–3.8)	62.5 (38.6–81.5)	6 (1–17)	12 (7–17)	18 (9–28)
Libyan Arab Jamahiriya	model	2.9 (0.0–8.0)	35.4 (0.0–75.1)	89 (8–190)	29 (0–65)	120 (21–210)
Morocco	DRS, 2006	0.5 (0.2–1.1)	12.2 (8.2–17.7)	160 (52–330)	38 (23–56)	200 (60–330)
Oman	DRS, 2008	2.2 (0.7–6.2)	8.3 (0.4–35.4)	8 (2–19)	0 (0–1)	8 (0–16)
Pakistan	model	2.9 (0.0–8.0)	35.4 (0.0–75.1)	14 000 (1 200–30 000)	1 700 (0–3 800)	15 000 (1 200–29 000)
Qatar	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	3 (0–11)	1 (0–3)	4 (0–10)
Saudi Arabia	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	210 (9–520)	4 (0–14)	210 (0–460)
Somalia	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	270 (8–610)	130 (0–340)	390 (56–730)
Sudan	model	0.9 (0.0–2.4)	14.4 (0.0–38.1)	510 (27–1 100)	350 (0–920)	850 (140–1 600)
Syrian Arab Republic	model	2.9 (0.0–8.0)	35.4 (0.0–75.1)	160 (14–340)	91 (0–200)	250 (58–440)
Tunisia	model	2.9 (0.0–8.0)	35.4 (0.0–75.1)	80 (7–170)	27 (0–60)	110 (21–190)
United Arab Emirates	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	8 (0–21)	1 (0–2)	9 (0–19)
Yemen	DRS, 2004	2.9 (1.8–4.8)	11.3 (5.3–22.6)	450 (250–710)	40 (6–90)	490 (260–720)

[a] Estimates based on subnational drug resistance data. DRS = drug resistance surveillance or survey data; CI = confidence interval; MDR-TB = multidrug-resistant TB

EUROPEAN REGION

Country	Source of estimates	% MDR among new TB cases (95% CI)	% MDR among previously treated TB cases (95% CI)	Number of MDR-TB among incident new and relapse TB cases (95% CI)	Number of incident acquired MDR-TB cases (95% CI)	Number of MDR-TB among incident total TB cases (95% CI)
Albania	model	0.4 (0.0–1.3)	5.6 (0.0–13.1)	2 (0–5)	0 (0–1)	3 (0–5)
Andorra	DRS, 2008	0.0 (0.0–56.1)	10.8 (0.0–34.5)	0 (0–1)	0 (0–0)	0 (0–0)
Armenia	DRS, 2007	9.4 (7.3–12.1)	43.2 (38.1–48.5)	260 (180–350)	220 (160–290)	480 (380–580)
Austria	DRS, 2005	1.9 (1.1–3.4)	12.5 (3.5–36.0)	—	—	—
Azerbaijan	DRS,[a] 2007	22.3 (19.0–26.0)	55.8 (51.6–59.9)	2 800 (2 200–3 500)	1 200 (940–1 600)	4 000 (3 300–4 700)
Belarus	model	12.5 (0.0–25.3)	42.1 (11.9–72.2)	660 (130–1 200)	140 (12–300)	800 (260–1 300)
Belgium	DRS, 2008	2.4 (1.4–3.9)	12.5 (5.9–24.7)	22 (12–35)	8 (2–17)	30 (17–43)
Bosnia and Herzegovina	DRS, 2005	0.4 (0.2–1.0)	6.6 (3.2–13.0)	8 (2–17)	1 (0–2)	9 (2–17)
Bulgaria	model	12.5 (0.0–25.3)	42.1 (11.9–72.2)	440 (81–810)	18 (2–38)	460 (99–810)
Croatia	DRS, 2005	0.5 (0.2–1.5)	4.9 (1.7–13.5)	6 (1–15)	2 (0–4)	8 (1–15)
Cyprus	DRS, 2008	0.0 (0.0–11.7)	33.3 (1.7–79.2)	2 (0–5)	0 (0–1)	2 (0–5)
Czech Republic	DRS, 2008	2.1 (1.1–3.8)	2.7 (0.1–13.8)	19 (9–33)	1 (0–5)	20 (8–33)
Denmark	DRS, 2008	0.0 (0.0–1.5)	0.0 (0.0–12.1)	16 (1–42)	4 (0–13)	20 (0–41)
Estonia	DRS, 2008	15.4 (11.6–20.1)	42.7 (32.1–53.9)	85 (64–110)	9 (5–13)	94 (71–120)
Finland	DRS, 2008	0.4 (0.0–2.3)	0.0 (0.0–29.9)	2 (0–6)	2 (0–7)	4 (0–8)
France	DRS, 2007	1.0 (0.5–1.7)	6.9 (3.4–13.5)	37 (19–61)	26 (8–52)	63 (33–93)
Georgia	DRS, 2006	6.8 (5.2–8.7)	27.4 (23.7–31.4)	360 (270–460)	310 (240–380)	670 (550–780)
Germany	DRS, 2008	0.7 (0.4–1.1)	11.0 (7.5–15.8)	31 (17–48)	25 (15–37)	56 (37–74)
Greece	DRS, 2008	2.7 (1.6–4.5)	50.0 (2.6–97.4)	17 (9–27)	42 (1–86)	58 (16–100)
Hungary	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	74 (2–190)	4 (0–15)	78 (0–170)
Iceland	DRS, 2008	20.0 (1.0–62.4)	10.8 (0.0–34.5)	1 (0–4)	0 (0–0)	1 (0–3)
Ireland	DRS, 2005	0.5 (0.0–2.8)	10.0 (0.5–40.4)	2 (0–7)	4 (0–13)	6 (0–13)
Israel	DRS, 2005	3.6 (1.8–6.9)	33.3 (1.7–79.2)	16 (7–28)	1 (0–2)	16 (6–27)
Italy	DRS,[a] 2005	1.6 (0.8–3.2)	17.7 (10.9–27.6)	65 (28–120)	54 (28–87)	120 (66–170)
Kazakhstan	DRS, 2001	14.2 (11.0–18.2)	56.4 (50.9–61.8)	5 300 (3 900–6 900)	2700 (2 100–3 500)	8 100 (6 400–9 700)
Kyrgyzstan	model	12.5 (0.0–25.3)	42.1 (11.9–72.2)	1 200 (230–2 300)	140 (13–310)	1 400 (350–2 400)
Latvia	DRS, 2008	12.1 (9.9–14.8)	31.9 (24.9–39.9)	160 (130–200)	4 (2–6)	170 (140–200)
Lithuania	DRS, 2008	9.0 (7.5–10.7)	47.5 (42.9–52.2)	270 (210–330)	68 (55–83)	330 (270–390)
Luxembourg	DRS, 2005	0.0 (0.0–9.6)	10.8 (0.0–34.5)	—	—	—
Malta	DRS, 2005	0.0 (0.0–25.9)	10.8 (0.0–34.5)	3 (0–6)	0 (0–0)	3 (0–6)
Monaco	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	—	—	—
Montenegro	DRS, 2008	0.0 (0.0–4.9)	0.0 (0.0–29.9)	1 (0–1)	0 (0–0)	1 (0–2)
Netherlands	DRS, 2008	1.6 (0.9–2.8)	6.3 (1.7–20.1)	18 (9–30)	1 (0–3)	19 (9–30)
Norway	DRS, 2008	0.6 (0.0–3.1)	14.3 (4.0–39.9)	2 (0–6)	4 (0–11)	6 (0–12)
Poland	DRS, 2004	0.3 (0.1–0.6)	8.2 (6.2–10.9)	31 (13–58)	43 (29–60)	74 (47–100)
Portugal	DRS, 2008	1.3 (0.8–2.0)	6.2 (3.3–11.4)	45 (27–68)	3 (1–6)	48 (28–69)
Republic of Moldova	DRS, 2006	19.4 (16.8–22.2)	50.8 (48.7–53.0)	1 500 (1 200–1 800)	620 (490–770)	2 100 (1 700–2 400)
Romania	DRS, 2004	2.8 (1.9–4.2)	11.0 (8.2–14.5)	1 100 (680–1 500)	190 (110–300)	1 300 (840–1 700)
Russian Federation	DRS,[a] 2008	15.8 (11.9–19.7)	42.4 (38.1–46.7)	26 000 (20 000–34 000)	12 000 (8 700–15 000)	38 000 (30 000–45 000)
San Marino	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	—	—	—
Serbia	DRS, 2008	0.7 (0.3–1.4)	7.7 (4.2–13.6)	14 (5–28)	5 (2–8)	19 (7–30)
Slovakia	DRS, 2008	0.3 (0.0–1.9)	3.2 (0.9–11.0)	3 (0–9)	0 (0–1)	3 (0–7)
Slovenia	DRS, 2008	0.5 (0.0–3.0)	7.7 (0.4–33.3)	1 (0–5)	0 (0–1)	2 (0–4)
Spain	DRS,[a] 2005	0.1 (0.0–0.4)	5.1 (0.0–13.7)	104 (3–385)	21 (2–51)	125 (0–313)
Sweden	DRS, 2008	2.0 (1.0–4.1)	13.3 (5.3–29.7)	11 (4–20)	5 (1–11)	15 (6–25)
Switzerland	DRS, 2008	1.2 (0.4–3.4)	2.9 (0.2–14.9)	4 (1–10)	1 (0–6)	6 (0–11)
Tajikistan	DRS,[a] 2008	16.5 (11.3–23.6)	61.6 (52.8–69.7)	2 500 (1 600–3 500)	1 500 (1 100–2 100)	4 000 (2 900–5 100)
TFYR of Macedonia	model	0.4 (0.0–1.3)	5.6 (0.0–13.1)	2 (0–5)	0 (0–1)	3 (0–5)
Turkey	model	0.4 (0.0–1.3)	5.6 (0.0–13.1)	100 (6–230)	47 (0–110)	150 (24–270)
Turkmenistan	DRS,[a] 2002	3.8 (1.5–9.4)	18.4 (11.9–27.2)	140 (40–300)	21 (9–35)	160 (35–290)
Ukraine	DRS,[a] 2002	16.0 (13.8–18.3)	44.3 (40.0–48.7)	8 200 (6 500–10 000)	440 (340–570)	8 700 (6 800–11 000)
United Kingdom of Great Britain and Northern Ireland	DRS, 2007	1.0 (0.7–1.3)	6.4 (3.3–12.1)	72 (48–100)	26 (9–51)	98 (66–130)
Uzbekistan	DRS,[a] 2005	14.2 (10.4–18.1)	49.8 (35.8–63.8)	5 700 (4 000–7 700)	3 000 (1 700–4 400)	8 700 (6 500–11 000)

[a] Estimates based on subnational drug resistance data. DRS = drug resistance surveillance or survey data; CI = confidence interval; MDR-TB = multidrug-resistant TB

SOUTH-EAST ASIA REGION

Country	Source of estimates	% MDR among new TB cases (95% CI)	% MDR among previously treated TB cases (95% CI)	Number of MDR-TB among incident new and relapse TB cases (95% CI)	Number of incident acquired MDR-TB cases (95% CI)	Number of MDR-TB among incident total TB cases (95% CI)
Bangladesh	model	2.2 (0.0–5.6)	14.7 (0.0–39.6)	8 900 (1 000–19 000)	940 (0–2 700)	9 800 (1 000–19 000)
Bhutan	model	2.2 (0.0–5.6)	14.7 (0.0–39.6)	29 (3–60)	4 (0–11)	33 (4–61)
DPR Korea	model	2.2 (0.0–5.6)	14.7 (0.0–39.6)	2 000 (220–4 200)	1900 (0–5 300)	3900 (658–7 200)
India	DRS,[a] 2005	2.3 (1.8–2.8)	17.2 (14.9–19.5)	55 000 (40 000–74 000)	43 000 (33 000–56 000)	99 000 (79 000–120 000)
Indonesia	DRS,[a] 2004	2.0 (0.5–6.9)	14.7 (0.0–39.6)	8 900 (1 100–25 000)	360 (0–1 000)	9 300 (0–21 000)
Maldives	model	2.2 (0.0–5.6)	14.7 (0.0–39.6)	3 (0–6)	0 (0–1)	3 (0–6)
Myanmar	DRS, 2007	4.2 (3.2–5.6)	10.0 (7.1–14.0)	8 900 (6 300–12 000)	450 (180–770)	9 300 (6 400–12 000)
Nepal	DRS, 2007	2.9 (1.9–4.3)	11.7 (7.6–17.6)	1 600 (980–2 400)	66 (30–110)	1 700 (990–2 300)
Sri Lanka	DRS, 2006	0.2 (0.0–1.0)	0.0 (0.0–10.2)	25 (1–94)	38 (0–110)	63 (0–130)
Thailand	DRS, 2006	1.7 (1.1–2.6)	34.5 (28.2–41.5)	1 700 (950–2 500)	1 300 (940–1 700)	2 900 (2 100–3 800)
Timor-Leste	model	2.2 (0.0–5.6)	14.7 (0.0–39.6)	130 (15–280)	3 (0–8)	130 (6–260)

[a] Estimates based on subnational drug resistance data. DRS = drug resistance surveillance or survey data; CI = confidence interval; MDR-TB = multidrug-resistant TB

WESTERN PACIFIC REGION

Country	Source of estimates	% MDR among new TB cases (95% CI)	% MDR among previously treated TB cases (95% CI)	Number of MDR-TB among incident new and relapse TB cases (95% CI)	Number of incident acquired MDR-TB cases (95% CI)	Number of MDR-TB among incident total TB cases (95% CI)
Australia	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	19 (9–33)	1 (0–2)	21 (9–32)
Brunei Darussalam	model	2.2 (0.0–10.7)	10.8 (0.0–34.5)	11 (0–29)	1 (0–3)	12 (0–26)
Cambodia	DRS, 2001	0.0 (0.0–0.6)	3.1 (1.1–8.8)	2 000 (112–4 900)	200 (0–580)	2 200 (0–4 600)
China	DRS, 2007	5.7 (5.0–6.6)	25.6 (22.6–28.3)	84 000 (65 000–106 000)	1 5000 (12 000–20 000)	100 000 (79 000–120 000)
Cook Islands	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	0 (0–0)	0 (0–0)	0 (0–0)
Fiji	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	5 (0–12)	1 (0–2)	5 (0–11)
Japan	DRS, 2002	0.7 (0.5–1.1)	9.8 (7.3–13.1)	220 (130–340)	64 (43–87)	290 (180–390)
Kiribati	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	10 (1–24)	1 (0–3)	11 (0–22)
Lao People's Democratic Republic	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	270 (13–650)	8 (0–23)	280 (0–590)
Malaysia	DRS,[a] 1997	0.1 (0.0–0.6)	0.0 (0.0–19.4)	31 (1–120)	74 (0–210)	104 (0–220)
Marshall Islands	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	4 (0–9)	0 (0–1)	4 (0–8)
Micronesia (Federated States of)	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	3 (0–7)	0 (0–0)	3 (0–6)
Mongolia	DRS, 1999	1.0 (0.4–2.5)	13.8 (0.0–36.2)	63 (17–140)	43 (0–120)	110 (21–190)
Nauru	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	0 (0–0)	0 (0–0)	0 (0–0)
New Zealand	DRS, 2008	0.0 (0.0–1.6)	0.0 (0.0–39.0)	15 (1–37)	1 (0–2)	15 (0–33)
Niue	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	—	—	—
Palau	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	0 (0–1)	0 (0–0)	0 (0–1)
Papua New Guinea	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	530 (9–1 300)	73 (0–210)	600 (0–1 200)
Philippines	DRS, 2004	4.0 (3.0–5.5)	20.9 (14.8–28.7)	11 000 (7 300–15 000)	2 000 (1 100–3 000)	13 000 (8 900–17 000)
Republic of Korea	DRS, 2004	2.7 (2.1–3.4)	14.0 (10.4–18.6)	1 400 (1 000–1 700)	490 (300–700)	1 900 (1 400–2 300)
Samoa	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	1 (0–2)	0 (0–0)	1 (0–2)
Singapore	DRS, 2008	0.1 (0.0–0.6)	2.9 (1.0–8.2)	2 (0–9)	1 (0–3)	4 (0–8)
Solomon Islands	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	18 (1–43)	3 (0–7)	20 (0–42)
Tonga	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	1 (0–2)	0 (0–0)	1 (0–2)
Tuvalu	model	1.9 (0.0–7.5)	13.8 (0.0–36.2)	0 (0–1)	0 (0–1)	1 (0–1)
Vanuatu	DRS, 2006	0.0 (0.0–11.7)	13.8 (0.0–36.2)	5 (0–12)	0 (0–1)	5 (0–11)
Viet Nam	DRS, 2006	2.7 (2.0–3.6)	19.3 (14.5–25.2)	5 600 (3 700–8 100)	280 (180–420)	5 900 (3 800–8 100)

[a] Estimates based on subnational drug resistance data. DRS = drug resistance surveillance or survey data; CI = confidence interval; MDR-TB = multidrug-resistant TB

ANNEX 7
Treatment outcomes

ANNEX 7A Treatment outcomes for new MDR-TB cases, 2006 (or 2004–2005)

Country or area	Year	New MDR-TB cases			Cured	Completed	Success[a]	Died		Failed		Defaulted		Transferred		Still on treatment	
		expected among TB cases notified[b]	detected and reported	with outcome reported	number	number	%	number	%	number	%	number	%	number	%	number	%
i) Data from sites using international standards of care[c]																	
Armenia	2006	120	65	9	2	1	33	1	11	1	11	4	44	0	0	0	0
Australia	2006	15	17	16	2	10	75	0	0	0	0	1	6	3	19	0	0
Bahrain	2006	4	2	2	2	0	100	0	0	0	0	0	0	0	0	0	0
Belgium	2006	17	8	8	7	0	88	1	13	0	0	0	0	0	0	0	0
Bolivia (Plurinational State of)	2006	82	34	4	1	1	50	1	25	1	25	0	0	0	0	0	0
Cambodia	2006	0	0	1	0	1	100	0	0	0	0	0	0	0	0	0	0
Canada	2006	8	8	9	0	7	78	0	0	0	0	0	0	1	11	1	11
China, Hong Kong SAR	2006	13	16	17	10	0	59	3	18	0	0	1	6	3	18	0	0
China, Macao SAR	2006	7	7	8	4	3	88	1	13	0	0	0	0	0	0	0	0
Costa Rica	2006	6	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Dominican Republic	2006	237	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Egypt	2006	151	7	2	2	0	100	0	0	0	0	0	0	0	0	0	0
El Salvador	2006	4	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Estonia	2006	53	36	36	19	2	58	10	28	1	3	4	11	0	0	0	0
Georgia	2006	208	111	—[d]	—	—	—	—	—	—	—	—	—	—	—	—	—
Germany	2006	27	65	56	18	17	63	4	7	0	0	7	13	0	0	10	18
Guam	2006	1	1	1	0	0	0	1	100	0	0	0	0	0	0	0	0
Guinea	2006	41	2	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Haiti	2005	249	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Honduras	2006	48	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Hungary	2005	37	9	9	4	2	67	1	11	1	11	0	0	0	0	1	11
Ireland	2004	1	0	2	0	2	100	0	0	0	0	0	0	0	0	0	0
Israel	2006	11	18	18	12	3	83	0	0	0	0	0	0	3	17	0	0
Jordan	2006	9	3	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Kenya	2006	0	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Kuwait	2006	8	10	10	0	6	60	0	0	0	0	0	0	4	40	0	0
Kyrgyzstan	2006	495	248	16	11	0	69	0	0	3	19	2	13	0	0	0	0

Country or area	Year	New MDR-TB cases			Cured	Completed	Success[a]	Died		Failed		Defaulted		Transferred		Still on treatment	
		expected among TB cases notified[b]	detected and reported	with outcome reported	number	number	%	number	%	number	%	number	%	number	%	number	%
Latvia	2006	123	85	75	52	9	81	5	7	2	3	7	9	0	0	0	0
Lebanon	2006	2	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Mexico	2006	344	61	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Nepal	2006	673	0	3	2	0	67	0	0	0	0	1	33	0	0	0	0
Netherlands	2004	12	1	9	0	6	67	1	11	0	0	2	22	0	0	0	0
New Zealand	2006	0	1	1	0	0	0	0	0	0	0	0	0	1	100	0	0
Nicaragua	2006	10	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Northern Mariana Islands	2004	5	1	1	0	0	0	0	0	0	0	0	0	1	100	0	0
Oman	2006	5	2	2	0	1	50	1	50	0	0	0	0	0	0	0	0
Peru	2006	1 385	736	168	66	36	61	10	6	12	7	29	17	3	2	12	7
Philippines	2006	5 668	19	1	0	0	0	0	0	0	0	1	100	0	0	0	0
Portugal	2004	33	12	35	2	19	60	7	20	1	3	1	3	1	3	4	11
Puerto Rico	2006	1	1	1	0	0	0	1	100	0	0	0	0	0	0	0	0
Qatar	2006	4	1	3	0	0	0	1	33	0	0	0	0	2	67	0	0
Republic of Moldova	2006	735	242	35	22	1	66	2	6	3	9	7	20	0	0	0	0
Romania	2006	478	95	33	19	12	94	0	0	1	3	1	3	0	0	0	0
Singapore	2006	1	3	3	2	0	67	1	33	0	0	0	0	0	0	0	0
Sweden	2006	6	2	2	2	0	100	0	0	0	0	0	0	0	0	0	0
Tunisia	2006	34	8	—[d]	—	—	—	—	—	—	—	—	—	—	—	—	—
United States of America	2006	120	91	105	0	79	75	13	12	0	0	4	4	9	9	0	0
Uzbekistan	2006	2 494	29	15	5	7	80	0	0	0	0	1	7	1	7	1	7
Total		**13 987**	**2 058**	**716**	**266**	**225**	**69**	**65**	**9**	**26**	**4**	**73**	**10**	**32**	**4**	**29**	**4**
ii) Data from sites with unknown standards of care																	
Albania	2006	1	1	1	0	0	0	0	0	1	100	0	0	0	0	0	0
Bhutan	2006	12	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Botswana	2006	239	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Brazil	2006	573	—	327	205	0	63	24	7	50	15	39	12	9	3	0	0
Burundi	2006	72	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Côte d'Ivoire	2004	372	0	37	2	0	5	11	30	10	27	14	38	0	0	0	0
Ecuador	2006	182	62	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Haiti	2006	242	—	2	0	2	100	0	0	0	0	0	0	0	0	0	0
Iraq	2006	144	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Kazakhstan	2006	2 447	1 028	141	122	12	95	0	0	0	0	3	2	2	1	2	1
Kenya	2006	0	0	1	1	0	100	0	0	0	0	0	0	0	0	0	0
Mauritius	2006	1	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—

Country or area	Year	New MDR-TB cases			Cured	Completed	Success[a]	Died		Failed		Defaulted		Transferred		Still on treatment	
		expected among TB cases notified[b]	detected and reported	with outcome reported	number	number	%	number	%	number	%	number	%	number	%	number	%
Mongolia	2006	29	9	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Montenegro	2006	0	0	1	0	0	0	0	0	1	100	0	0	0	0	0	0
Morocco	2006	71	—	117	46	0	39	10	9	7	6	28	24	5	4	21	18
Panama	2006	26	10	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Papua New Guinea	2006	153	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Paraguay	2004	43	0	1	0	0	0	0	0	0	0	1	100	0	0	0	0
Poland	2006	21	19	17	4	6	59	4	24	0	0	1	6	0	0	2	12
Romania	2006	478	33	81	25	1	32	5	6	2	35	16	20	3	4	3	4
Rwanda	2006	232	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Sri Lanka	2006	13	3	16	3	3	38	3	19	0	0	7	44	0	0	0	0
Syrian Arab Republic	2006	55	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Turkey	2006	45	133	131	29	72	77	8	6	2	2	9	7	3	2	8	6
Uruguay	2006	0	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Venezuela (Bolivarian Republic of)	2006	26	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Total		**5 477**	**1 299**	**873**	**437**	**96**	**61**	**65**	**7**	**99**	**11**	**118**	**14**	**22**	**3**	**36**	**4**

[a] Success = cured or completed
[b] Estimated proportion of MDR-TB among new TB cases multiplied by the number of new TB cases reported the same year.
[c] Including cohorts from programmes approved by the Green Light Committee (underlined) or sites applying Green Light Committee-type standards in management and drugs.
[d] outcome data not shown if ≥20% of the cohort is "still on treatment".
MDR-TB = multidrug-resistant TB

ANNEX 7B Treatment outcomes for previously treated MDR-TB cases, 2006 (or 2004–2005)

Country or area	Year	Previously treated MDR-TB cases			Cured	Completed	Success[a]	Died		Failed		Defaulted		Transferred		Still on treatment	
		expected among TB cases notified[b]	detected and reported	with outcome reported	number	number	%	number	%	number	%	number	%	number	%	number	%
i) Data from sites using international standards of care[c]																	
Armenia	2006	241	150	18	5	3	44	2	11	4	22	4	22	0	0	0	0
Australia	2006	8	10	3	0	2	67	0	0	0	0	0	0	1	33	0	0
Bahrain	2006	0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Belgium	2006	11	8	—[d]	—	—	—	—	—	—	—	—	—	—	—	—	—
Bolivia (Plurinational State of)	2006	33	—	11	10	0	91	0	0	1	9	0	0	0	0	0	0
Cambodia	2006	46	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Canada	2006	6	2	3	1	1	67	1	33	0	0	0	0	0	0	0	0
China, Hong Kong SAR	2006	20	18	17	9	0	53	3	18	0	0	1	6	4	24	0	0
China, Macao SAR	2006	3	0	1	0	1	100	0	0	0	0	0	0	0	0	0	0
Costa Rica	2006	2	1	1	1	0	100	0	0	0	0	0	0	0	0	0	0
Dominican Republic	2006	117	24	24	18	0	75	3	13	3	13	0	0	0	0	0	0
Egypt	2006	305	112	26	15	1	62	6	23	3	12	1	4	0	0	0	0
El Salvador	2006	10	—	8	4	1	63	1	13	0	0	2	25	0	0	0	0
Estonia	2006	35	16	17	6	0	35	2	12	1	6	8	47	0	0	0	0
Georgia	2006	544	155	31	2	8	32	4	13	5	16	6	19	1	3	5	16
Germany	2006	45	13	17	4	3	41	2	12	2	12	0	0	6	35	0	0
Guam	2006	0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Guinea	2006	162	17	2	1	0	50	0	0	1	50	0	0	0	0	0	0
Haiti	2005	28	—	30	23	0	77	4	13	0	0	3	10	0	0	0	0
Honduras	2006	21	—	2	1	0	50	0	0	0	0	1	50	0	0	0	0
Hungary	2005	37	8	8	3	0	38	0	0	5	63	0	0	0	0	0	0
Ireland	2004	3	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Israel	2006	1	1	2	1	0	50	0	0	1	50	0	0	0	0	0	0
Jordan	2006	4	11	19	11	0	58	3	16	0	0	1	5	4	21	0	0
Kenya	2006	0	89	1	1	0	100	0	0	0	0	0	0	0	0	0	0
Kuwait	2006	0	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Kyrgyzstan	2006	391	88	50	22	1	46	5	10	6	12	16	32	0	0	0	0
Latvia	2006	59	57	67	36	0	54	10	15	6	9	14	21	0	0	1	1
Lebanon	2006	5	3	3	3	0	100	0	0	0	0	0	0	0	0	0	0
Mexico	2006	352	62	22	4	6	45	4	18	5	23	3	14	0	0	0	0
Nepal	2006	342	0	156	100	0	64	13	8	9	6	34	22	0	0	0	0
Netherlands	2004	2	0	1	0	1	100	0	0	0	0	0	0	0	0	0	0

Country or area	Year	Previously treated MDR-TB cases			Cured	Completed	Success[a]	Died		Failed		Defaulted		Transferred		Still on treatment	
		expected among TB cases notified[b]	detected and reported	with outcome reported	number	number	%	number	%	number	%	number	%	number	%	number	%
New Zealand	2006	0	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Nicaragua	2006	18	0	3	1	0	33	0	0	2	67	0	0	0	0	0	0
Northern Mariana Islands	2004	0	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Oman	2006	0	0	1	0	0	0	1	100	0	0	0	0	0	0	0	0
Peru	2006	1 293	534	502	186	102	57	37	7	31	6	88	18	1	0	57	11
Philippines	2006	1 059	384	132	78	6	64	25	19	2	2	21	16	0	0	0	0
Portugal	2004	25	10	14	0	6	43	4	29	1	7	1	7	0	0	2	14
Puerto Rico	2006	0	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Qatar	2006	0	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Republic of Moldova	2006	879	798	53	34	2	68	2	4	10	19	5	9	0	0	0	0
Romania	2006	724	435	80	31	20	64	8	10	8	10	12	15	0	0	1	1
Singapore	2006	5	3	3	2	0	67	0	0	1	33	0	0	0	0	0	0
Sweden	2006	1	1	1	1	0	100	0	0	0	0	0	0	0	0	0	0
Tunisia	2006	13	—	16	0	1	6	10	63	1	6	1	6	0	0	3	19
United States of America	2006	—	—	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Uzbekistan	2006	1 094	54	121	42	30	60	9	7	17	14	20	17	2	2	1	1
Total		**7 944**	**3 064**	**1 466**	**656**	**195**	**58**	**159**	**11**	**125**	**9**	**242**	**17**	**19**	**1**	**70**	**5**
ii) Data from sites with unknown standards of care																	
Albania	2006	2	0	0	0	0	—	0	—	0	—	0	—	0	—	0	—
Bhutan	2006	9	0	11	10	0	91	1	9	0	0	0	0	0	0	0	0
Botswana	2006	45	—	8	6	1	88	0	0	1	13	0	0	0	0	0	0
Brazil	2006	482	—	44	14	0	32	8	18	8	18	14	32	0	0	0	0
Burundi	2006	16	0	15	9	0	60	1	7	0	0	1	7	4	27	0	0
Côte d'Ivoire	2004	85	36	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Ecuador	2006	181	62	43	22	0	51	4	9	13	30	4	9	0	0	0	0
Haiti	2006	38	—	12	0	10	83	0	0	0	0	0	0	0	0	2	17
Iraq	2006	213	—	20	5	4	45	3	15	5	25	3	15	0	0	0	0
Kazakhstan	2006	11 124	3 089	487	364	28	80	23	5	18	4	24	5	8	2	22	5
Kenya	2006	0	89	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Mauritius	2006	1	2	2	1	0	50	1	50	0	0	0	0	0	0	0	0
Mongolia	2006	61	89	50	23	10	66	7	14	2	4	6	12	2	4	0	0
Montenegro	2006	0	2	2	2	0	100	0	0	0	0	0	0	0	0	0	0
Morocco	2006	0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Panama	2006	33	5	10	5	0	50	3	30	0	0	1	10	0	0	1	10

Country or area	Year	Previously treated MDR-TB cases			Cured	Completed	Success[a]	Died		Failed		Defaulted		Transferred		Still on treatment	
		expected among TB cases notified[b]	detected and reported	with outcome reported	number	number	%	number	%	number	%	number	%	number	%	number	%
Papua New Guinea	2006	143	—	1	0	0	0	1	100	0	0	0	0	0	0	0	0
Paraguay	2004	12	2	3	0	1	33	1	33	0	0	1	33	0	0	0	0
Poland	2006	79	13	13	2	2	31	5	38	0	0	3	23	0	0	1	8
Romania	2006	724	435	537	114	9	23	112	21	165	31	99	18	7	1	31	6
Rwanda	2006	52	—	50	41	2	86	5	10	1	2	0	0	0	0	1	2
Sri Lanka	2006	0	13	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Syrian Arab Republic	2006	57	8	10	7	0	70	2	20	0	0	1	10	0	0	0	0
Turkey	2006	111	116	118	33	43	64	15	13	0	0	11	9	0	0	16	14
Uruguay	2006	3	1	1	1	0	100	0	0	0	0	0	0	0	0	0	0
Venezuela (Bolivarian Republic of)	2006	53	21	8	6	0	75	1	13	0	0	1	13	0	0	0	0
Total		**13 524**	**3 983**	**1 445**	**665**	**110**	**54**	**193**	**13**	**213**	**15**	**169**	**12**	**21**	**1**	**74**	**5**

[a] Success = cured or completed

[b] Estimated MDR-TB prevalence among previously treated TB cases multiplied by the number of previously treated TB cases reported the same year.

[c] Including cohorts from programmes approved by the Green Light Committee (underlined) or sites applying Green Light Committee-type standards in management and drugs.

[d] outcome data not shown if ≥20% of the cohort is "still on treatment".

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