

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

- 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.

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.

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 countries¹ 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 less than US\$ 0.5 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

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.

with MDR-TB were reported to have been enrolled in 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.