Tuberculosis control

Progress and long-term planning
Prevention and control of multidrug-resistant tuberculosis
and extensively multidrug-resistant tuberculosis

Report by the Secretariat

1. In 2007 the Health Assembly, in resolution WHA60.19, noted the progress made since 1991 towards the international targets for global tuberculosis control: to detect 70% of cases and to cure 85% of sputum smear-positive patients with pulmonary tuberculosis under treatment. It also noted the development of the Stop TB Strategy\(^1\) as a comprehensive approach to overcoming the factors hindering efforts to control tuberculosis, and welcomed the Stop TB Partnership’s Global Plan to Stop TB 2006–2015,\(^2\) which is underpinned by the Strategy. The Health Assembly also requested the Director-General, inter alia, to report to the Sixty-third World Health Assembly through the Executive Board on progress made in implementing the Global Plan, including mobilization of resources, and on progress made in achieving the international targets for tuberculosis control by 2015, with an evaluation of the performance of national programmes and of the impact of control on the tuberculosis epidemic. In May 2009, recognizing the emergence and spread of multidrug-resistant and extensively drug-resistant tuberculosis, the Health Assembly, in resolution WHA62.15, urged all Member States 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. This document responds to the Health Assembly’s request to the Director-General to report on overall progress made.

2. WHO’s latest estimates of the global burden of tuberculosis refer to cases occurring in 2008: 9.4 million new cases, of which 1.4 million (15%) were in patients infected with HIV. Most new cases were in the South-East Asia and Western Pacific regions (together 55%) and the African Region (30%), with fewer in the Eastern Mediterranean Region (7%), the European Region (5%) and the Region of the Americas (3%). Of the HIV-positive cases, 78% were in the African Region. WHO’s estimates also indicate that in 2008 there were 11 million prevalent cases of tuberculosis, with 1.3 million deaths, and an additional 520 000 deaths associated with HIV/tuberculosis coinfection. The estimated total number of multidrug-resistant cases worldwide in 2008 was 440 000 (uncertainty range: 390 000–510 000), with 27 Member States accounting for 85% of global cases. The proportion of multidrug-resistant cases globally that are extensively drug-resistant is not yet known, but is

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\(^1\) The six components of the Stop TB Strategy are: (i) pursue high-quality DOTS expansion and enhancement; (ii) address tuberculosis/HIV co-infection, multidrug-resistant tuberculosis, and the needs of poor and vulnerable populations; (iii) contribute to health system strengthening based on primary health care; (iv) engage all care providers; (v) empower people with tuberculosis and communities through partnership; and (vi) enable and promote research.

estimated to be around 5%. By 2009, 58 countries, had reported at least one case of extensively drug-resistant tuberculosis.

3. The progress made in implementing interventions for the control of tuberculosis, multidrug-resistant tuberculosis and HIV-associated tuberculosis as measured over three years against milestones contained in the Global Plan is summarized in the Table. The internationally agreed target for 2005 of a treatment success rate of at least 85% under the DOTS strategy was reached globally in 2007, but the case detection rate in 2008 of 62% of patients with sputum smear-positive pulmonary tuberculosis lagged behind the 71% target contained in the Global Plan. Progress has been made in testing tuberculosis patients for HIV infection, but provision of co-trimoxazole prophylaxis and antiretroviral therapy, the two crucial interventions for HIV-positive tuberculosis patients, is about one third of that targeted in the Global Plan. Screening people living with HIV for tuberculosis and giving prophylactic or curative treatment also fell far short of the Global Plan targets. Furthermore, progress in control of multidrug-resistant tuberculosis has also been slow. In 2008, less than 3% of estimated multidrug-resistant cases of tuberculosis were diagnosed and treated according to WHO guidelines, compared with the Global Plan milestone of 23%.

Table. Progress in tuberculosis control compared with Global Plan milestones for the years 2006, 2007 and 2008

<table>
<thead>
<tr>
<th>Global Plan component and indicators</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
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<tr>
<td><strong>DOTS strategy</strong></td>
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<tr>
<td>Case detection rate, smear-positive cases (%)</td>
<td></td>
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<tr>
<td>Global Plan</td>
<td>65</td>
<td>68</td>
<td>71</td>
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<tr>
<td>Actual progress</td>
<td>60</td>
<td>60</td>
<td>62</td>
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<tr>
<td>Treatment success rate, smear-positive cases (%)</td>
<td></td>
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<tr>
<td>Global Plan</td>
<td>83</td>
<td>84</td>
<td>84</td>
</tr>
<tr>
<td>Actual progress</td>
<td>84</td>
<td>86</td>
<td>Not available</td>
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<tr>
<td><strong>Tuberculosis/HIV coinfections</strong></td>
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<td></td>
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<tr>
<td>Tuberculosis patients tested for HIV (%)</td>
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<tr>
<td>Global Plan</td>
<td>47</td>
<td>56</td>
<td>64</td>
</tr>
<tr>
<td>Actual progress</td>
<td>12</td>
<td>20</td>
<td>22</td>
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<tr>
<td>Number of HIV-positive tuberculosis patients treated with co-trimoxazole (millions)</td>
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<td></td>
<td></td>
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<tr>
<td>Global Plan</td>
<td>0.5</td>
<td>0.6</td>
<td>0.7</td>
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1 Projected figures based on 2004 data.
2 Projected figures based on 2003 data.
4. As a result of intensive global efforts between 1995 and 2008, a cumulative total of 36 million tuberculosis patients were successfully treated in DOTS programmes. Furthermore, during that period, up to 6 million deaths were averted compared with the numbers that would have occurred had the performance of tuberculosis control remained constant at the 1995 level. The case detection rate in 2008 of 62% against the internationally agreed target of 70% and the treatment success rate in 2007 of 86% against the target of 85% together demonstrate the overall performance national programmes, as stipulated by the relevant indicator (Proportion of tuberculosis cases detected and cured under DOTS) within target 8 (Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases) of Millennium Development Goal 6 (Combat HIV/AIDS, malaria and other diseases). The latest data suggest that the annual incidence rate of tuberculosis has been slowly declining globally since 2004 and the world as a whole is on track to achieve target 8. However, the absolute number of cases has been rising as the rate of decline of incidence has been too slow to offset increases in population. One indicator within target 8 relates to the prevalence and death rates associated with tuberculosis. In this regard, the Stop TB Partnership has set a further target of halving prevalence and mortality rates by 2015 compared with their 1990 level. Specifically, this means reducing prevalence to no more than 155 cases per 100 000 population, and reducing the annual mortality rate to no more than 14 per 100 000 by 2015, including people coinfected with tuberculosis and HIV. The latest projections for prevalence and deaths due to tuberculosis suggest that the target of halving these rates will be met in five of WHO’s six regions, but may not be achieved in the African Region, wherein the tuberculosis burden grew rapidly for more than a decade after 1990.

5. The resources available for implementation of tuberculosis control have increased each year, reaching in 2010 a figure about 2.5 times higher than in 2002, when WHO began financial monitoring. In 2009, a total of US$ 4100 million was available for care and control of tuberculosis, multidrug-resistant tuberculosis and HIV-associated tuberculosis in 118 countries that reported financial data (and that accounted for 94% of the world’s estimated total number of cases). Of this total, 86% was funding from governments, 9% was in the form of grants from the Global Fund to Fight AIDS, Tuberculosis and Malaria and 3% came from other donors. Overall, funding is highest in the European Region (US$ 1900 million in 2010, mostly for the Russian Federation), followed by the African Region (US$ 500 million in 2010) and the Western Pacific Region (US$ 300 million in 2010). The estimated need reported by countries was US$ 4900 million and, despite the growth in funding, the shortfall in 2010 amounted to US$ 800 million. Compared with the funding expectations set out in the Global Plan, the gap in 2010 is higher still, at US$ 2100 million. Most of the extra funding required according to the Global Plan is for diagnosis and treatment of multidrug-resistant tuberculosis in the
South-East Asia and Western Pacific regions (mostly for China and India), and for collaborative activities against tuberculosis and HIV and for implementation of the DOTS strategy in the African Region. Surveys of funding for research and development have found that about US$ 500 million per year were available between 2005 and 2007, which was half the sum required annually according to the Global Plan. Tracking of financing for technical assistance has been limited to date, but suggests that funding falls far short of the US$ 300 million per year estimated to be required in the Global Plan.

6. In its efforts to achieve the international targets through established and growing partnerships, WHO continues to host and support the Stop TB Partnership’s secretariat; coordination is effective at all levels of the Organization. The Strategic and Technical Advisory Group for Tuberculosis, which provides the Director-General with advice and evaluation of the Organization’s work on tuberculosis, has played a crucial role in guiding development of major new policies on diagnosis and treatment of tuberculosis. Technical advisory groups in most regions also guide WHO in responding to the challenges of policy implementation in diverse epidemiological and health system settings. WHO hosts the secretariats of several working groups and subgroups of the Stop TB Partnership, whose work helps to inform policy development and plays a major role in building the evidence base, forging consensus and coordinating provision of support to Member States in implementing policies. WHO responds to Member States’ demands for technical assistance in coordination with all relevant partners and donor agencies through the TB Technical Assistance Mechanism, whose secretariat it also hosts. WHO continues to rely on flexible mechanisms such as time-limited task forces that can rapidly provide policy advice and guidance in order to overcome specific obstacles to implementation. Since 2006 these task forces have focused on the global response to extensively drug-resistant tuberculosis, health system strengthening and tuberculosis control, ethics in tuberculosis care, and measuring the impact of control efforts. A growing array of partners together with Member States rely on WHO’s unique tuberculosis monitoring, evaluation and financing databases, reports and coordinated surveillance support.

PROGRESS IN IMPLEMENTING CORE COMPONENTS OF THE STOP TB STRATEGY

7. Care of tuberculosis patients and control of the disease have improved significantly over the past decade. From 1995 to 2008, more than 40 million tuberculosis patients have been treated through DOTS programmes. By 2007, 94% of the world population lived in countries that had adopted the DOTS strategy and more than 98% of reported cases were diagnosed and treated in DOTS programmes. In 180 countries smear microscopy is being used as the basic diagnostic test for tuberculosis; access to culture facilities, which help to detect and confirm more cases, is still limited. To ensure the quality of diagnosis, about 70% of laboratories in countries with a high burden of tuberculosis have been included in external quality-assurance mechanisms. WHO’s recommended standardized treatment has been used globally, and fixed-dose drug combinations as a measure to prevent occurrence of drug-resistant tuberculosis have been used by more than 70 Member States. WHO has contributed to the setting and promotion of the International Standards for Tuberculosis Care in order to help to ensure the provision of high-quality care across the spectrum of health-care providers. Patient-centred approaches are promoted to ensure adherence to, and completion of, treatment regimens and their wider application is now required. WHO is finalizing a guidance document in order to promote ethical standards in care and control of tuberculosis and is collaborating with relevant partners in this area. The Global Drug Facility, a Stop TB Partnership project, has been important in enabling countries to have access to timely supplies of quality-assured medicines through its procurement mechanism, to manage their medicine stocks better, and to have access to emergency supplies in the event of unexpected shortages. Between 2001 and 2009 the Global Drug Facility
organized the delivery of 13.9 million treatments to 110 countries. Improved national recording and reporting systems, with increasing use of electronic reporting, have enhanced the quality and comprehensiveness of data. Tuberculosis services are integrated into primary health-care services and their delivery therefore depends on the quality of general health services in most countries. Evidence from a variety of countries and programmes indicates that tuberculosis programmes can contribute to the strengthening of health systems and services in various ways. Examples include involving patients and communities in tuberculosis care and control; implementing tuberculosis care as a part of WHO’s Practical Approach to Lung Health; and engaging diverse public, voluntary, private and corporate providers in care and control activities through public–private mix approaches. Some countries have successfully expanded all these programmatic approaches, but much remains to be done. A large proportion of cases – an estimated 39% in 2008 – still remain undetected or unreported and may receive care of questionable quality. Access to free diagnosis and treatment is not yet within the reach of all poor and vulnerable populations, occasional shortages of medicines are still reported and weaknesses in recording and reporting persist.

8. In 2008, 1.4 million tuberculosis patients (representing 22% of all notified cases globally) were tested for HIV across 142 countries, in 50 of which at least 75% of tuberculosis patients were tested for HIV. The rapid expansion of the testing of tuberculosis patients for HIV infection has been especially noteworthy in the African Region, where 45% of notified tuberculosis patients were tested for HIV in 2008. In 11 Member States in that Region, more than 75% of all newly diagnosed tuberculosis patients were tested for HIV in 2008. Furthermore, in 2008, about 200 000 HIV-positive tuberculosis patients were given co-trimoxazole prophylaxis and 100 000 were receiving antiretroviral therapy. At the same time, in 2008, 1.4 million people worldwide living with HIV were screened for tuberculosis and around 50 000 people living with HIV were offered prophylactic treatment with isoniazid. Overall, implementation of collaborative activities against tuberculosis and HIV fell short of the targets contained in the Global Plan for 2008.

9. In 2008, less than 7% of the estimated 440 000 cases of multidrug-resistant tuberculosis and an even smaller fraction of patients with extensively drug-resistant tuberculosis were diagnosed through national tuberculosis programmes. These low rates are the result of years of neglect of laboratory services and the extremely slow rate of transfer of new diagnostic technologies to developing countries. In order to rectify the insufficiencies in diagnostic capacity, the Stop TB Partnership’s Global Laboratory Initiative is spearheading an unprecedented effort to improve and expand tuberculosis laboratory services, guided by the Initiative’s secretariat, hosted by WHO, and its network of international partners. At the same time, the number of new tuberculosis diagnostic methods in development is growing. WHO regularly assesses new technologies for rapid deployment and policy guidance. Two such approaches – the use of liquid media for mycobacterial culture and line probe assays for rapid diagnosis of multidrug-resistant tuberculosis – are being given top priority in the 27 countries most affected by multidrug-resistant tuberculosis, the work being supported by several international partners and with funding mainly from UNITAID. Innovative partnerships are being formed in order to secure resources while ensuring that laboratory quality standards, appropriate infrastructure and adequate technical capacity are put in place. The rapid advances in tuberculosis diagnostics mean that country strategies and plans must be dynamic and responsive to any new policy guidance from WHO. Provision of tuberculosis laboratory services is, however, constrained, mainly by cross-cutting health systems issues such as poor infrastructure and inadequate human resources, and requires bold policies and a coordinated, integrated approach to laboratory capacity strengthening within the context of national laboratory strategies and plans.
10. In May 2009, the Health Assembly in resolution WHA62.15 welcomed the Beijing Call for Action on tuberculosis and patient care, and urged Member States to achieve universal access to diagnosis and treatment of multidrug-resistant and extensively drug-resistant tuberculosis, recalling the commitments made in resolution WHA60.19 on implementation of long-term plans for prevention and control of tuberculosis. Subsequently, plans to implement resolution WHA62.15 have been prepared by 20 of the 27 countries with a high burden of multidrug-resistant tuberculosis. By June 2009, the Green Light Committee (established by WHO and partners in order to ensure the supply of quality-assured second-line antituberculosis medicines) had approved treatments for about 59,000 patients in 108 projects spanning 68 countries. By 2009, a total of 19,637 patients with multidrug-resistant tuberculosis had been enrolled in 44 countries. The treatment success rate in these projects between 2000 and 2006 was 65%. Currently, however, only about 2% of the estimated 500,000 cases of multidrug-resistant tuberculosis that occur each year are being treated through the Green Light Committee mechanism. Further action to enrol an additional 100,000 patients by 2013 is necessary. In 2008, 114 countries, reported survey data on drug resistance. In 2009, eight additional drug resistance surveys were started, and 15 more are likely to start in 2010. Updated guidelines for the programmatic management of multidrug-resistant and extensively drug-resistant tuberculosis are due to be issued by the end of 2010. A new WHO policy on tuberculosis infection control was published in 2009 and training material is being produced. Work has also begun on defining specifications for commodities and equipment, and estimating the costs of implementing the policy. Global efforts on prevention and control of multidrug-resistant tuberculosis have been further reinforced by resolutions passed in 2009 by the regional committees for Africa (resolution AFR/RC59/R2) and the Eastern Mediterranean (resolution EM/RC56/R.8). Despite increased attention from all stakeholders, major obstacles to expanding the response to multidrug-resistant tuberculosis remain. The facilities to which patients with multidrug-resistant tuberculosis are admitted lack proper infection control; social support networks are absent or too weak to enable patients to comply with treatment regimens; inadequate systems make reporting of valid data on treatment outcomes difficult or impossible; and customs regulations prevent patients from accessing the best quality medicines available on the market.

11. The WHO Global Task Force on TB Impact Measurement was established in 2006, with the mandate of producing robust, rigorous and endorsed assessments of progress towards reducing incidence, prevalence and mortality rates in line with global targets set for 2015. In 2007, the Global Task Force defined three major strategic actions to be taken: (i) improve surveillance of cases (through routine notification systems) and deaths (through vital registration systems); (ii) institute nationwide population-based surveillance of the prevalence of tuberculosis in priority countries including 21 global focus countries; and (iii) periodically review and update methods used to estimate incidence, prevalence and mortality from surveillance and survey data. The related policies and recommendations have been set out in a WHO policy paper. In 2008 and 2009, WHO’s partners have

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1 See document A62/20 Add.1.
3 More information on the WHO Global Task Force on TB Impact Measurement is available on the WHO web site (http://www.who.int).
4 More information on the 21 global focus countries, as defined by the WHO Global Task Force on TB Impact Measurement is available on the WHO web site (http://www.who.int).
worked closely with countries to implement these policies and recommendations. Regional workshops in four regions and country missions have been used to carry out systematic analyses of surveillance data, to update estimates of incidence, prevalence and mortality; to identify areas where surveillance needs to be strengthened; and to develop related plans for strengthening surveillance systems. Regional workshops are planned for countries in the African and Western Pacific regions in 2010, and subsequently it is expected that such workshops will be held for all regions on a biennial basis. Countries where prevalence surveys are recommended have been supported to design and conduct these surveys through workshops and country missions, with a recent focus on overcoming the most common obstacles to starting implementation. These difficulties, which are seen particularly in the 12 priority countries in the African Region, include funding shortfalls and delays in procurement of X-ray equipment. The first major update of the methods used to produce WHO’s estimates of incidence, prevalence and mortality was completed in 2009.

12. Achieving tuberculosis-related targets of the Millennium Development Goals will not be possible without better tools to prevent, diagnose and cure tuberculosis. Research is therefore a major component of the Global Plan, which recommends investment of an estimated US$ 11 000 million for the development of such tools over the period 2006–2015. Much progress in this research has been made over the past three years. In diagnostics, a major breakthrough has been the introduction of a new item of technology, the molecular line probe assay, which can detect multidrug-resistant tuberculosis in a few days instead of weeks. Five novel candidate anti-tuberculosis medicines are in clinical trials and eight further compounds are in preclinical development. Two phase III clinical trials of four-month treatment regimens for tuberculosis will be completed by 2012. As regards vaccines, preclinical investigations are being undertaken on at least 29 candidates. Eight candidate vaccines have entered clinical trials, three in phase II. Through the commitment of public–private partnerships, the engagement of major public funding agencies and the willingness of regulatory authorities to help expedite approvals of new products, there is a potential for new tools to be available before 2015. Although, according to a survey by the Treatment Action Group, tuberculosis research and funding rose worldwide from US$ 363 million in 2005 to US$ 429 million in 2006 and US$ 482 million in 2007, this growth is insufficient. A minimum of US$ 1000 million per year will be required to support the overall research that is necessary to develop and use more effective tools to help to eliminate tuberculosis.

13. It is now clear that the operational targets set for 2005 – at least 70% detection of smear-positive cases and a treatment success rate of at least 85% – are not adequate benchmarks for the work ahead. Member States will need to move urgently towards universal access to tuberculosis prevention, early diagnosis and proper treatment, to the maximum extent possible. To realize this aspiration, early detection of all cases of tuberculosis in all its forms is needed. Early detection and effective care will also rely on more attention being paid to those most at risk for tuberculosis and the social, economic and clinical determinants of these risks. Reinforcing the foundations of health systems, formulating bold policies to meet the challenges, and abolishing the financial barriers to implementing those policies across the health sector will be essential. The system foundations that are crucial to strengthened tuberculosis care and control include: sound human resources through resolution of the crisis that is crippling health services in many countries; regulatory systems and enforcement capacity that ensure the availability of quality-assured medicines and their rational use by all care providers; airborne infection control in health-care and other settings where people congregate; expansion,

1 These groups include, for example, very poor people, women and children, indigenous peoples, migrant workers, refugees and internally displaced persons, tobacco smokers, substance abusers, and people with co-morbidities including malnutrition, HIV infection and diabetes.
accreditation and quality assurance of laboratories supporting public health services; strong service-delivery networks that include all care providers throughout the public, voluntary, private and corporate sectors; expanded health information systems, including death registration and electronic means of recording and reporting data and for validating them; and, most importantly, greater awareness among, and demand expressed by, affected persons and communities.

14. Realizing the Stop TB Strategy’s vision of a tuberculosis-free world will also require policies and actions beyond the remit of tuberculosis-control programmes and, indeed, the health sector, that help to eradicate the key determinants of the tuberculosis epidemic, such as poverty, undernutrition and unhygienic living conditions. Sustained and simultaneous efforts are therefore necessary to strengthen actions in four broad areas: continuing to scale up early diagnosis and appropriate treatment in line with the Stop TB Strategy, formulating and enforcing bold health system policies that enable universal access to health and tuberculosis care, intensifying research to develop new tools for tuberculosis control and rapid transfer of technologies to countries with a high burden of tuberculosis, and joining forces for addressing social determinants and risk factors that help to drive the tuberculosis epidemic. WHO and its Stop TB partners are committed to providing support to Member States in order to implement fully the Stop TB Strategy and the Global Plan and to sustain advocacy to ensure that tuberculosis control remains high on the broad political agenda.

15. In January 2010 the Executive Board, at its 126th session, noted an earlier version of this report.1

ACTION BY THE HEALTH ASSEMBLY

16. The Health Assembly is invited to note the report.

1 See document EB126/2010/REC/2, summary record of the ninth meeting.