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From Basic Science  
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## Chapter 7: Global Burden of Tuberculosis

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### 7.1. Global epidemiology of tuberculosis

The consequences of tuberculosis (TB) on society are immense. Worldwide, one person out of three is infected with *Mycobacterium tuberculosis* – two billion people in total. TB accounts for 2.5 % of the global burden of disease and is the commonest cause of death in young women, killing more women than all causes of maternal mortality combined. TB currently holds the seventh place in the global ranking of causes of death. Unless intensive efforts are made, it is likely to maintain that position through to 2020, despite a substantial projected decline in disease burden from other infectious diseases (Dye 1999, Smith 2004).

Effective drugs to treat and cure the disease have been available for more than 50 years, yet every 15 seconds, someone in the world dies from TB. Even more alarming: a person is newly infected with *M. tuberculosis* every second of every day. Left untreated, a person with active TB will infect an average of 10 to 15 other people every year (Dye 2005).

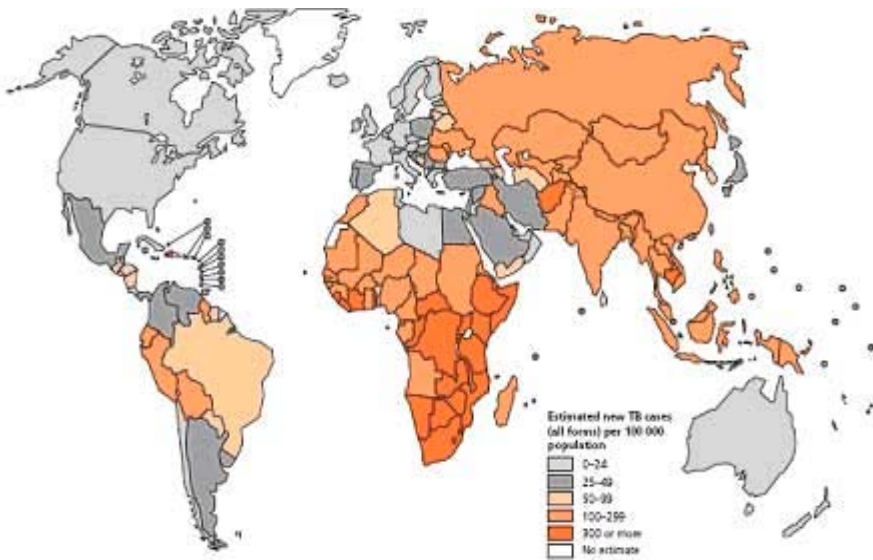
TB hinders socioeconomic development: 75 % of people with TB are within the economically productive age group of 15-54 years. Ninety-five per cent of all cases and 99 % of deaths occur in developing countries, with the greatest burden in sub-Saharan Africa and South East Asia. Household costs of TB are substantial (Dye 2006, World Health Organization 2006a).

In most countries, more cases of TB are reported among men than women. This difference is partly due to the fact that women have less access to diagnostic facilities in some settings, but the broader pattern also reflects real epidemiological differences between men and women, both in exposure to infection and in susceptibility to disease. In regions where the transmission of *M. tuberculosis* has been stable or increasing for many years, the incidence rate is highest among young adults, and most cases are caused by recent infection or reinfection. As transmission falls, the caseload shifts to the older age groups, and a higher proportion of cases come from the reactivation of latent infection (Borgdorff 2000).

While the human immunodeficiency virus (HIV) infection has clearly had a profound effect on TB epidemiology, other potentially important risk factors have been somewhat neglected. In the coming years, more attention needs to be given to the interaction between chronic diseases and TB, including diabetes, undernutri-

tion, and respiratory illnesses caused by tobacco and air pollution (Corbett 2003, World Health Organization 2004).

Although the “direct costs” of diagnosis and treatment are significant for poor families, the greatest economic loss occurs as a result of “indirect” costs, such as loss of employment, travel to health facilities, sale of assets to pay for treatment-related costs, and in particular, lost productivity from illness and premature death (Smith 2004, Floyd 2003, World Health Organization 2005a).



Source: WHO report, 2006

Figure 7-1: Estimated TB incidence rates, 2004

The World Health Organization (WHO) estimated 8.9 million new cases of TB in 2004 (140/100,000 population). About 3.9 million cases (62/100,000) were acid fast bacilli (AFB) sputum smear-positive, the most infectious form of the disease. There were 14.6 million prevalent cases (229/100,000), of which 6.1 million were AFB sputum smear-positive (95/100,000). An estimated 1.7 million people (27/100,000) died from TB in 2004, including those co-infected with HIV (248,000). The WHO African region has the highest estimated incidence rate (356/100,000), but the majority of patients with TB live in the most populous countries of Asia; Bangladesh, China, India, Indonesia, and Pakistan together ac-

count for half (48 %) of the new cases that arise every year (Figure 7-1). In terms of the total estimated number of new TB cases arising annually, about 80 percent of new cases occur in the 22 top-ranking countries (Dye 2006, World Health Organization 2006a).

In 2004, the estimated TB incidence per capita was stable or falling in five out of six WHO regions, although it was still growing at 0.6 % per year globally. The exception is the African region, where the incidence of TB was still rising, in line with the spread of HIV. However, the rate of increase in the number of cases notified from the African region is slowly decreasing each year, probably because the HIV epidemic in African countries is also slowing. In Eastern Europe (mostly countries of the former Soviet Union), the incidence per capita increased during the '90s, peaked around 2001, and has since fallen. The average downturn in case notifications in Eastern Europe is mainly due to data from Russia and the Baltic States of Estonia, Latvia, and Lithuania; however, incidence rates might still be increasing in the central Asian republics of Tajikistan and Uzbekistan (Dye 2006, World Health Organization 2006a).

In all other regions (Table 7-1), the incidence rate was stable or decreasing continuously between 1990 and 2003. The downfall was relatively quick in Latin America, Central Europe and the established market economies. In summary, the global trend in incidence rate was increasing most quickly at 1.5 % per year in 1995 but has since been decelerating. If the trends suggested by the case notifications are correct, and if these trends persist, the global incidence rate will reach about 150 per 100,000 in 2015, resulting in more than 10 million new cases in that year (Dye 2006, World Health Organization 2006a, World Health Organization 2006 b).

Global efforts to control TB were reinvigorated in 1991, when a World Health Assembly resolution recognized TB as a major global public health problem. Two targets for TB control were established as part of this resolution – detection of 70 % of new AFB smear-positive cases, and cure of 85 % of such cases by the year 2000. Despite intensified efforts, these targets were not met; more than 80 % of known cases are successfully treated, but only 45 % of cases are detected (World Health Organization 1993, World Health Organization 1994, World Health Organization 2006a).

Table 7-1: Estimated incidence, prevalence and TB mortality, 2004

WHO region	Incidence				Prevalence	TB Mortality		
	All forms	Smear-positive						
Africa	2 573* (29 <sup>§</sup> )	356 <sup>§</sup>	1 098*	152 <sup>§</sup>	3 741*	518 <sup>§</sup>	587*	81 <sup>§</sup>
The Americas	363* (4 <sup>§</sup> )	41 <sup>§</sup>	161*	18 <sup>§</sup>	466*	53 <sup>§</sup>	52*	5.9 <sup>§</sup>
Eastern Mediter- ranean	645* (7 <sup>§</sup> )	122 <sup>§</sup>	289*	55 <sup>§</sup>	1 090*	206 <sup>§</sup>	142*	27 <sup>§</sup>
Europe	445* (5 <sup>§</sup> )	50 <sup>§</sup>	199*	23 <sup>§</sup>	575*	65 <sup>§</sup>	69*	7.8 <sup>§</sup>
South East Asia	2 967* (33 <sup>§</sup> )	182 <sup>§</sup>	1 327*	81 <sup>§</sup>	4 965*	304 <sup>§</sup>	535*	33 <sup>§</sup>
Western Pacific	1 925* (22 <sup>§</sup> )	111 <sup>§</sup>	865*	50 <sup>§</sup>	3 765*	216 <sup>§</sup>	307*	18 <sup>§</sup>
<b>Global</b>	<b>8 918* (100<sup>§</sup>)</b>	<b>140<sup>§</sup></b>	<b>3 939*</b>	<b>62<sup>§</sup></b>	<b>14 602*</b>	<b>229<sup>§</sup></b>	<b>1 693*</b>	<b>27<sup>§</sup></b>

\* number (thousands)

<sup>§</sup> % of global total<sup>§</sup> per 100,000 pop.

Source: WHO, 2006

Since 2000, the United Nations Millennium Development Goals have provided a framework for evaluating implementation and impact under target 8 (among 18), which is to “*have halted by 2015 and begun to reverse the incidence of malaria and other major diseases*” (including TB). Although the objective is expressed in terms of incidence, the Millennium Development Goals also specify that progress be measured in terms of the reduction in TB prevalence and deaths. The target for these two indicators, based on a resolution passed at the 2000 Okinawa (Japan) summit of G8 industrialized nations, and subsequently adopted by the Stop TB Partnership ([www.stoptb.org](http://www.stoptb.org)), is to halve TB prevalence and death rates between 1990 and 2015 (evolution TB control). These additional targets are much more of a challenge, especially in Africa and Eastern Europe (World Health Organization 2000, World Health Organization 2005b, United Nations Statistics Division 2006).

### High-burden countries

In March 2000, the Ministers of Health and Finance from 20 countries harboring 80 % of the world’s TB cases met in Amsterdam and issued the Amsterdam Declaration. This stated that the global situation was “*both alarming and unacceptable*”, and that “*We commit ourselves to accelerate action against TB through expansion of DOTS*” (World Health Organization, International Union Against Tuberculosis

and Lung Disease 2001, World Health Organization 2002a, World Health Organization 2006a).

There are 22 high-burden countries, which account for approximately 80 % of the estimated number of new TB cases (all forms) arising worldwide each year. These countries (Table 7-2) are the focus of intensified efforts in Directly Observed Treatment, Short-course (DOTS) expansion ([www.who.int/tb/dots/whatisdots/en/index.html](http://www.who.int/tb/dots/whatisdots/en/index.html)). The high-burden countries are not necessarily those with the highest incidence rates per capita; many of the latter are medium-sized African countries with high rates of TB/HIV co-infection (Dye 2006, World Health Organization 2006a, World Health Organization 2006b).

TB death rates in high-burden countries varied dramatically, from 9 per 100,000 population in Brazil to 139 per 100,000 in South Africa. In these two countries, the overall case fatality rates for TB were 13 % and 27 %, respectively, and the difference was due largely to the difference in HIV infection rates (Dye 2006, World Health Organization 2006a).

In 2004, only six high-burden countries (Democratic Republic of Congo, Myanmar, the Philippines, South Africa, Thailand and Viet Nam) reached the detection rate of new AFB smear-positive cases (70 %) by DOTS, and the estimate for at least one of these countries (Democratic Republic of Congo) is uncertain (Dye 2006, World Health Organization 2006a).

Eight high-burden countries met the 85 % target for treatment success based on the 2003 cohort. All of them are in South-East Asia or Western Pacific regions, with the exception of Afghanistan, where the case detection rate by the DOTS program is relatively low. Among high-burden countries, only the Philippines and Viet Nam had met the targets for both case detection and treatment success by the end of 2004 (Dye 2006, World Health Organization 2006a).

The progress made in global TB control by the end of 2005 depended greatly on what had been previously achieved in eight countries, which were inhabited by 61 % of the patients who were undetected in 2004. For this reason, Bangladesh, Ethiopia, Nigeria, Pakistan, and the Russian Federation will be under close scrutiny, in addition to China, India, and Indonesia (Dye 2006, World Health Organization 2006a).

Table 7-2: Estimated TB burden, 2004

	Incidence		Prevalence, all forms per 100,000 pop. per year	Mortality, all forms per 100,000 pop. per year	HIV preva- lence, in incident TB cases %
	All forms per 100,000 pop.	Smear positive per 100,000 pop. per year			
1. India	168	75	312	30	5.2
2. China	101	46	221	17	0.9
3. Indonesia	245	110	275	46	0.9
4. Nigeria	290	125	531	82	27
5. South Africa	718	293	670	135	60
6. Bangladesh	229	103	435	51	0.1
7. Pakistan	181	81	329	40	0.6
8. Ethiopia	353	154	533	79	21
9. Philippines	293	132	463	48	0.1
10. Kenya	619	266	888	133	29
11. DR Congo	366	159	551	79	21
12. Russian Fed.	115	51	160	21	6.8
13. Viet Nam	176	79	232	22	3.0
14. UR Tanzania	347	147	479	78	36
15. Uganda	402	175	646	92	19
16. Brazil	60	26	77	7.8	17
17. Afghanistan	333	150	661	92	0.0
18. Thailand	142	63	208	19	8.5
19. Mozambique	460	191	635	129	48
20. Zimbabwe	674	271	673	151	68
21. Myanmar	171	76	180	21	7.1
22. Cambodia	510	226	709	94	13
<b>High Burden Countries</b>	<b>178</b>	<b>79</b>	<b>301</b>	<b>34</b>	<b>0.0</b>

Source: WHO, report 2006

Community participation in TB control is part of the National Tuberculosis Control Programme strategy in 14 high-burden countries. The number of high-burden countries with national strategies for advocacy, communication, and social mobili-

zation has increased from two in 2002 to 11 in 2005, and is expected to reach 19 by 2007 (Dye 2006, World Health Organization 2006a).

High-burden countries are in various stages of developing collaborations within and among public and private health sectors (through PPM-DOTS). While Bangladesh, China, India, Indonesia, Kenya, Myanmar, and the Philippines have already improved links between National Tuberculosis Control Programmes, hospitals and other healthcare providers, PPM-DOTS is still at an early stage in most other high-burden countries (Dye 2006, World Health Organization 2006a).

The total cost of TB control, which includes the general health system staff and the infrastructure used for TB control, in addition to the National Tuberculosis Control Programme budget requirements, is projected to be US\$ 1.6 billion in the 22 high-burden countries in 2006, compared with US\$ 876 million in 2002. The Russian Federation and South Africa have by far the largest costs, with a combined total of US\$ 810 million. Assuming that health systems have had the capacity to manage a growing number of TB patients in 2006, the funding gap for total TB control costs in 2006 will have been the same as for the National Tuberculosis Control Programme budgets, i.e. US\$ 141 million. Total costs increase to US\$ 2.0 billion, and the funding gap increases to US\$ 180 million when all 74 countries that reported data are included. These 74 countries represent 89 % of TB cases globally (Dye 2006, World Health Organization 2006a).

All but one of the 22 high-burden countries that increased spending between 2003 and 2004 also increased the number of new AFB smear-positive cases that were detected and treated in DOTS programs. Cambodia increased spending, but did not increase the total number of AFB smear-positive patients treated by DOTS (Dye 2006, World Health Organization 2006a).

Among the 22 high-burden countries, five (India, Indonesia, Myanmar, the Philippines, and Viet Nam) were in the best financial position to reach the World Health Assembly targets in 2005; two (Cambodia and China) were well placed to do so, if able to make up funding shortfalls (Dye 2006, World Health Organization 2006a).

## 7.2. Tuberculosis and the interaction with the HIV epidemic

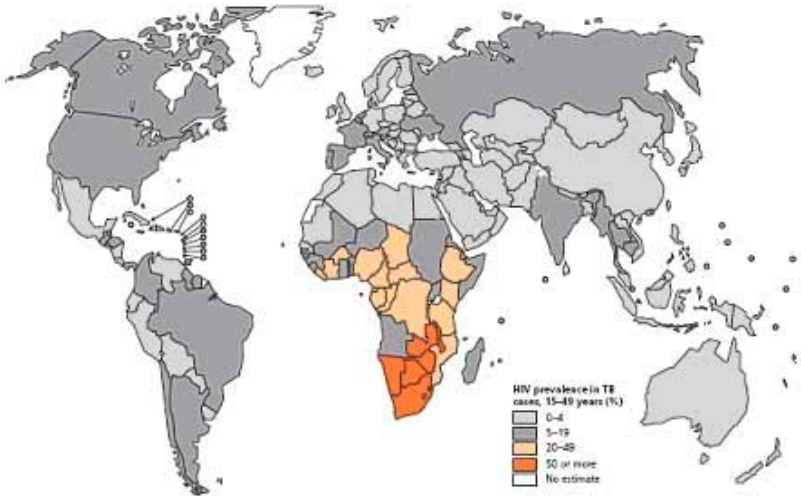
HIV and TB form a lethal combination, each speeding the other's progress. HIV infection is a potent risk factor for TB. Not only does HIV increase the risk of re-activating latent *M. tuberculosis* infection, it also increases the risk of rapid TB progression soon after *M. tuberculosis* infection or reinfection. In persons infected with *M. tuberculosis* only, the lifetime risk of developing TB ranges between 10 %

and 20 %. In persons co-infected with *M. tuberculosis* and HIV, however, the annual risk can exceed 10 %. The TB burden in countries with a generalized HIV/AIDS epidemic has therefore increased rapidly over the past decade, especially in the severely affected countries of eastern and southern Africa. TB is one of the most common causes of morbidity and the most common cause of death in HIV-positive adults living in less-developed countries, yet it is a preventable and treatable disease (Corbett 2003, Aaron 2004, World Health Organization 2006b).

It is possible that, in addition to increasing individual susceptibility to TB following *M. tuberculosis* infection, a high burden of HIV-associated TB cases also expands *M. tuberculosis* transmission rates at the community level, threatening the health and survival of HIV-negative individuals as well. In several countries, HIV has been associated with epidemic outbreaks of TB. Many of the reported outbreaks involved multidrug-resistant (MDR) strains, which respond poorly to standard therapy - the growing burden of TB (Corbett 2003, Aaron 2004, World Health Organization 2006a, World Health Organization 2006b).

According to a study published by Corbett et al., an estimated 8.3 million new TB cases were reported in 2000 worldwide. Nine percent (7 %-12 %) of all new TB cases in adults (aged 15-49 years) were attributable to HIV infection, but the proportion was much greater in the WHO African Region (31 %) and some industrialized countries, notably the United States (26 %). There were an estimated 1.8 million deaths from TB, of which 12 % were attributable to HIV. In turn, TB was the cause of 11 % of all adult AIDS deaths. The worldwide prevalence of *M. tuberculosis*-HIV co-infection in adults was 0.36 % (11 million people). Co-infection prevalence rates equaled or exceeded 5 % in eight African countries. In South Africa alone there were 2 million co-infected adults (Corbett 2003, Corbett 2004).

Other studies published by Dye *et al.* reported that much of the observed increase in the incidence of global TB since 1980 is attributable to the spread of HIV in Africa. Globally, an estimated 13 % of adults with newly diagnosed TB were infected with HIV in 2004, but there was great variation among regions — from 34 % in the African region to 1.4 % in the Western Pacific region. Rates of HIV infection in patients with TB have so far remained below 1 % in Bangladesh, China, Indonesia, and Pakistan. In African populations with high rates of HIV infection, a relatively high proportion of patients with TB are women aged between 15 and 24 years. The rise in the number of TB cases is slowing in Africa, almost certainly because HIV infection rates are beginning to stabilize or fall. HIV has probably had a smaller effect on TB prevalence than on incidence because the virus significantly reduces the life expectancy of patients with TB (Figure 7-2) (Asamoah-Odei 2004, Dye 2005, Dye 2006).



Source: WHO report, 2006

Figure 7-2: Estimated HIV prevalence in new adult TB cases, 2004.

In regions where HIV infection rates are high in the general population, they are also high among patients with TB; estimates for 2004 exceeded 50 % in Botswana, South Africa, Zambia, and Zimbabwe, among other countries (Corbett 2003, Dye 2005, Dye 2006, World Health Organization 2006a).

The survival rate of HIV-positive TB patients varies according to AFB smear status and regimen. It is generally higher for AFB smear-positive than for smear-negative patients, and it is lowest with rifampicin-based regimens (Corbett 2003, Dye 2005, Dye 2006, World Health Organization 2006a).

In summary, the HIV pandemic presents a massive challenge for global TB control. The prevention of HIV and TB, the extension of WHO DOTS programs, and a focused effort to control HIV-related TB in areas of high HIV prevalence are matters of great urgency (World Health Organization 2002a,b; Aaron 2004, World Health Organization 2006a). The WHO and its international partners have formed the TB/HIV Working Group ([www.stoptb.org/wg/tb\\_hiv](http://www.stoptb.org/wg/tb_hiv)), which is developing a global policy on the control of HIV-related TB, providing advice on how those fighting against TB and HIV can work together to tackle this lethal combination. The temporary policy on collaborative TB/HIV activities describes steps to create mechanisms of collaboration between TB and HIV/AIDS programs, to reduce the burden of TB among people with HIV and the burden of HIV among TB patients.

These activities should be included in national TB control plans (Aaron 2004, World Health Organization 2002a, World Health Organization 2002b; World Health Organization 2006a).

### 7.3. Progress of the DOTS strategy

In 1994, the internationally recommended control strategy, later named DOTS, was launched. It stands for Directly Observed Treatment, Short-course, and its key components include:

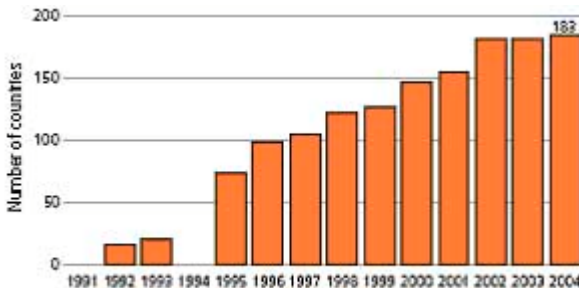
- government commitment;
- case detection by predominantly passive case finding;
- standardized short-course chemotherapy for, at least, all confirmed sputum AFB smear-positive cases, provided under proper case management conditions;
- a system of regular drug supply; and
- a monitoring system for program supervision and evaluation.

A six-month supply of drugs for DOTS costs less than US\$ 10 in some parts of the world. The World Bank has ranked the DOTS strategy as one of the “most cost-effective of all health interventions”. Countries that employ DOTS have been able to prevent an expected increase in drug resistance. Some countries using DOTS, such as Cuba and Nepal, have even begun to see declining levels of drug resistance (World Health Organization 1994, World Health Organization 2002c).

A total of 183 countries and territories were implementing the DOTS strategy in 2004. By the end of 2004, 83 % of the world’s population lived in countries covered by DOTS. DOTS programs notified 4.4 million new and relapse TB cases in 2004, of which 2.1 million were new AFB smear-positive. In total, 21.5 million TB patients, and 10.7 million AFB smear-positive patients, were treated in DOTS programs over the 10-year period 1995-2004 (Sharma 2006, World Health Organization 2006a).

Globally, the case detection rate by DOTS programs increased almost linearly from 11 % in 1995 to 28 % in 2000, and then accelerated to 45 % in 2003. If the 7 % global increase in detection between 2002 and 2003 was maintained, it would have reached approximately 60 % by 2005, 10 % below target. Comparing different parts of the world in 2003, case detection was highest in the Latin American (48 %)

and Western Pacific regions (50 %), and lowest in Eastern Europe (22 %). The recent acceleration has been mostly due to rapid implementation in India, where case detection increased from 1.7 % in 1998 to 47 % in 2003, and in China, where case detection increased from 30 % in 2002 to 43 % in 2003. India and China together accounted for 63 % of the increase in case notification by DOTS programs between 2002 and 2003. With this display of growing coverage, governments, donors, and other supporting agencies were beginning to ask for evidence that DOTS is having the expected epidemiologic impact (Figure 7-3) (De Cock 1999, World Health Organization 2002b, World Health Organization 2002c; Dye 2005, Frieden 2005, Sharma 2006, World Health Organization 2006a).



Source: WHO report, 2006

Figure 7-3: Number of countries implementing DOTS (out of a total of 211 countries), 1991-2004.

The global treatment success rate under DOTS has been high since the first observed cohort in 1994 (77 %). Since 1998, it has remained above 80 %, even though the cohort size has increased 6-fold to 1.4 million patients. There is, however, much variation between regions. Treatment success exceeded the 85 % target in the Western Pacific region, largely because China reported a 93 % success rate. Clearly, the biggest failure of DOTS has been in Africa, where rates of TB continue to rise, seemingly unabated. In 2002, the African region showed less than 75 % cure rates, and death rates were as high as 8 % in patients co-infected with *M. tuberculosis* and HIV. Whether this statistic indicates a failure of DOTS, or is the result of the rapid spread of the HIV epidemic, is debatable. Eastern Europe, another region plagued by poor health systems and an expanding HIV epidemic, witnessed continued increases in TB incidence rates throughout the 1990s, though the increase now seems to have peaked. Increases in incidence rates of disease are

also noted in Central Asian countries, though the death rate in DOTS recipients remains stable at 5 %. Both Eastern Europe and Central Asia are also hotspots of MDR-TB (Dye 2005, Frieden 2005, Sharma 2006, World Health Organization 2006a).

Although the decline in TB has almost certainly been accelerated by good chemotherapy programs in countries such as Chile, Cuba, and Uruguay, there have only been few recent, unequivocal demonstrations of the impact of DOTS in high-burden countries. Two examples come from Peru and China. In Peru, the incidence rate of pulmonary TB has decreased annually by 6 % since the nationwide implementation of DOTS in 1991. In 13 provinces of China that implemented DOTS, the prevalence rate of culture-positive TB was cut by 30 % between 1990 and 2000 (Dye 2005, World Health Organization 2006a).

Despite substantial success with DOTS expansion, most countries will probably not meet the target of the United Nations Millennium Development Goals of halving the prevalence of TB and the associated death rates between 1990 and 2015. Further innovative steps need to be taken as the public-health community moves beyond DOTS expansion to global TB control. The main objectives are: to continue DOTS expansion with more funding and oversight, build on existing DOTS programs to pursue DOTS-Plus, increase funding for research into improved diagnostics, therapeutics, and vaccines, revisit strategies of chemoprophylaxis and active case finding, and use DOTS to strengthen public-sector infrastructure and community-based health programs and insurance schemes (Sharma 2006, World Health Organization 2006a).

### **DOTS-Plus**

Based upon DOTS, DOTS-Plus is a comprehensive management strategy under development and testing that includes the five tenets of the DOTS strategy. DOTS-Plus takes into account specific issues (such as the use of second-line anti-tuberculosis drugs) that need to be addressed in areas where there is high prevalence of MDR-TB. These drugs should be stored and dispensed at specialized health centers with appropriate facilities and well-trained staff. Thus, DOTS-Plus works as a supplement to the standard DOTS strategy. By definition, it is impossible to conduct DOTS-Plus in an area without having an effective DOTS-based TB control program in place. It is vital that DOTS-Plus pilot projects follow WHO recommendations in order to minimize the risk of creating drug resistance to second-line TB drugs (which are more toxic and expensive, and less effective, than first-line drugs). The regimen includes two or more second-line TB drugs to which the isolate is susceptible, including one drug given parenterally for six months or

more. The total duration of treatment is 18-24 months. This treatment is directly observed and should be either individualized according to drug susceptibility test results of *M. tuberculosis* isolate identified on culture, or given as a standardized regimen to patients who fail supervised re-treatment (for example, when culture and drug susceptibility testing are not performed) (World Health Organization 2002d, Sharma 2006).

DOTS-Plus is not intended to be a universal strategy, and is not required in all settings. DOTS-Plus should be implemented in selected areas with moderate to high levels of MDR-TB in order to combat an emerging epidemic. Via the Green Light Committee review process, DOTS-Plus is already being implemented in Bolivia, Costa Rica, Estonia, Haiti, Karakalpakstan (Uzbekistan), Latvia, Malawi, Mexico, Peru, Philippines and the Russian Federation (Arkhangelsk, Ivanono, Tomsk and Orel Oblasts). More recently, DOTS-Plus projects have also been approved in Georgia, Honduras, Jordan, Kenya, Kyrgyzstan, Lebanon, Nepal, Nicaragua, Romania, and Syria (Gupta 2002, Sharma 2006, World Health Organization 2002d).

The Working Group on DOTS-Plus for MDR-TB identified the lack of access to second-line anti-tuberculosis drugs as one of the major obstacles to the implementation of DOTS-Plus pilot projects. The working group has made arrangements with the pharmaceutical industry to provide concessionally-priced second-line anti-tuberculosis drugs to DOTS-Plus pilot projects that meet the standards outlined in the Guidelines for Establishing DOTS-Plus Pilot Projects for the Management of MDR-TB. Currently, prices have been reduced by up to 99 % compared with prices on the open market. It is the task of the Green Light Committee to review the applications from potential DOTS-Plus pilot projects and to determine whether or not they are in compliance with the Guidelines for Establishing DOTS-Plus Pilot Projects (Gupta 2002, World Health Organization 2002c, World Health Organization 2002d; Sharma 2006).

## 7.4. The new Stop TB strategy

The first Global Plan to Stop TB set out the actions that were needed in TB control over the period 2001-2005 and helped to steer global TB control efforts during that time. Current rates of progress are insufficient to allow the targets of halving TB mortality and prevalence by 2015 to be achieved. Particularly urgent action is needed in regions where the epidemic is worsening, notably in Africa but also in Eastern Europe (Dye 2005, World Health Organization 2001, World Health Organization 2006c).

As a global movement to accelerate social and political action to stop the spread of the disease, the Stop TB Partnership provides the platform for international organizations, countries, donors (public and private sector), governmental and non-governmental organizations, patient organizations, and individuals to contribute to a collective and concerted campaign to Stop TB. Making the most of partners' efforts, in terms of effectiveness and efficiency, requires a plan. The Stop TB Partnership has developed a Global Plan to Stop TB that covers the period 2006–2015 (Squire 2006, World Health Organization 2006d).

Within the Partnership's strategic approaches for the next decade, the Plan sets out the activities that will make an impact on the global burden of TB. This involves reducing TB incidence - in line with the Millennium Development Goals - and reaching the Partnership's targets for 2015 of halving TB prevalence and deaths compared with 1990 levels. TB is a long-haul disease: the Plan represents a step towards the elimination of TB as a global public health problem by 2050, and the realization of the Partnership's vision of a TB-free world. It sets out the resources needed for actions, underpinned by sound epidemiological analysis with robust budget justifications; and it supports the need for long-term planning for action at the regional and country level (United Nations Statistics Division 2006, World Health Organization 2006a, World Health Organization 2006c).

The Plan will serve to stimulate political commitment, financial support, effective intervention, patient involvement, and community participation; and it will also indicate the potential of the new tools to control TB, which are currently under development (improved drugs, diagnostics and vaccines). There is no truly effective vaccine against TB, and the limitations of the available tools for diagnosis and treatment (smear microscopy testing and "short-course" chemotherapy) make standard TB care demanding for both patients and healthcare providers. The need to rely on the available tools has substantially hindered the pace of progress in global TB control. Facilitating the concerted efforts of the Stop TB Partnership's Working Groups on New Diagnostics, Drugs, and Vaccines for TB is thus, a key component of the Stop TB Strategy. In the spirit of partnership, TB control programs should actively encourage and participate in this process. Countries should advocate the development of new tools, help to speed up the field testing of new products, and prepare for swift adoption and roll-out of new diagnostics, drugs and vaccines as they become available (Squire 2006, World Health Organization 2006d).

The development of the Plan has relied on contributions from the Stop TB Partnership's seven working groups — DOTS expansion, DOTS-Plus for MDR-TB, TB-HIV, new TB diagnostics, new TB drugs, new TB vaccines, advocacy, communi-

cation and social mobilization — coordinated by the Partnership Secretariat (Squire 2006, World Health Organization 2006d).

The Working Groups have contributed to the two key dimensions of the Plan:

- regional scenarios (projections of the expected impact and costs of activities oriented towards achieving the Partnership's targets for 2015 in each region), and
- the strategic plans of the working groups and the Secretariat (Squire 2006, World Health Organization 2006c, World Health Organization 2006d).

The Stop TB Strategy is divided into four major sections (World Health Organization 2006c, World Health Organization 2006 d):

**The Stop TB Strategy at a glance.** Provides an overview of the strategy.

- **Vision, goal, objectives, targets and indicators.** Explains the goal and related objectives, targets and indicators of the Stop TB Strategy, as well as the overall vision to which the Strategy will contribute.
- **The six principal components of the Stop TB Strategy.** (see below).
- **Measuring global progress and impact.** Explains how progress towards TB control targets will need to be measured and evaluated.

The six components of the Stop TB Strategy are (World Health Organization 2006a, World Health Organization 2006c, World Health Organization 2006d):

1. **Pursuing high-quality DOTS expansion and enhancement.** Making high-quality services widely available and accessible to all those who need them, including the poorest and most vulnerable, requires DOTS expansion to even the remotest areas. In 2004, 183 countries (including all 22 of the high-burden countries which account for 80 % of the world's TB cases) were implementing DOTS in at least part of the country.
2. **Addressing TB/HIV, MDR-TB and other challenges.** Addressing TB/HIV, MDR-TB and other challenges requires much greater action and input than DOTS implementation and is essential in order to achieve the targets set for 2015, including the United Nations MILLENNIUM DEVELOPMENT GOALS relating to TB (Goal 6; Target 8).

3. **Contributing to health system strengthening.** National Tuberculosis Control Programmes must contribute to overall strategies to advance financing, planning, management, information and supply systems, and innovative service delivery scale-up.
4. **Engaging all care providers.** TB patients seek care from a wide array of public, private, corporate and voluntary healthcare providers. To be able to reach all patients and ensure that they receive high quality care, all types of healthcare providers are to be engaged.
5. **Empowering people with TB, and communities.** Community TB care projects have shown how people and communities can undertake some essential TB control tasks. These networks can mobilize civil societies and also ensure political support and long-term sustainability for National Tuberculosis Control Programmes.

**Enabling and promoting research.** While current tools can control TB, improved practices and elimination will depend on new diagnostics, drugs and vaccines.

With the implementation of the strategy:

- equitable access for all to quality TB diagnosis and treatment will be expanded,
- over the ten years of this Plan, about 50 million people will be treated for TB under the Stop TB Strategy, including about 800,000 patients with MDR-TB; in addition, about 3 million patients who have both TB and HIV will be enrolled on antiretroviral therapy (in line with UNAIDS plans for universal access) ([www.unaids.org/en](http://www.unaids.org/en)),
- some 14 million lives will be saved from 2006 to 2015,
- for the first time in 40 years, a new TB drug will be introduced in 2010, with a new short TB regimen (1–2 months) shortly after 2015,
- by 2010, diagnostic tests at the point of care will allow rapid, sensitive, and inexpensive detection of active TB. By 2012, a diagnostic toolbox will accurately identify people with latent TB infection and those at high risk of progression to disease, and
- by 2015, a new, safe, effective, and affordable vaccine will be available with the potential to have a significant impact on TB control in later years (World Health Organization 2006 a, World Health Organization 2006c, World Health Organization 2006d).

The total cost of the Plan — US\$ 56 billion — represents a three-fold increase in the annual investment in TB control compared with the first Global Plan. This total includes US\$ 9 billion for research and development and US\$ 47 billion for implementation of current interventions (US\$ 44 billion are country-level costs, representing about 80 % of the Plan's total cost (Squire 2006, World Health Organization 2006c, World Health Organization 2006d).

In a resolution adopted by the 58<sup>th</sup> World Health Assembly in 2005, on 'sustainable financing for TB prevention and control', all countries made a commitment to ensure the availability of sufficient domestic and external resources to achieve the Millennium Development Goals relevant to TB. National governments and donors must fulfill this commitment by mobilizing the funds to increase current levels of funding and fill the US\$ 31 billion gap. With the will, the funds and the action, together we can Stop TB (World Health Organization 2005a, World Health Organization 2006b; Squire 2006).

If the Stop TB Strategy is implemented as set out in the Global Plan, the resulting improvements in TB control should reverse the rise in the incidence of TB by 2015, and halve the prevalence and death rates in all regions except Africa and Eastern Europe (Squire 2006, World Health Organization 2006a, World Health Organization 2006c, World Health Organization 2006d).

The 2006 WHO report Global TB Control concluded that three (of six) WHO regions – namely the Americas, South-East Asia, and the Western Pacific - are likely to have met both the 2005 targets. Seven of the 22 high-burden countries are likely to have met the 2005 targets: Cambodia, China, India, Indonesia, Myanmar, the Philippines and Viet Nam (World Health Organization 2006a).

## References

1. Aaron L, Saadoun D, Calatroni I, et al. Tuberculosis in HIV-infected patients: a comprehensive review. *Clin Microbiol Infect* 2004; 10: 388-98.
2. Asamoah- Odei E, Garcia Calleja JM, Boerma JT. HIV prevalence and trends in sub-Saharan Africa: no decline and large sub-regional differences. *Lancet* 2004; 364: 35-40.
3. Borgdorff MW, Nagelkerke NJ, Dye C, Nunn P. Gender and tuberculosis: a comparison of prevalence surveys with notification data to explore sex differences in case detection. *Int J Tuberc Lung Dis* 2000; 4: 123-32.
4. Corbett EL, Charalambous S, Moloi VM, et al. Human immunodeficiency virus and the prevalence of undiagnosed tuberculosis in African gold miners. *Am J Respir Crit Care Med* 2004; 170: 673-9.
5. Corbett EL, Watt CJ, Walker N, et al. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. *Arch Intern Med* 2003; 163: 1009-21.

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6. De Cock KM, Chaisson RE. Will DOTS do it? a reappraisal of tuberculosis control in countries with high rates of HIV infection. *Int J Tuberc Lung Dis* 1999; 3: 457-65.
7. Dye C, Scheele S, Dolin P, Pathania V, Raviglione MC. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. *JAMA* 1999; 282: 677-86.
8. Dye C, Watt CJ, Bleed DM, Mehran Hosseini S, Raviglione MC. Evolution of tuberculosis control and prospects for reducing tuberculosis incidence, prevalence, and deaths globally. *JAMA* 2005; 293: 2767-75.
9. Dye C. Global epidemiology of tuberculosis. *Lancet* 2006; 367: 938-40.
10. Floyd K. Costs and effectiveness-the impact of economic studies on TB control. *Tuberculosis* 2003; 83: 187-200.
11. Frieden TR, Munsiff SS. The DOTS strategy for controlling the global tuberculosis epidemic. *Clin Chest Med* 2005; 26: 197-05.
12. Gupta R, Cegielski JP, Espinal MA, et al. Increasing transparency in partnerships for health-introducing the Green Light Committee. *Trop Med Int Health* 2002; 7: 970-6.
13. Sharma SK, Liu JJ. Progress of DOTS in global tuberculosis control. *Lancet* 2006; 367: 951-2.
14. Smith I. What is the health, social, and economic burden of tuberculosis. p. 233-7. In: Frieden T. (ed). *Toman's tuberculosis case detection, treatment, and monitoring: questions and answers*. 2<sup>nd</sup> ed. Geneva, WHO, 2004. WHO/HTM/TB/2004.334.
15. Squire SB, Obasi A, Nhlema-Simwaka B. The Global Plan to Stop TB: a unique opportunity to address poverty and the Millennium Development Goals. *Lancet* 2006; 367: 955-7.
16. United Nations Statistics Division. Millennium Development Goal Indicators database. [http://unstats.un.org/unsd/mi/mi\\_goals.asp](http://unstats.un.org/unsd/mi/mi_goals.asp) (accessed March 19, 2007).
17. World Health Organization (2006b), Fact sheet, N° 104, March 2006.
18. World Health Organization, International Union Against Tuberculosis and Lung Disease, Royal Netherlands Tuberculosis Association. Revised international definitions in tuberculosis control. *Int J Tuberc Lung Dis* 2001; 5: 213-5.
19. World Health Organization (2005a). Addressing poverty in tuberculosis control: options for national TB control programmes. Geneva, WHO, 2005 (WHO/HTM/TB/2005.352).
20. World Health Organization (2002a). An expanded DOTS framework for effective tuberculosis control. Geneva, Switzerland: WHO, 2002. (WHO/CDS/TB/2002.297).
21. World Health Organization (2002c). Expanding DOTS in the context of a changing health system. Geneva, WHO, 2002 (WHO/CDS/TB/2002.318).
22. World Health Organization (2006a). Global tuberculosis control: surveillance, planning and financing. Geneva, Switzerland: WHO; 2006. Publication WHO/HTM/TB/2006.362.
23. World Health Organization. Resolution WHA44.8. Tuberculosis control programme. In: *Handbook of resolutions and decisions of the World Health Assembly and the Executive Board*. Vol III, 3<sup>rd</sup> ed. (1985-1992). Geneva, WHO, 1993 (WHA44/1991/REC/1): 116.
24. World Health Organization. Resolution WHA53.1. Stop Tuberculosis Initiative. In: *Fifty-third World Health Assembly*. Geneva, 15-20 May 2000. Resolutions and decisions. Geneva, WHO, 2000 (WHA53/2000/REC/1), Annex: 1-2.
25. World Health Organization (2005b). Resolution WHA58.14. Sustainable financing for tuberculosis prevention and control. In: *Fifty-eighth World Health Assembly*. Geneva, 16-25 May 2005. Resolutions and decisions. Geneva, WHO, 2005 (WHA58/2005/REC/1), Annex: 79-81.

26. World Health Organization (2006c). Stop TB Partnership. The Stop TB Strategy. Building on and enhancing DOTS to meet the TB-related Millennium Development Goals. Geneva, WHO, 2006 (WHO/HTM/TB/2006.368).
27. World Health Organization (2002b). Strategic framework to decrease the burden of TB/HIV. Geneva, WHO, (WH/CDS/TB/2002.296).
28. World Health Organization (2006d). The Global Plan to Stop TB, 2006-2015. Actions for life-towards a world free of tuberculosis. Geneva, WHO, 2006 (WHO/HTM/STB/2006.35).
29. World Health Organization. The Global Plan to Stop Tuberculosis. Geneva, WHO, 2001 (WHO/CDS/STB/2001.16).
30. World Health Organization (2002d). The newsletter of the global partnership movement to Stop TB. 2002; 7.
31. World Health Organization. The world health report 2004: changing history. Geneva: WHO, 2004.
32. World Health Organization. WHO Tuberculosis Programme: framework for effective tuberculosis control. Geneva, WHO, 1994 (WHO/TB/94.179).

