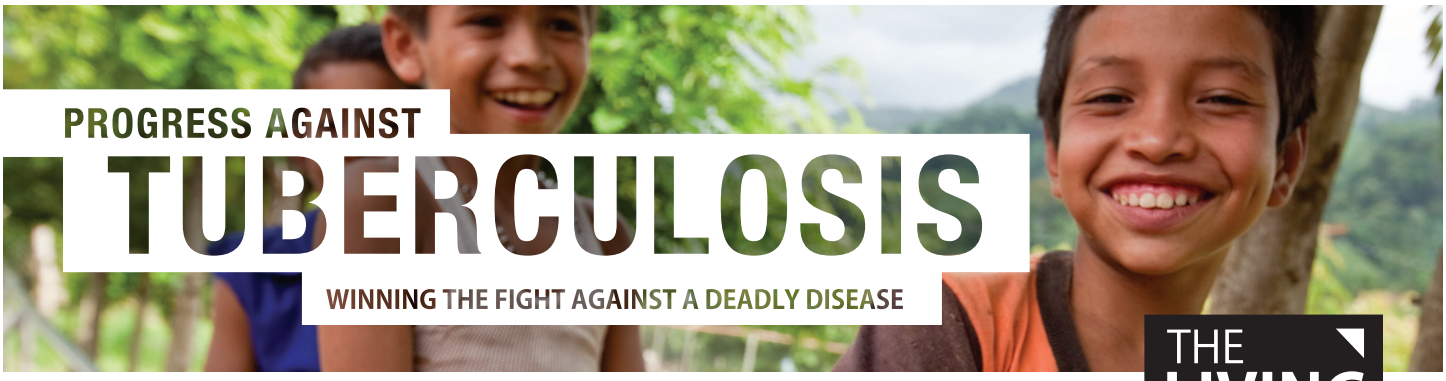


PROGRESS AGAINST TUBERCULOSIS

WINNING THE FIGHT AGAINST A DEADLY DISEASE

THE LIVING PROOF PROJECT

U.S. investments in global health are working.

The number of people dying from tuberculosis continues to decline worldwide, due to improved treatment protocols and an impressive global campaign to bring increased financial resources and attention to fight this deadly infectious disease.

The fight against tuberculosis (TB) gained momentum in the early 1990s with the declaration of TB as a global emergency by the World Health Assembly, and with the introduction of a new treatment protocol, known as "Directly Observed Therapy, Short-course" (DOTS). Global efforts were further scaled up in response to the United Nations' sixth Millennium Development Goal (MDG 6)—to reduce rates of TB infection and to halve global prevalence and mortality rates by 2015 compared to 1990 levels. If trends continue, infection rates will be halved by 2015 in the Americas, the Eastern Mediterranean, Southeast Asia, and the Western Pacific. However, in Africa and Eastern Europe, progress is slow, particularly due to the added challenges of emergent drug resistance and complications related to human immunodeficency virus (HIV) co-infection.

Global Progress

Funding in the 22 high-burden countries that account for 80 percent of the world's TB cases nearly doubled from $1.2 billion (U.S.) in 2002 to $2.2 billion (U.S.) in 2009. In 2009, available investments for TB total approximately $3 billion (U.S.).[1]

Public and private organizations across the world have come together to launch global partnerships for the fight against TB:

- The **Stop TB Partnership (Stop TB)**, launched in 1998 and hosted by the World Health Organization (WHO), is a global network of public and private organizations, including TB control programs, technical agencies, service delivery organizations, research scientists, and donors. Stop TB raises awareness about the global TB burden and coordinates the activities of partners in key areas, including advocacy, technical support, and research and development.
- The **Global Drug Facility**, run by the Stop TB Partnership, was established in 2001 to expand access to high-quality, affordable anti-TB drugs and diagnostics, and to carry out drug procurement for GLC-approved programs.
- In 2000, the **Green Light Committee (GLC)** Initiative was established to expand access to second-line anti-TB drugs for the treatment of strains of TB that are resistant to standard first-line drugs, known as multidrug-resistant TB (MDR-TB).[2] The GLC is administered by WHO.
- The **Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund)** is the world's largest international source of financing for the global response to TB. It was created in 2002 as an innovative financing mechanism to raise and disburse funding to countries. As a global public-private partnership, the Global Fund uses a demand-driven, performance-based model. Countries apply for grants to fund their response to TB, and continued financing is dependent on achievement of agreed-upon targets. By the end of 2008, the Global Fund had approved $3.1 billion (U.S.) in grants to TB programs.[3] In 2008, the Global Fund contributed 57 percent of all international (non-domestic) investments for TB.[4]

Innovation and Scientific Advances

Less than a decade ago, the research and development (R & D) pipeline for new TB drugs, diagnostics, and vaccines was relatively dry. Today much more effort is being put into the development of new technologies:

- Rapid and accurate diagnosis of symptomatic patients is key to successfully combating TB. Sputum smear-microscopy, used as the diagnostic method in countries where disease is endemic, has a low sensitivity, detecting only about half of all TB cases. Moreover, it requires a trained microscopist, presenting a challenge in many low-resource settings. The **Foundation for Innovative New Diagnostics (FIND)** is working to develop rapid diagnostics to more efficiently and reliably detect TB and MDR-TB.[5]
- Led by the **Global Alliance for TB Drug Development (TB Alliance),** TB drug development focuses on shortening

the duration of TB therapy, treating MDR-TB and ensuring compatibility with antiretroviral drugs to treat HIV. Several drugs in advanced stages of development may help shorten TB therapy from six to eight months to three to four months. Other anti-TB drug candidates are active against MDR-TB.[6] With nine products in pre-clinical development or later, the global TB drug pipeline looks richer than it has over the past 40 years.[7]

- The **Aeras Global TB Vaccine Foundation** is supporting research into new TB vaccines, including working to make a modified BCG vaccine. A modestly effective vaccine (50 to 70 percent efficacious) combined with antibiotics to treat the disease could save millions of lives, and a highly effective vaccine could bring TB to very low levels worldwide.

WHAT IS TUBERCULOSIS?

Tuberculosis (TB) is an infectious disease caused by a bacterium called Mycobacterium tuberculosis. The bacterium spreads from person to person through the air. One-third of the world's population is infected with the TB bacterium, but only 5 to 10 percent of those infected become sick or contagious.

TB is one of the leading causes of death from an infectious disease worldwide, and a major killer of people living with HIV/Acquired Immune Deficiency Syndrome (AIDS). About 1.8 million people died from TB in 2007, including 456,000 people living with HIV.[19] Ninety percent of all cases and deaths occur in developing countries. The economic impact of TB for developing countries is also huge. It is estimated that high-burden countries in Asia suffer from productivity loss due to TB of 4 to 7 percent of GDP per year.[20]

The goal of the Stop TB Strategy is a world free of TB.[21] One of the pillars of this strategy is Directly Observed Treatment, Short-Course (DOTS), the internationally recommended approach for the diagnosis and treatment of tuberculosis.[22] The DOTS treatment protocol requires the supervision of a TB patient's treatment by an independent observer to ensure that the patient takes the treatment regularly, usually over a six-month period. DOTS has been proven highly cost-effective at reducing incidence of tuberculosis in high-burden settings.[23] All 22 high-burden countries have had DOTS programs since 2000.

In terms of prevention, the Bacille Calmette-Guérin (BCG) vaccine provides some protection against severe forms of pediatric TB, but has a very limited protective effect against adult pulmonary TB, which is the most common form of TB worldwide.[24]

Results

The results achieved in the global fight against TB are impressive, both in terms of coverage (case detection, access to DOTS, and treatment success rates) and impact (decline in TB cases and reduced mortality). The progress in the fight against TB shows that a global commitment can have a significant impact on one of the world's most common and serious diseases.

Case Detection

Due to significant global efforts in case detection, TB patients are identified more quickly today, and are thus able to receive treatment.

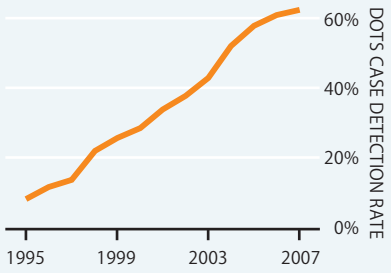
- Globally, the case detection rate of new TB cases under DOTS increased from 11 percent in 1995 to 63 percent in 2007.[8]
- The target set by the World Health Assembly in 1991 to detect 70 percent of new TB cases under DOTS programs by the year 2000 was achieved in 2007 in the Americas (73 percent) and the Western Pacific (77 percent), and the target was close to being met in Southeast Asia (69 percent). In Africa, the Eastern Mediterranean, and Eastern Europe, case detection has also been scaled up but remains below 70 percent.[9]

Access to DOTS

The number of countries implementing DOTS increased from zero in 1991 to 180 in 2007. Approximately 32 million patients were treated under DOTS between 1995 and 2007.[10]

SCALING UP CASE DETECTION

Global Case Detection Rates of New TB Cases Under DOTS, 1995–2007



Source: World Health Organization, *Global Tuberculosis Control: Epidemiology, Strategy, Financing 2009.*

Treatment Success Rate

In 2006, the global treatment success rate for new smear-positive cases under the DOTS program reached the target of 85 percent set by the World Health Assembly in 1991. Three regions (Eastern Mediterranean, Western Pacific, and Southeast Asia) exceeded the target. Africa (75 percent), the Americas (75 percent), and Eastern Europe (70 percent) are still approaching the target.

Decline in incidence and prevalence: Globally, the Millennium Development Goal (MDG) target 6, calling for declining incidence of TB, was met in 2005. The global incidence rate peaked at 142 cases per 100,000 population in 2004, and has been declining globally since then, except in Eastern Europe, where rates are stable. By 2015, TB prevalence will be halved relative to 1990 levels in all regions except Africa and Europe if the current trends persist. However, the decline in incidence needs to be further accelerated to achieve the target of eliminating TB by 2050.[11]

Reduced Mortality

TB deaths are declining globally. The Eastern Mediterranean, the Americas, and Southeast Asia are on track to at least halve mortality rates by 2015 compared to 1990. The Western Pacific region will just miss the target unless

the current rate of decline accelerates. In all four regions, mortality rates have been declining since 1990.

In Africa, in parallel with the increase in HIV/AIDS rates, and Eastern Europe, because of drug resistance and deterioration in public health services, mortality rates grew significantly during the 1990s. While this trend has been reversed (in 2000 in Eastern Europe, and in 2005 in Africa), mortality rates in 2007 were still substantially higher than in 1990 in Africa and just back to the 1990 level in Eastern Europe. Globally, the annual number of deaths from TB among people living with HIV/AIDS peaked in 2005 at 480,000 deaths, compared to 456,000 deaths in 2007.[12]

Moving Forward

Tackling the TB crisis in Africa and Eastern Europe: Neither the MDG-specified prevalence nor the mortality targets will be achieved in Africa or Eastern Europe by 2015, unless urgent action is taken. Addressing this crisis will require focused action in three areas:

- Increasing case detection through strengthened health infrastructures and improvement in the quality of primary health care services: In Africa, only 47 percent of estimated cases are being detected. Also, Russia and many Eastern European countries have case detection rates under 50 percent. To increase detection, effective quality-assured diagnostic tests and laboratory systems are required, and need to be combined with HIV/AIDS testing and treatment. In addition, more active outreach is needed to vulnerable populations, such as poor migrant populations, prisoners, and drug users.
- Diagnosing and treating HIV/TB co-infection: TB is one of the most common opportunistic infections associated with HIV's attack on the immune system—an estimated one-third of the people living with HIV/AIDS are infected with TB, many of them in Africa.[13] Both infections reinforce each other: HIV/AIDS-infected people are more likely to develop TB after infection and are more likely to die without prompt treatment. At the same time, TB bacteria can fuel the progression of HIV, causing patients to become sicker more rapidly. In countries heavily affected by HIV/AIDS, incidence rates of TB have increased about fourfold since the early 1990s.[14] However, only 32 percent of TB cases in people living with HIV received both antiretroviral- and anti-tuberculosis treatment in 2007. Collaborative TB/HIV activities need to be expanded to ensure that those who are HIV-positive, with and without TB, have access to effective TB prevention, diagnosis, and treatment.[15]
- Fighting MDR- and XDR-TB: The growing proportion of multidrug-resistant TB (MDR-TB—strains of TB that are resistant to standard first-line drugs) and extensively drug-resistant TB (XDR-TB—TB strains that are also resistant to most second-line drugs) is another challenge requiring urgent action. MDR-TB emerges as a result

COUNTRY SPOTLIGHT: FIGHTING MDR-TB IN LATVIA

Only a decade ago, Latvia was considered one of the countries most heavily affected by MDR-TB. Latvia's rates of TB (including MDR-TB) increased dramatically, along with other countries of the former Soviet Union, following the collapse of Latvia's national health system in the 1990s. MDR-TB is a serious problem in Eastern Europe—of the 27 high-burden MDR-TB countries worldwide, 15 are in Eastern Europe. TB prevalence peaked in 1998, with 90 cases per 100,000 population, and 13 percent of all reported TB cases had MDR-TB. Latvia's overall TB burden is particularly heavy among the more vulnerable members of society, such as prisoners, the homeless, drug users, and alcoholics.

With the introduction of DOTS in Latvia in 1995, the national TB control program was able to make significant progress in diagnosing and treating TB across the country. The national case detection rate increased from 71 percent in 1995 to 89 percent in 2007, and the treatment success rate increased from 61 percent in 1995 to 73 percent in 2006. By 2007, the TB prevalence had dropped to 55 per 100,000 people. [25]

As overall TB rates dropped, however, MDR-TB continued to make up an increasing proportion of all TB cases. In 1999, Latvia launched a "DOTS-Plus" pilot program to diagnose and treat MDR-TB. The program provided drug-susceptibility testing to all TB patients, used molecular diagnostic tools to rapidly screen for MDR-TB, and provided second-line TB treatment to cure patients diagnosed with MDR-TB. Latvia has also been working in partnership with the Green Light Committee to further increase the country's access to second-line treatment and enable the country to treat all patients diagnosed with MDR-TB.

Today, Latvia has made significant progress in bringing MDR-TB under control. Treatment success rates for 2005 (the latest MDR-TB figures available) were 71 percent. Even more impressive, between 2002 and 2007 the total annual number of detected MDR-TB cases per 100,000 people decreased by an average of 14 percent per year. Latvia has also recently opened the first WHO collaborating center for MDR-TB management training, where public health officials from other countries can learn how to respond effectively to MDR-TB. A remaining challenge is the low treatment success rate of XDR-TB patients thus far. Out of 48 patients treated against XDR-TB

between 2000 and 2005, 18 were cured.[26] This demonstrates the necessity for more R & D on effective XDR drugs.

Overall, Latvia's experience in managing MDR-TB is promising and can serve as a model for controlling MDR-TB in other countries. It demonstrates that combined international and national efforts to fight MDR-TB through a program which is well integrated into the national TB strategy can have significant impact on the disease.

of poor TB treatment, and accounts for more than 110,000 deaths each year.[16] An estimated 511,000 new MDR-TB cases occurred in 2007, with three countries accounting for 56 percent of all global cases: China, India, and Russia. However, globally, only 3,681 people were put on treatment in projects approved by the GLC in 2007 and are receiving treatment according to international guidelines. This is equal to 1 percent of the estimated global total of MDR-TB cases. In addition, WHO estimates that 40,000 cases of XDR-TB occur each year.[17] As diagnosis is difficult and current treatment options are seriously limited, research on better diagnosis and TB drugs, and on how to further improve DOTS programs, is critical.

To maintain and accelerate progress toward combating TB, new resources are needed. The total cost of the Global Plan to Stop TB for the period 2006–2015 is estimated at $56.1 billion (U.S.), compared to the $25 billion (U.S.) global financial commitment for TB control, leaving a funding gap of $30.8 billion (U.S.).[18]

Endnotes

1. This is the total funding available for the 94 countries that account for 93 percent of the global TB burden.
2. Second-line drugs are used when the standard first-line drugs fail. http://www.stoptb.org/gdf/drugsupply/drugs_available.asp.
3. This is the five-year proposed total budget; the two-year budget is $1.2 billion (U.S.).
4. Global Fund to Fight AIDS, Tuberculosis, and Malaria, *Scaling up for Impact: Results report,* 2009.
5. These new diagnostic tools are called molecular line probe assays.
6. See "New Laboratory Diagnostic Tools for Tuberculosis Control, WHO and Stop TB Partnership, Retooling Task Force, 2008" at http://www.stoptb.org/resource_center/assets/documents/Diagnostic_Brochure_Final_Dec_08.pdf.
7. P. Chatterjee, "Challenges Remain to New Tuberculosis Drugs, Delegates Told," *Lancet Infectious Disease* 8, no. 6 (June 2008): 356.
8. Case detection rate under DOTS and non-DOTS programs increased from 35 percent in 1995 to 64 percent in 2007.
9. The regional case detection rate was 60 percent in the Eastern Mediterranean Region, 51 percent in the European Region, and 47 percent in the African Region. World Health Organization: *Global Tuberculosis Control: Epidemiology, Strategy, Financing,* 2009.
10. WHO and Stop TB Partnership, *Implementing the Stop TB Strategy in 2008.* http://www.who.int/tb/publications/2008/factsheet_april08.pdf; World Health Organization, *Global Tuberculosis Control: Epidemiology, Strategy, Financing,* 2009.
11. The Stop TB partnership has set the target to eliminate TB as a public health problem by 2050. See L. J. Abu-Raddad, L. Sabatelli, Lorenzo, J. T. Achterberg, J. D. Sugimoto, I. M. Longini, C. Dye, M. E. Halloran, "Epidemiological Benefits of More-Effective Tuberculosis Vaccines, Drugs, and Diagnostics," *PNAS* 106, no. 33 (18 August 2009): 13980–13985.
12. WHO, *Global Tuberculosis Control: Epidemiology, Strategy, Financing,* 2009.
13. http://www.who.int/tb/hiv/faq/en/.
14. The Joint United Nations Programme on HIV/AIDS (UNAIDS), Frequently asked questions about Tuberculosis and HIV. http://data.unaids.org/pub/FactSheet/2006/TB_HIV_QA.pdf.
15. UNAIDS, *Report on the Global HIV/AIDS Epidemic 2008,* August 2008.
16. WHO, *Tuberculosis. MDR-TB & XDR-TB. The 2008 Report,* 2008.
17. WHO, *Global Tuberculosis Control: Epidemiology, Strategy, Financing,* 2009. World Health Organization, Tuberculosis. MDR TB &XDR-TB. *The 2008 Report,* 2008.
18. Stop TB Partnership and WHO, *The Global Plan to Stop TB 2006-2015*.
19. WHO, *Global Tuberculosis Control: Epidemiology, Strategy, Financing,* 2009.
20. C. Harper, "Tuberculosis, A Neglected Opportunity," *Nature Medicine* 13 (2007): 309–312.
21. WHO and Stop TB Partnership: The Stop TB Strategy: Building on and enhancing DOTS to meet the TB related Millennium Development Goals, 2006.
22. The DOTS strategy has five components: government commitment for TB control, diagnosis based on sputum-smear microscopy tests done on patients reporting TB symptoms, direct observation short-course chemotherapy treatments, a definite drug supply, and standardized reporting of cases and treatment outcomes.
23. P.G. Suárez, C.J. Watt, E. Alarcón, et al., "The Dynamics of Tuberculosis in Response to 10 Years of Intensive Control Effort in Peru," *J Infect Dis,* 184, no. 4 (15 August 2001): 473–8; China Tuberculosis Control Collaboration, "The Effect of Tuberculosis Control in China," *Lancet*, 364 (2004): 417–22.
24. http://www.who.int/vaccine_research/diseases/tb/vaccine_development/bcg/en/.
25. WHO, *Global Tuberculosis Control: Epidemiology, Strategy, Financing,* 2009.
26. V. Leimane, "Treatment and Management of MDR-TB in Latvia," *Bulletin of the World Health Organization* 85 (May 2007): 5.

The Living Proof Project is a multimedia initiative intended to highlight successes of U.S.-funded global health initiatives. Millions of lives have already been transformed and saved with effective, affordable solutions. We have the knowledge, innovative technologies and proven tools to do much more. The content for this progress sheet was developed by the Global Health Group at the University of California, San Francisco and SEEK Development in Berlin. It is also available online at www.livingproofproject.org.