


ACCELERATING IMPACT: EXPANDING ACCESS TO CARE

U.S. Government Report on International Foreign Assistance for TB FY 2011/2012

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PEPFAR
U.S. President's Emergency Plan for AIDS Relief



Cover Photo: DOTS Supporter at work, Zimbabwe

Credit: B Nyathi, TB CARE I, The Union

References to the U.S. Government (USG) in this report refer to specific interagency collaborative activities. This report does not represent the full breadth of each agency's activities.

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EXECUTIVE SUMMARY

Since 1990, the world has made progress toward meeting global targets for reducing the number of tuberculosis (TB) cases and deaths. We are on track to meet the global target of a 50 percent reduction in mortality by 2015. Still, many significant challenges remain. TB is a contagious airborne bacterial disease that continues to be a serious global public health threat. People living with HIV have a high chance of developing TB, particularly in places where TB is common, and an even higher chance of dying from it. In 2011, there were an estimated 8.7 million new cases of TB, and 1.4 million people died from the disease, 430,000 of whom were co-infected with HIV. The rapid emergence of multidrug-resistant TB (MDR-TB) is a public health emergency. Slow progress in identifying and providing adequate care in countries with a high burden of MDR-TB has the potential to reverse what has been accomplished in global TB care and treatment to date.

The impact of TB goes beyond the immediate loss of income and productivity for the household member who is sick. Other family members may be pulled out of work and school temporarily to provide care. In many places, families must pay for daily or weekly transport to a health facility even if TB diagnosis and treatment are available free of charge. At the national level, it is estimated that some countries lose from four to seven percent of their GDP because of TB.¹

The U.S. Government (USG) is a global leader in combating TB. The missions of the agencies working on TB are aligned and cover all aspects of biomedical, operational, domestic and international public health research, and implementation. Each agency, using its comparative advantage, works to improve understanding of the disease; develop and implement new tools for diagnosis, prevention, and treatment; and ensures programmatic efficiencies. The U.S. Agency for International Development (USAID) is the lead agency for international TB care and treatment activities and supports a comprehensive response to TB, TB/HIV, and MDR-TB through national TB care and treatment programs in host countries. The Office of the Global AIDS Coordinator (OGAC) is the lead for the USG response to TB/HIV co-infection as part of the President's Emergency Plan for AIDS Relief (PEPFAR). The U.S. Centers for Disease Control and Prevention (CDC) is the lead agency for domestic TB prevention and care efforts, and provides international technical support for global TB care and treatment in collaboration with USAID and OGAC. While it does not provide foreign assistance of any kind, including for TB care and treatment, the National Institutes of Health (NIH), working with the CDC, leads USG research efforts for the development of new TB diagnostics, drugs, and vaccines. Within NIH, the National Institute of Allergy and Infectious Diseases (NIAID) is the lead institute for TB research. The Department of Defense (DoD) has laboratories in numerous priority countries that monitor the quality of TB diagnostic services. DoD conducts operational research, and mobile care units deployed in crisis and conflict settings are used in support of efforts to ensure adequate TB services in those challenging circumstances.

¹ TB Alliance, "Economic Impact of TB"; World Bank, "Economic Benefit of TB Control," 2007.

ACHIEVEMENTS

In 2011, over 1.5 million smear-positive TB patients were successfully treated in countries supported by USAID.

TB prevalence and mortality are decreasing in USAID's priority countries.

The number of people with MDR-TB enrolled in treatment through USG-supported programs increased from 19,000 in 2010 to 44,000 in 2011.

The USG works closely with the World Health Organization (WHO) and the Stop TB Partnership, as well as public and private product development organizations. The USG, through NIH, is the world's largest funder of TB biomedical research, and the single largest contributor to the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund). Through its model for providing technical assistance to help implement Global Fund grants, USAID prioritizes support for a set of countries with the largest amount of Global Fund resources. These countries comprise 70 percent of the TB funds available, as well as 88 percent of TB prevalence, 88 percent of the MDR-TB burden, and 84 percent of TB/HIV co-infection among all countries who are TB grant recipients.

In every country where it works, the USG works with Ministries of Health and national HIV/AIDS and national TB programs (NTPs) to build and sustain national capacity. The USG's work on TB prevention and care focuses on those countries with the highest burdens of TB and HIV/AIDS, the poorest program performance, and increasing rates of MDR-TB. In 2011, in line with the Secretary of State's Quadrennial Diplomacy and Development Review, USAID began concentrating and focusing its work to ensure that its TB care and treatment program has the greatest impact. This has led to continued investments to build country ownership and strengthen the capacity of NTPs. For example, Brazil (highlighted in this report) is now transferring knowledge to other high TB burden countries, while continuing to improve TB case detection among its own vulnerable populations.

Between 1990 and 2011, TB mortality and prevalence decreased by 35 percent and 37 percent, respectively, in USAID-supported countries. More than 1.5 million sputum smear-positive TB patients were successfully treated in 2011, representing an 86 percent treatment success rate. Over 44,000 people with MDR-TB were enrolled in treatment through USG-supported programs, a significant increase from 2010 when just over 19,000

people were enrolled. This increase is largely a result of the USG's intensified MDR-TB case finding and expansion of access to care, a continuing challenge to reaching global and national targets for MDR-TB.

Universal access, which is the expansion of access to care, is a pillar of the USG's TB care and treatment program. Between 2010 and 2012, great strides were made to intensify TB case finding. USAID developed and scaled up a five-pronged approach to improve universal access to TB care: (1) providing TB care in communities in addition to health care facilities, (2) improving the quality and performance of TB laboratories, (3) addressing TB in prisons, (4) working with the private sector to ensure proper treatment for TB according to public health guidelines, and (5) actively finding TB cases.

The USG has been a leader in supporting the development and implementation of a new rapid diagnostic test, Cepheid Xpert® MTB/RIF assay (Xpert). Xpert has the potential to greatly improve diagnosis of TB and MDR-TB with test results in less than two hours. Its development was based on research supported by the NIAID at NIH. In FY 2012, PEPFAR and USAID partnered with the Bill & Melinda Gates Foundation and UNITAID in an innovative public-private partnership to reduce the price of Xpert test cartridges by 40 percent.

Despite the progress in TB prevention, care, and treatment, challenges remain. Continued efforts are needed to secure universal access, especially by extending the delivery of quality services provided by the private sector and reaching poor and vulnerable populations. The USG continues to address the MDR-TB epidemic, and aims to ensure that achievements endure. While Xpert may have a considerable impact on TB diagnosis, the development of new drugs, additional diagnostics, and notably, a vaccine, still are needed. The USG will continue to work closely with its partners to scale-up all components of the Stop TB Strategy to ensure that achievements continue.

This report outlines the global TB context; the coordinated USG approach to TB care and treatment; USAID's achievements in TB prevention, diagnosis, and treatment at the global and country levels; USG collaborative interagency activities; and the partnership with the Global Fund. USG agencies involved in global TB research and development are mentioned in specific areas of the report to highlight the broader contributions of the USG; however, this is not a comprehensive account of all USG efforts in global TB prevention, care, and research. References to the "USG" refer to specific interagency collaborative activities, but do not represent the full breadth of each agency's activities.

GLOBAL TB CONTEXT

Globally, TB prevalence and mortality have decreased significantly compared to 1990 levels. The world is on track to reach the 2015 Millennium Development Goal (MDG) of reducing TB mortality by 50 percent, and will have made significant gains to reach the MDG of reducing TB incidence by 50 percent. Despite these successes, there were an estimated 8.7 million new cases of TB in 2011 and 1.4 million deaths, including 430,000 TB deaths among people living with HIV (PLHIV). An estimated one-third of new TB cases occurred among women, and about 500,000 women died from TB. In 2011, approximately 327,000 children under the age of 15 were notified that they had TB disease, and over 60,000 children died.²

TB is an airborne disease caused by *Mycobacterium tuberculosis*. Throughout the world, an estimated two billion people are infected with the bacteria responsible for TB. Of those infected, most people do not become ill, but will harbor the infection (“latent TB”) for their entire lives, becoming vulnerable to the active disease if their immune systems are weakened. HIV/AIDS, diabetes, and other illnesses can make a person more vulnerable to TB, as do malnutrition and smoking.³ Some populations, like prisoners, miners, slum dwellers, and people living in poverty are more vulnerable to both infection and disease, given their crowded living and working conditions and often precarious health status.

Although men are more likely to be infected with TB, women are more likely to develop active TB disease. TB is one of the leading causes of death among women worldwide. WHO estimates that almost half a million women die of TB each year. In addition, evidence suggests that TB during pregnancy leads to complications for both mothers and infants. TB places a significant economic burden on families and households. Besides the immediate loss of income and productivity for the household member who is sick, other family members may be pulled temporarily out of work and school to provide care. In many places, families must pay for daily or weekly transport to a health facility even if TB diagnosis and treatment are available free of charge. At the national level, it is estimated that some countries lose from four to seven percent of their GDP because of TB.⁴

Today, most countries have aligned their national TB strategic plans with the internationally recommended WHO Stop TB Strategy (see textbox). Numerous NTPs are improving their diagnostic techniques, and are using fixed-dose combination drugs to treat TB, which reduces the number of pills taken and thereby improves the correct use of TB drugs. Additionally, a number of NTPs are tapping private sector providers and pharmacists to work with public TB services and are using community-based volunteers to find TB cases and monitor

² This is an estimate as it is difficult to diagnose TB disease in children, and data is limited.

³ WHO estimates that over 20% of the world’s TB cases are attributable to smoking.

⁴ TB Alliance, “Economic Impact of TB”; World Bank, “Economic Benefit of TB Control,” 2007.

THE STOP TB STRATEGY

1. Pursue high-quality DOTS expansion and enhancement
2. Address TB/HIV, MDR-TB, and the needs of poor and vulnerable populations
3. Contribute to health system strengthening based on primary health care
4. Engage all care providers
5. Empower people with TB and communities through partnerships
6. Enable and promote research



Health worker consulting a TB patient while providing DOT in an urban health facility in Afghanistan

Credit: Sayed Mirza Sayedi, TB CARE | Afghanistan, MSH

treatment, thus expanding access to diagnosis and treatment. Since 1995, these approaches have resulted in the successful treatment of 51 million people and have saved 20 million lives.

Despite these advances, challenges remain. There has been slow progress toward the development of new diagnostics, drugs, and a TB vaccine. Moreover, about a third of the estimated number of people with TB has not been able to access quality diagnosis and treatment services. At the regional level, most notably in Eastern Europe and Central Asia, drug resistance has grown steadily during the last decade. There are about 630,000 estimated cases of MDR-TB. The development of MDR-TB is exacerbated by clinical and programmatic mismanagement of TB. For example, providers may not prescribe the proper regimen, may use low-quality drugs, or patients do not receive adequate treatment

support. MDR-TB is much more difficult to diagnose and treat, requiring specialized laboratory expertise and infrastructure and an 18- to 24-month regimen of expensive drugs with potentially toxic effects.

The HIV epidemic continues to drive the spread of TB in countries where both diseases are highly prevalent. At least one-third of the 34 million PLHIV are infected with latent TB and almost 80 percent of these patients live in sub-Saharan Africa. PLHIV often have different symptoms than those with TB alone and are more difficult to diagnose with the standard tests used worldwide. When patients are diagnosed with both TB and HIV, they may have to visit more than one clinic to receive care for both illnesses. In 2011, only 48 percent of all HIV-positive TB patients were started on antiretroviral treatment (ART).

THE COORDINATED U.S. GOVERNMENT APPROACH TO TB PREVENTION, TREATMENT, AND CARE

As one of the largest contributors to TB programs, the USG utilizes a well-coordinated interagency model to promote efficiency and effectiveness. The USG also works in close collaboration with international partners and the Global Fund to ensure coordination, reduce duplication of effort, and ensure funds are used to support projects in line with globally-recommended models of care, and that are responsive to Ministry of Health strategies.

USG agencies working to address the global challenge of TB form the U.S. Federal TB Task Force, which is charged, in part, with assisting translation of biomedical research into programmatic strategies to support TB prevention, diagnosis, treatment, and care (Figure 1). Each agency brings specific technical expertise and country presence to the USG response to TB. Practically speaking, USG support for global TB efforts is coordinated through monthly conference calls of an International Working Group, which includes representatives from USAID, CDC, NIH, OGAC, and DoD. Collaboration and coordination among USAID, CDC, NIAID, and State/OGAC have contributed to support for NTPs and global TB partners through programmatic interventions and research relevant to TB programs, with each agency bringing comparative expertise to address the many challenges of TB.

USAID is the USG lead agency supporting international TB care and treatment efforts. During the reporting period, USAID supported a comprehensive response to TB, MDR-TB, and TB/HIV by strengthening NTPs and health systems in 40 countries. In addition, USAID is one of the major implementers of PEPFAR-funded TB/HIV programs, along with CDC. USAID also supports international normative and policy development for TB programs in endemic countries; capacity building for TB program implementation; operational research to improve the effectiveness and efficiency of TB diagnosis and treatment services; accelerated implementation of new diagnostic and treatment technologies and implementation methodologies; and improved prevention and care in developing countries.

OGAC coordinates the USG response to HIV/AIDS across federal agencies, and **leads the USG's international response to TB/HIV co-infection as part of PEPFAR.** Efforts to address TB/HIV co-infection are prioritized within HIV prevention, care, and treatment programs. These smart investments are based on science that will save lives and target populations where HIV is found. Ending HIV-associated TB among PLHIV is possible through a combination of widespread ART coverage, early identification and treatment of TB, isoniazid preventive therapy (IPT), and infection control activities. These high-impact interventions will be critical to achieving an AIDS-free generation and are integral to PEPFAR planning and program implementation, as articulated in the PEPFAR Blueprint released in December 2012.

NIH leads USG efforts in TB biomedical and translational research by conducting research and supporting scientists and product developers domestically and internationally. NIH-supported science is focused on improving the fundamental understanding of TB and TB/HIV by supporting basic, applied, and clinical biomedical research for drug-sensitive and drug-resistant TB, as well as investing in the discovery and development of new drugs, vaccines and diagnostics. **Within NIH, NIAID is the lead institute for TB research.**

CDC leads domestic TB prevention and care efforts and leverages this expertise to provide critical technical support to Ministries of Health in 41 countries on development of TB control policies and guidelines, surveillance and epidemiology, laboratory strengthening, and building in-country technical capacity. CDC is

a major implementer (with USAID) of PEPFAR’s TB/HIV programs. CDC conducts clinical and operational research to evaluate promising diagnostic and treatment strategies and inform the efficient use of traditional and novel approaches to the management of TB, TB/HIV and MDR-TB. CDC funds the TB Epidemiologic Studies Consortium to fill knowledge gaps in approaches to TB control, and the TB Clinical Trials Consortium to identify shorter, safer, more effective treatments for TB.

DoD’s laboratories in numerous priority countries **monitor the quality of TB diagnostic services and conduct operational research.** In addition, mobile care units deployed in crisis and conflict settings are used in support of efforts to ensure adequate TB services in those challenging circumstances.

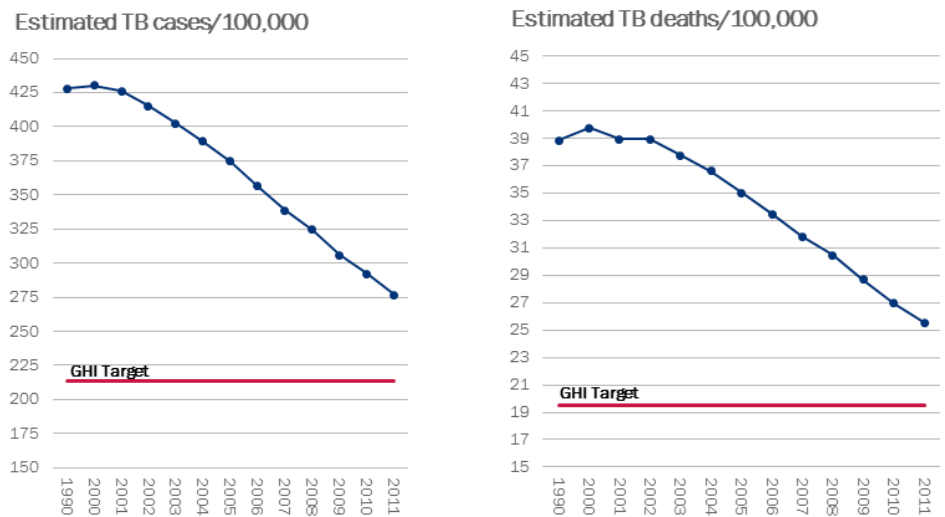
Figure 1. International Working Group of the Federal TB Task Force: USG Agencies Involved in TB Programs

Agency	Leadership Role/Comparative Strengths	Key Achievements in 2011-2012
U.S. Agency for International Development	Lead for international TB efforts covering 40 countries with technical assistance in universal access, MDR-TB, and laboratory strengthening; implementer for OGAC-funded TB/HIV programs	Over 1.5 million smear-positive TB patients successfully treated in 2011 in USAID’s priority countries. Over 44,000 people with MDR-TB were enrolled in treatment through USG-supported programs.
Department of State/Office of the U.S. Global AIDS Coordinator (OGAC)/PEPFAR	Lead for activities to address TB/HIV co-infection	High rates of HIV testing among TB patients in many of the countries where PEPFAR works. In 2011, 69 percent of reported TB patients in the African region had a reported HIV test. Contributed to an estimated 1.3 million lives saved from 2005-2011 through collaborative TB/HIV interventions.
U.S. Centers for Disease Control and Prevention	Lead for domestic TB program and international lab support; conducts operational research and provides technical support to 41 countries; implementer for OGAC-funded TB/HIV programs	Assisted national TB programs in 11 countries to develop laboratory strategic plans and trained laboratory staff from 14 countries on existing and new diagnostics. Provided evidence leading to new international guidelines for diagnosing TB among PLHIV, managing MDR-TB, and scaling-up new diagnostics.
National Institute of Allergy and Infectious Diseases, National Institutes of Health	Lead for biomedical and translational research and training in research	Critical contributor to the development of Cepheid Xpert MTB/RIF assay. NIAID’s investments in biomedical and translational research have contributed to 6 diagnostics, 7 drug and 7 vaccine candidates that are, as part of the current global product pipeline, in clinical development.

USAID'S WORK IN SCALING-UP TB PREVENTION, TREATMENT, AND CARE

The USG TB Strategy provides the framework for the program's goals and objectives. The USG has committed to contributing to global TB goals of reducing prevalence and mortality by 50 percent by 2015 by successfully treating at least 2.6 million new sputum smear-positive TB patients, and supporting the diagnosis and treatment of at least 57,200 MDR-TB patients. In cooperation with partners at global, regional, national, and local levels, USAID worked in 40 countries during the FY 2011-2012 reporting period. This section specifically highlights activities supported by TB funds appropriated to USAID. In the 40 countries supported by USAID, TB mortality and prevalence have decreased by 35 percent and 37 percent, respectively, since 1990 (Figure 2). Over 1.5 million sputum smear-positive TB patients were successfully treated in 2011, and over 44,000 people with MDR-TB were enrolled on treatment through USAID-supported programs.

Figure 2. Trends in TB Prevalence^a and Mortality in USAID-Supported Countries



^a =TB prevalence is defined as the number of existing cases per 100,000 population as of July 1 for each year (the mid-year point in time). TB mortality is defined as the number of TB deaths per 100,000 population as of July 1 for each year (the mid-year point in time). Prevalence and mortality estimates are taken from the WHO Global TB Database and weight-averaged across the 40 priority countries to produce the trend in decline since 1990.

STRATEGICALLY INVESTING TO ACHIEVE SUCCESS

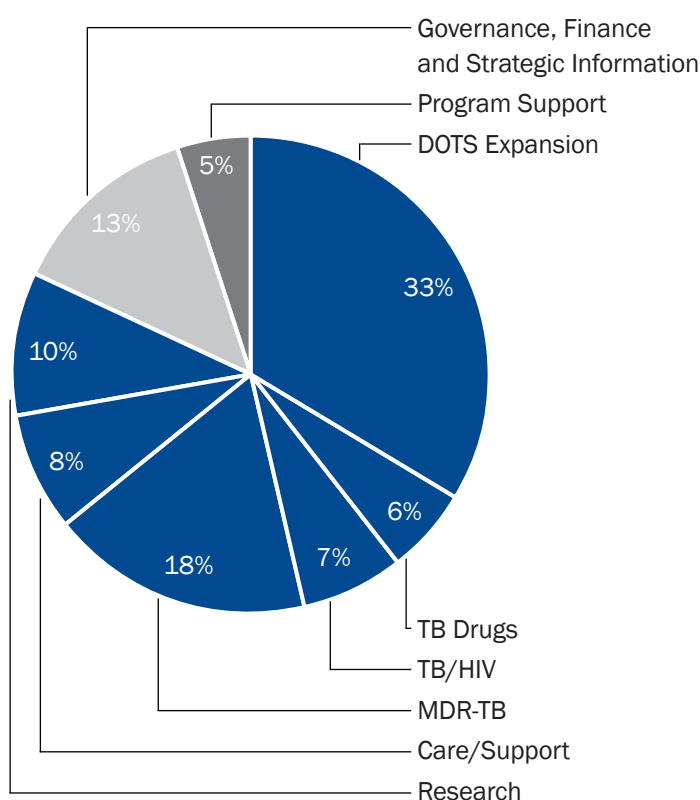
USAID focuses its investments on technical areas and interventions that will have the greatest impact on improving TB prevention, diagnosis, and treatment services. In FY 2011 and FY 2012, \$238 million and \$256 million, respectively, were appropriated to USAID to support TB programs worldwide. As is shown in Figure 3, 82 percent of USAID's TB resources were programmed to directly support

patient services for DOTS expansion, MDR-TB, TB/HIV, TB drugs, and for care and social support for TB patients. Ten percent of the budget was invested in late-stage operational and implementation research.

STRENGTHENING COUNTRY OWNERSHIP

One of the core principles of USAID’s TB program is to work closely with Ministries of Health and NTPs, providing technical support that directly responds to their national TB strategies. As the largest single funder of the Global Fund, the USG supports the implementation of Global Fund grants. Robust national strategic plans are

Figure 3. USAID TB Expenditures in FY 2011-2012



at the center of the Global Fund’s new funding model. USAID supported the development of these strategic plans in 13 countries in FY 2011 and FY 2012.

USAID has developed a technical assistance model to improve support for the implementation of national strategic plans, which will lead to better performing programs and allow for more strategic investments by the government and donors. USAID works closely with NTPs to ensure that technical assistance is aligned with their national plans and convenes all partners who are providing assistance in a collaborative way. During the reporting period, USAID provided technical assistance support for Global Fund grant implementation in 22 countries.

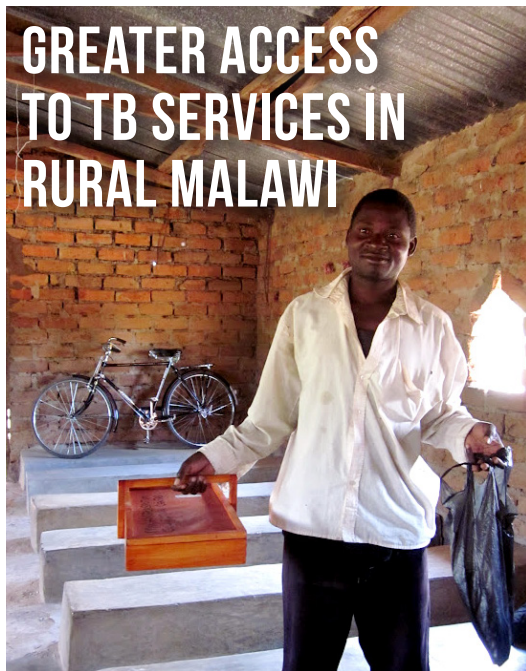
USAID supports NTPs to advocate within their own governments for increased investments in TB programs that could lead to greater program sustainability. For example, the Government of India, one of the highest burden countries, has quadrupled its investment in TB prevention, diagnosis, and treatment services over the past year, stepping up to meet the challenges. However, the country still has not scaled-up MDR-TB diagnosis and treatment with only one in ten of their estimated MDR-TB cases diagnosed. In Indonesia, USAID supported the NTP to develop and publish a donor exit strategy so the NTP could own the process going forward. Brazil has exemplified strong country ownership of its TB program after ten years of partnership with USAID.

BUILDING HUMAN RESOURCE CAPACITY

A strong work force is essential for a well-functioning health system, and USAID works with NTPs and other key partners to increase the expertise of healthcare workers through training, supervision, and mentorship activities. During the reporting period, USAID funds supported national-level training for all components of the Stop TB Strategy. For example, USAID has developed a mentorship program to build the capacity

WITH USG SUPPORT IN FY11 AND FY12

- 13 countries had in-depth reviews of their national TB programs
- 13 countries finalized their national strategic plans
- 10 countries completed field work for a drug resistance survey
- 22 countries received technical support for the implementation of their Global Fund grants
- 30 countries received technical assistance to strengthen their lab network
- 29 countries were supported in scaling-up the programmatic management of MDR-TB
- 13 countries developed national TB infection control guidelines
- 13 countries received training for health care providers on pediatric TB



Community volunteer visiting rural areas by bicycle

In some parts of rural Malawi, it is common for people to travel over 50 kilometers to access health centers where they can receive TB treatment. In 2010, a woman was diagnosed with TB at a health center 3 kilometers from her village, but she had to travel 56 kilometers to the district hospital to start treatment since her local health center did not provide this service. Two years later, she had a relapse of TB and dreaded the thought of making the long journey back to the hospital.

Understanding the need to address this challenge, USAID supported a treatment initiation center and a community volunteer program at this TB patient's local health center. The woman received a visit from a community volunteer who brought her to the health center on a bicycle and supported her throughout her treatment, even bringing her sputum samples to the health center for follow-up testing. She was cured six months later. USAID supports community volunteers with bicycles, training in community-based TB services, sputum transportation boxes and other resources to help them help community members like this woman. She is one of many people in rural Malawi who has faced challenges like this one.

of national and international TB consultants on infection control. Eighteen international consultants have been trained through this new program, including architects, biosafety experts, and public health practitioners. These consultants now have the capacity to provide technical support to countries in their regions and globally. USAID also supports a fellowship program in the Latin America and Caribbean Region through the Pan American Health Organization, whereby consultants are trained to provide TB technical assistance within the region to further expand South-to-South collaboration.

COLLABORATING TO ADDRESS TB/HIV

TB is a major cause of death for people living with HIV, especially in sub-Saharan Africa. Thirteen percent of people with TB also have HIV. USG agencies coordinate closely to accelerate access to TB/HIV activities, including expanding access to diagnosis and treatment services for PLHIV who develop TB. These efforts are led by OGAC/PEPFAR. USAID TB funds leverage these resources to ensure maximum outcomes.

TACKLING THE GROWING MDR-TB EPIDEMIC

USAID's investment in MDR-TB aims to improve the prevention, detection, and treatment of MDR-TB through support provided globally and at the country level to develop and implement policies, guidelines, scale-up plans, and treatment support. The consequences of a poorly performing MDR-TB program could be

devastating for a country. Before USAID began its support for MDR-TB, most countries did not have MDR-TB programs, lacked the personnel with expertise in this area, and did not have the capacity to manage the side effects of treatment. USAID builds the capacity of these workers through training and mentoring. These efforts have shown tremendous progress in recent years. In 2011, over 44,000 people with MDR-TB were enrolled on treatment through USG-supported programs, a significant increase from 2010 when over 19,000 people with MDR-TB were enrolled. Since the implementation of a successful MDR-TB program is complex and labor intensive, countries must develop a plan for introducing and expanding their program to manage MDR-TB. These plans include strategies for increasing the detection and treatment of individuals, a budget associated with implementation, and a plan to get the needed finances. By the end of FY 2012, USAID had provided support to 29 countries in scaling-up program management of MDR-TB, including the development of new plans, transition plans to move from pilot projects to large-scale implementation, and trainings on implementation under the stewardship of national TB programs. The improvement of infection control practices in facilities is a critical component of USAID's support, particularly the implementation of the WHO's TB Infection Control Policy.⁵ Strengthening

5 WHO's Infection Control Policy can be found online at: http://whqlibdoc.who.int/publications/2009/9789241598323_eng.pdf.

TEN YEARS IN BRAZIL: ACHIEVING SUCCESS AND SUPPORTING COUNTRY OWNERSHIP

FY 2012 marked the final year of USAID's ten-year TB program in Brazil. Since 2002, USAID has partnered with the Government of Brazil to achieve success through the adoption and expansion of DOTS. This support, in collaboration with assistance from the Global Fund and other donors, has contributed to a 15.9 percent decrease in the TB incidence rate and a 22.5 percent decrease in mortality rates over the same period. Brazil is on track to meet the Millennium Development Goals to reduce TB prevalence and deaths by 50 percent by 2015.

In some USAID-supported municipalities, DOTS coverage increased from less than 10 percent to the current estimate of 90 percent. USAID helped build a cadre of health care workers who have been functioning as DOTS trainers for new health care workers who will also become trainers and so on, using a cascade method. Working with USAID to ensure WHO pre-qualification, Brazilian manufacturers will begin producing fixed-dose combination drugs in the next couple of years. USAID support helped the Prof. Hélio Fraga National Reference Laboratory to receive certification for TB and other lung diseases.

MDR-TB treatment centers expanded from 63 in 2004 to nearly 200 in 2012. These centers offer high quality care, a reliable supply of quality assured second-line drugs, and improved access to diagnosis and treatment services for patients. Between 2004 and 2010, the MDR-TB cure rate increased from 40 percent to 62 percent, and mortality and treatment failure rates decreased by 50 percent with the support of these interventions. USAID also contributed to a significant improvement in the diagnosis of MDR-TB, as the number of MDR-TB case notifications more than doubled between 2004 and 2012.



Dots Observers Meeting

Credit: B Nyathi, TB CARE | Zimbabwe, The Union

and expanding the capacity of laboratories to test for resistance to first-line drugs is an important first step toward identifying MDR-TB. This is highlighted in the centerfold of this report.

Treating MDR-TB is very complex as it requires taking drugs for up to two years. The second-line drugs (SLDs) used to treat MDR-TB have serious side effects such as profound hearing loss and persistent nausea, making it very difficult for people to work and care for their families (see textbox). In FY 2012, USAID helped finance social support programs for MDR-TB patients in nine countries, thus increasing the chances that they will

complete the long, difficult treatment regimen. This support includes food, funds for hospitalization fees, biochemical tests to monitor treatment side effects, and funds for transportation fees to health facilities. In addition, USAID supported the implementation of vocational training for MDR-TB patients and training of community-based treatment supporters.

Another challenge for MDR-TB is the high cost of treatment and ensuring that quality drugs are available. While the cost of drugs to treat drug-sensitive TB is around the equivalent of \$22, treating MDR-TB with the currently recommended regimen can cost between

USAID'S FIVE-PRONGED APPROACH

Involvement of private sector providers who operate outside of the NTP or public sector system is critical for achieving global TB goals. Many people with TB first seek care at a local pharmacist, traditional healer, or hospital that is not linked with the NTP. These providers may not diagnose and treat TB according to the international standards of care and they may not refer symptomatic individuals to the public sector DOTS program. This practice can lead to poor outcomes and the potential development of MDR-TB. USAID supported the first work in public-private mix (PPM) and works closely with countries on the development of PPM strategies.

- In Bangladesh, USAID supported initiatives to expand PPM by linking with 3,416 private practitioners to increase referrals of people with TB symptoms to public health facilities. In FY 2012, these private practitioners referred over 43,000 people to public health facilities.
- Involving private facilities and doctors is particularly important in Nigeria, where about 60 percent of all health care services are provided in the private sector. In 2011, Nigeria reported that 25 percent of all TB cases were reported to the NTP by facilities operating outside the public sector. This finding represents great progress from previous years, when the NTP received reports primarily from public sector health facilities.

PRIVATE SECTOR INVOLVEMENT

USAID is leading the way in supporting countries to identify the best approaches to active case finding that will yield high returns in terms of additional cases diagnosed and started on treatment. USAID has supported WHO to develop guidelines on contact investigation in developing countries to promote screening of household and community members of individuals who have been diagnosed with infectious TB. Effective contact investigations often result in the detection of a significant number of TB cases, especially among children, who are likely to develop active disease after being exposed to an adult with TB. USAID supported the development of guidelines to report TB among health care workers and encourages NTPs to implement surveillance of active TB among health care providers.

- With support from USAID and WHO, the National Department of Health in South Africa updated its guidelines for the Practical Approach to Lung Health (PAL). PAL is an approach to managing patients who visit primary health care centers with respiratory symptoms and leads to improvements in the quality of respiratory case management. This is a comprehensive health systems approach to improving the respiratory health of adults, while also ensuring people are not misdiagnosed with acute respiratory infection when they may actually have TB.
- In Mexico, where an estimated 25 percent of all TB patients are diabetic, the NTP is piloting a cross-referral strategy between TB and diabetes clinics with USAID support. This activity focuses on strengthening TB screening among diabetics and diabetes screening among TB patients and ensuring referrals and follow-up care where patients with both conditions are identified.

ACTIVE CASE FINDING

EXPANDED ACCESS TO SERVICES

TO EXPANDING ACCESS TO SERVICES



The overarching goal of USG laboratory strengthening activities is to ensure access to and availability of high quality, reliable laboratory support for the detection, treatment, and monitoring of TB patients. At the global level, USAID supports the Global Laboratory Initiative (GLI) of the Stop TB Partnership. At the country level, USAID partners support NTPs and national TB reference laboratories by developing or updating National TB Laboratory Strategic Plans, improving sputum transport networks, building technical and managerial capacity of laboratory staff, and improving diagnostic infrastructure. The USG provided significant support to the roll-out and scale-up of Xpert in countries through a coordinated technical approach (see details in the section on Xpert).

- With USAID support, the NTP in Zimbabwe has partnered with an international non-profit organization called Riders for Health on specimen transportation. This NGO supports the program by transporting specimens from peripheral areas to the nearest laboratory. TB patients are now diagnosed more quickly, and specimen turnaround time dropped from 11 to 3 days in 2012, meaning that patients are initiating treatment earlier.
- The Uganda National TB Reference Laboratory received the 2012 award for the African Society for Laboratory Medicine's Best Practice in Laboratory Medicine. CDC, with USAID funding, has provided a significant amount of technical assistance for improving this laboratory.



Community-based DOTS (CB-DOTS) is increasingly promoted as a key intervention to improve TB case detection and treatment adherence, especially in settings where there are many barriers to care. USAID's efforts in this area include the following activities:

- In Zimbabwe, 1,036 community volunteers were mobilized in ten districts to support TB patients and to ensure that they completed treatment. The lessons learned from this program will inform the development of a standard national community TB treatment support program and subsequent expansion.
- In Mozambique, USAID is supporting local NGOs to improve case detection and treatment outcomes. Over 500 volunteers have been trained in CB-DOTS to provide education and screening for TB and malaria throughout their communities. From January through November 2012, approximately one quarter of all new sputum smear-positive TB patients reported in the 11 districts were identified through these activities.



Prisoners are at a high risk for becoming infected with TB and/or developing TB disease due to poor ventilation of prison buildings, overcrowding, and poor nutrition. These conditions can set the stage for significant outbreaks of TB. According to WHO, the prevalence of TB in prisoners is up to 100 times higher than in the civilian population. Poorly managed TB in prison settings can affect the surrounding community as well, since prison staff and visitors are at risk of exposure to TB and then possible transmission of active TB to their families and communities. USAID is working in several countries to address the issue of TB in prisons.

- In Kyrgyzstan, USAID-supported programs have established critical referral and linkage services for prisoners who are discharged from correctional facilities with active TB and in need of treatment continuation.
- In Indonesia, 30,941 prisoners were screened for TB in FY 2012 with USAID support.

\$4,000 and \$8,000 for the drugs alone. This high cost is driven by the limited market for high-quality SLDs. Because of the limited capacity to diagnose and treat MDR-TB in many countries, the quantity of SLDs is very small for each country and does not provide sufficient incentive to manufacturers of active pharmaceutical ingredients and finished pharmaceutical products. To improve the availability of and access to high quality SLDs and influence market forces, USAID is working with the Global Drug Facility (GDF) and other partners through a financing initiative to encourage manufacturers to produce the four most expensive MDR-TB drugs. It has also supported manufacturers' capacity and access to the WHO prequalification system. In

A DOCTOR'S STRUGGLE

Dr. Dalene von Delft was working in a large state hospital in South Africa, where she believes she contracted TB. An X-ray revealed a three-centimeter hole in her lung and further testing showed that she had MDR-TB, with resistance to four drugs. Dalene knows of 15 colleagues who have contracted TB, although she is the first in her circle of friends to contract MDR-TB.

Dalene's doctor put her on a six-drug treatment, with injections of amikacin, known to cause hearing loss which could have ended her career as a pediatrician. Although Dalene started feeling better after two and a half months, her hearing began to deteriorate. Fortunately, in 2011, she became a candidate for special compassionate use of a new drug called bedaquiline, which was approved by the U.S. Food and Drug Administration in late 2012. Dalene's only alternatives had been permanent deafness, prematurely ending her career, or possibly even death. She completed her treatment and is now alive and well, joining the minority of South Africans cured of MDR-TB. She has become an activist clinician and widely shares her ideas on TB prevention and treatment. Dalene's story exemplifies the hardships that MDR-TB patients have to endure.

Dalene's story is taken with permission from Chris Bateman's contribution to the South African Medical Journal.

addition, it facilitates purchase by country governments through the Global Drug Facility's pooled procurement mechanism, which was established in 2001 to expand access to, and availability of, high-quality TB drugs.

RESEARCH

Despite advances in prevention and treatment, MDR-TB, extensively drug-resistant TB (XDR-TB),⁶ and the global HIV epidemic threaten to undermine recent progress in preventing, diagnosing, and successfully treating TB. Moreover, the success of TB programs is hampered by a number of factors: (1) a limited number of tools that can accelerate the detection of TB; (2) the lack of more effective drugs that can shorten treatment, improve outcomes, and prevent the development of drug resistance; and (3) the lack of a vaccine to prevent new cases.

The USG's global leadership in all aspects of research through the missions of USAID, CDC, and NIAID/NIH involves continued investment in biomedical, operational, and implementation research that contributes to the development of new drugs, vaccines, and diagnostics and assures that new interventions are appropriately integrated into global TB treatment and care programs. In 2012, USAID continued to support a study to determine the requirements for successful utilization of the line probe assay, a molecular-based diagnostic tool used to detect MDR-TB. If successfully implemented, this tool can substantially reduce the time to diagnosis of MDR-TB, leading to faster initiation of appropriate SLDs regimens and reduction in transmission.

Another facet of this strategic approach is the support of clinical studies contributing to the development of shorter TB drug regimens that are effective against all forms of TB, can be used with ART, and are suitable for children. In FY 2011 and FY 2012, USAID continued to support the STREAM study, which aims to evaluate the efficacy and safety of a standardized short-course regimen for the treatment of MDR-TB. If successful, the results of this study could have a major effect on expanding MDR-TB programs, improving treatment outcomes, and catalyzing the development of new MDR-TB drugs. Additionally, another USAID-supported study that aims to reduce the length of treatment for drug-susceptible TB patients by two months has completed patient enrollment and is now in the follow-up phase. USAID is also supporting a number of research studies to evaluate the efficacy and safety of TB drug regimens that include novel TB drugs and can reduce the duration of treatment of drug-susceptible and drug-resistant TB to four to six months.

6 XDR-TB is defined by WHO as resistant to at least four of the core TB drugs.

AFGHANISTAN: USING COMMUNITY BASED (CB) APPROACHES TO EXPAND ACCESS TO TB SERVICES



Afghanistan is one of the 22 WHO-designated high burden countries for TB and has some of the lowest health indicators worldwide. TB prevalence is extremely high at 351 per 100,000 population and unlike most other countries where TB is more prevalent among men, TB affects a larger proportion of women in Afghanistan. Because of the challenging security situation, access to health care services and adherence to TB treatment are difficult for people with TB. Despite these challenges, the CB-DOTS program has expanded throughout the country, greatly increasing access to TB diagnosis and treatment. In FY 2012, 1,181 smear-positive TB cases were identified by community health workers at USAID-supported sites, a significant increase from the baseline of 359 in 2009. In addition, the number of TB patients receiving treatment support from community health workers increased dramatically from 853 in 2010 to 2,209 in 2012. Treatment success rates have been consistently higher than the national average in all USAID-supported provinces.

In densely populated Kabul, USAID adapted the community-based model to the urban setting where quality TB services are limited because of poor health infrastructure and overcrowding. The number of urban DOTS centers has increased to 68, focusing on more referrals of people with TB symptoms and improving treatment adherence. As a result, referrals have increased from only 1,200 in 2009 to over 13,000 in 2012.

USAID also built the capacity of NTP staff in 18 provinces to provide quality TB diagnosis and treatment services. USAID supported the implementation of the country's first ever electronic reporting system which now receives TB reports from 90 percent of the provinces. Health care workers from poorly performing facilities travel to model DOTS facilities for on-the-job training. In FY12, 156 female staff members from the five most insecure provinces in the country were trained on standard operating procedures for case detection, treatment, infection control, and management of pediatric TB so they can provide services for other women who often face barriers in accessing health care services.



CAMBODIA: A DOTS SUCCESS STORY

Children at a TB clinic in Cambodia

Credit: TB CARE | Cambodia

Cambodia has made impressive progress in providing TB prevention, diagnosis, and treatment services. It serves as a strong example of what can be achieved in a low-income country with a high burden of TB through the expansion of quality DOTS programs and implementation of the Stop TB Strategy. Since 2002, TB prevalence has decreased 45 percent and Cambodia is on track to meet the MDG target of halving TB deaths by 2015, relative to the 1990 baseline. The country has been at the forefront in terms of piloting new approaches to case detection and treatment support and scaling up successful models.

Strong country ownership and the government's commitment to addressing the TB burden have been central to Cambodia's success. Cambodia has had a dedicated NTP manager since 2001 who knows the intricate details of the program, has strong technical skills, and is well-respected in the Ministry of Health and in the global TB community. Providing support to Cambodia's NTP (CENAT) starting in 2001, USAID has worked closely with the NTP manager in partnership

with international and local NGOs. The NTP manager often adopts successful initiatives by civil society and NGOs and scales them up through the NTP strategy.

COMMUNITY-BASED DOTS

CB-DOTS was introduced in Cambodia in 2002 in an effort to bring TB services closer to patients. Cambodia is divided into 24 provinces, which are further divided into 77 operational districts for the organization of public sector health care services. In 2003, USAID began its involvement in CB-DOTS through the implementation of a pilot activity in five operational districts. Since then, CB-DOTS has been scaled up and is now implemented in 68 high-burden districts, significantly increasing access to TB services.

USAID support has also helped increase community involvement in TB programs, especially by working with local organizations and encouraging country ownership and sustainability. Community volunteers, called "DOTS watchers," are trained to directly observe

treatment for TB patients in their communities, including monitoring for side effects and recording and reporting dosages. Additionally, volunteers play an important role in increasing awareness about TB and promoting earlier case detection by identifying and referring TB suspects to health centers.

PUBLIC/PRIVATE MIX

As in other Asian countries, private sector providers are an important part of Cambodia's health system as many people with TB symptoms first seek care at a pharmacy or private medical office. With USAID support, CENAT has been working with pharmacists since 2005 to integrate them with the DOTS program through a referral network for TB diagnosis and treatment services. This has included developing a PPM strategy, providing technical assistance to pilot and scale-up a referral network between private pharmacists and public sector DOTS centers in selected provinces, and supporting scale-up at national level and sustainability planning. USAID has also supported training pharmacists on how to guide people to TB diagnosis and treatment. These PPM interventions have resulted in increased referral rates, case notifications, and access to treatment. CENAT has led the process, working closely with USAID to identify the approach to expand PPM efforts. USAID is supporting PPM implementation in 26 operational districts in seven provinces by engaging over 1,200 private providers.



Child receiving a Tuberculin Skin Test (TST), Cambodia

Credit: TB CARE | Cambodia



Patient Centered Approach Focus Group Discussion, Cambodia

Credit: Pichenda Koeut, CENAT

DRUG MANAGEMENT

The presence of counterfeit and poor-quality TB drugs in any country with a high TB burden is a major reason for treatment failure and the increasing emergence of MDR-TB. Since 2003, USAID has been working with Cambodia to strengthen its capacity on sustaining quality assurance and quality control for TB drugs. This has included building the capacity of the Department of Drugs and Food (DDF) to conduct quality monitoring on drugs across the country and providing robust data to support enforcement actions. Additional USAID efforts include strengthening the National Health Product Quality Control Laboratory's capacity to comply with international standards; training department inspectors; and raising the awareness of health workers and the general public about the potential dangers of using substandard and counterfeit drugs. Sentinel sites for basic testing of the quality of drugs were established in 2009 and 2010.

As a result of these joint activities, the percentage of poor quality drugs, including TB drugs, has declined from 24.8 percent in 2003 to 2.3 percent in 2011. The DDF has shut down illegal health services and pharmacy outlets in the country. In November 2009, there were 1,081 illegal drug outlets in the country, and by December 2011, there were none. USAID and WHO have been instrumental in assisting the DDF with a ban on the importation and sale of TB drugs, thus ensuring that only internationally quality-assured drugs are used in the treatment of MDR-TB patients.

COUNTRY HIGHLIGHTS

Afghanistan

CDR^a: 46% | TSR^b: 90%

While the country is successfully treating 90 percent of its TB cases, the case detection rate remains low at 46%. USAID is working to strengthen community-based TB activities.

Bangladesh

CDR: 44% | TSR: 92%

One of USAID's main activities in Bangladesh is increasing access to TB services, which aims to improve the case detection rate, currently low at 44%. The number of people diagnosed and started on treatment for MDR-TB increased from 98 in 2008 to 390 in 2011.

Cambodia

CDR: 63% | TSR: 94%

USAID has prioritized supporting the NTP to increase case detection. Referrals of people with TB symptoms by community volunteers and private providers increased from 52% to 82% in less than a year at USAID-supported sites.

Democratic Republic of The Congo

CDR: 50% | TSR: 90%

USAID is working to improve the low case detection rate of 50% through active engagement with community volunteers, including former TB patients, who are trained to identify people with TB symptoms and refer them to health facilities for testing.

Ethiopia

CDR: 71% | TSR: 83%

The case detection rate increased from 61% to 71% between 2008 and 2011. USAID-supported private providers are contributing to TB case detection, and in 2011, private health facilities detected 18,061 TB cases. To improve the treatment success rate, the USG is supporting community-based TB activities to ensure that people with TB have additional support.

Georgia

CDR: 84% | TSR: 76%

Between 2008 and 2011, the TB case detection rate increased from 72% to 84%. USAID is supporting implementation of quality MDR-TB diagnosis and treatment and improved management of anti-TB drugs, the cause of the low treatment success rate.

Ghana

CDR: 77% | TSR: 86%

The case detection rate increased from 62% to 77% between 2008 and 2011. A prevalence survey is underway to determine the true burden of TB.

India

CDR: 60% | TSR: 88%

USAID prioritized engagement with private providers to increase case detection, expansion of MDR-TB diagnosis and treatment, and increased political commitment. As a result, the government has quadrupled its investment in TB prevention, diagnosis, and treatment over the past year.

Indonesia

CDR: 71% | TSR: 90%

To improve access to diagnosis and treatment for MDR-TB, USAID is supporting the development of model MDR-TB sites and plans to scale up the model sites in five provinces.

Kazakhstan

CDR: 87% | TSR: 61%

USAID is collaborating with partners, including the Global Fund, to improve the treatment success rate and address the related widespread MDR-TB issue.

Kenya

CDR: 81% | TSR: 87%

USAID is supporting the capacity building and increased commitment of the district level TB programs through training and supervision.

Kyrgyzstan

CDR: 80% | TSR: Data not available

USAID is focusing its support on improving the quality of MDR-TB services, including the implementation of the new Xpert technology.

Malawi

CDR: 67% | TSR: 87%

USAID has supported the development of community sputum collection points in remote areas nationally, enabling increased access to TB diagnosis.

Mozambique

CDR: 34% | TSR: 85%

To address the low case detection rate, USAID continues to support an innovative community-based program, focusing on finding more TB cases. USAID is supporting approaches to integrate laboratory systems and capacity building for TB and malaria.

Namibia

CDR: 64% | TSR: 85%

Significant progress has been made with increasing the case detection rate from 54% to 64% from 2008-2011. The country has made great efforts in sustainability and country ownership by scaling up successful donor-supported interventions.

Nigeria

CDR: 46% | TSR: 84%

Although the CDR is low at 46%, it has increased from 39% in 2008. It should continue to increase with the roll-out of Xpert in a number of states in Nigeria with USAID support.

Pakistan

CDR: 64% | TSR: 91%

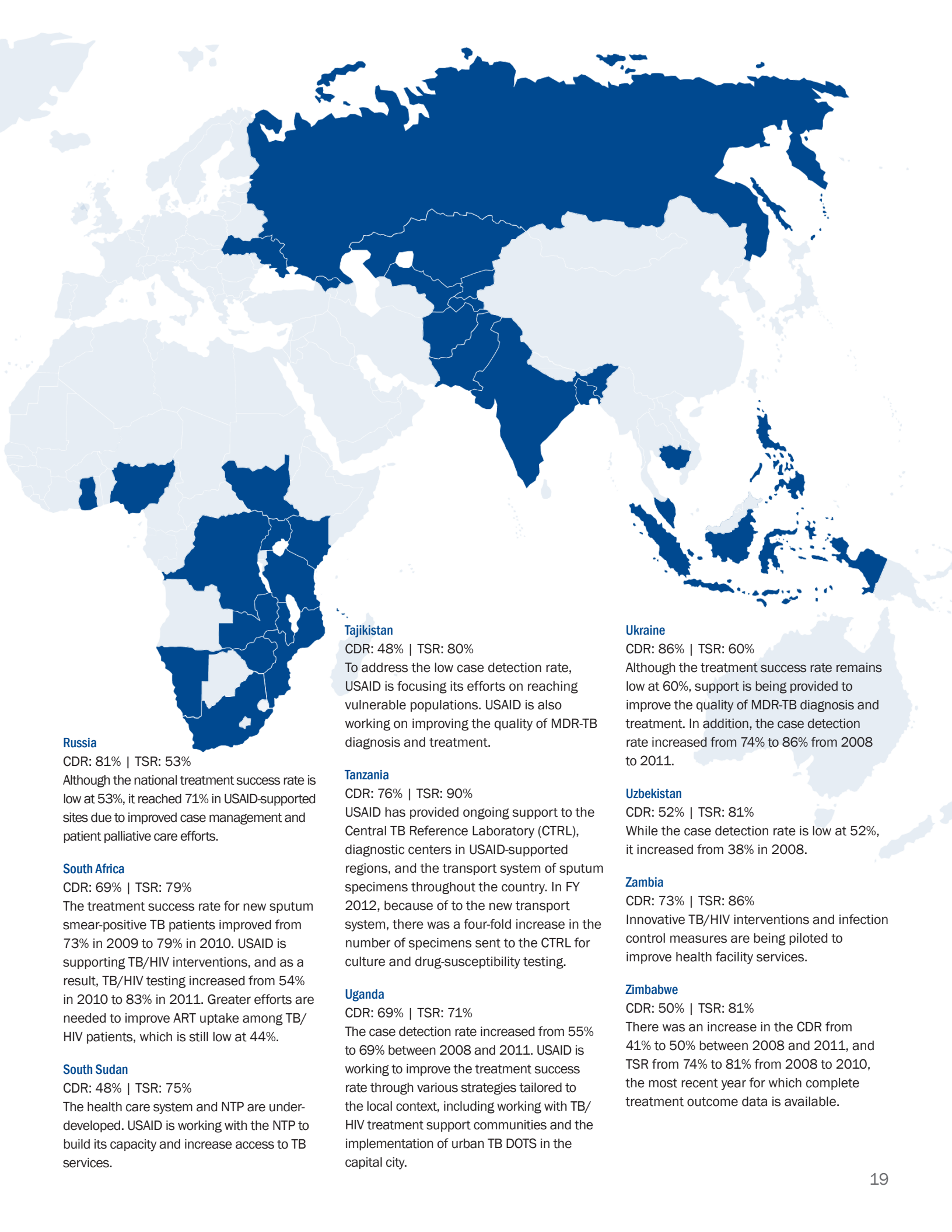
USAID supported the country's first national TB disease prevalence survey to estimate the burden of TB. The survey was completed in 2012.

Philippines

CDR: 75% | TSR: 91%

The case detection rate increased from 54% to 75% between 2008 and 2011. USAID is supporting improved case finding in geographically-isolated regions and other areas without access.

a = case detection rate; b = treatment success rate



Russia

CDR: 81% | TSR: 53%

Although the national treatment success rate is low at 53%, it reached 71% in USAID-supported sites due to improved case management and patient palliative care efforts.

South Africa

CDR: 69% | TSR: 79%

The treatment success rate for new sputum smear-positive TB patients improved from 73% in 2009 to 79% in 2010. USAID is supporting TB/HIV interventions, and as a result, TB/HIV testing increased from 54% in 2010 to 83% in 2011. Greater efforts are needed to improve ART uptake among TB/HIV patients, which is still low at 44%.

South Sudan

CDR: 48% | TSR: 75%

The health care system and NTP are underdeveloped. USAID is working with the NTP to build its capacity and increase access to TB services.

Tajikistan

CDR: 48% | TSR: 80%

To address the low case detection rate, USAID is focusing its efforts on reaching vulnerable populations. USAID is also working on improving the quality of MDR-TB diagnosis and treatment.

Tanzania

CDR: 76% | TSR: 90%

USAID has provided ongoing support to the Central TB Reference Laboratory (CTRL), diagnostic centers in USAID-supported regions, and the transport system of sputum specimens throughout the country. In FY 2012, because of the new transport system, there was a four-fold increase in the number of specimens sent to the CTRL for culture and drug-susceptibility testing.

Uganda

CDR: 69% | TSR: 71%

The case detection rate increased from 55% to 69% between 2008 and 2011. USAID is working to improve the treatment success rate through various strategies tailored to the local context, including working with TB/HIV treatment support communities and the implementation of urban TB DOTS in the capital city.

Ukraine

CDR: 86% | TSR: 60%

Although the treatment success rate remains low at 60%, support is being provided to improve the quality of MDR-TB diagnosis and treatment. In addition, the case detection rate increased from 74% to 86% from 2008 to 2011.

Uzbekistan

CDR: 52% | TSR: 81%

While the case detection rate is low at 52%, it increased from 38% in 2008.

Zambia

CDR: 73% | TSR: 86%

Innovative TB/HIV interventions and infection control measures are being piloted to improve health facility services.

Zimbabwe

CDR: 50% | TSR: 81%

There was an increase in the CDR from 41% to 50% between 2008 and 2011, and TSR from 74% to 81% from 2008 to 2010, the most recent year for which complete treatment outcome data is available.

ACCELERATING GAINS IN GLOBAL TB: HIGHLIGHTS OF U.S. GOVERNMENT INTERAGENCY ACTIVITIES

XPERT MTB/RIF— JOINT CONTRIBUTIONS OF THE USG TO THE DEVELOPMENT AND IMPLEMENTATION OF A RAPID TB DIAGNOSTIC TEST

The USG has been a leader in supporting both the development of the Xpert assay and implementation of projects to introduce and scale-up the assay in countries. Xpert is a molecular diagnostic test with tremendous potential to greatly improve detection and diagnosis of TB and MDR-TB. In less than two hours, it can detect *Mycobacterium tuberculosis* DNA and changes in the DNA that are associated with rifampicin resistance directly from sputum, while traditional culture techniques to confirm drug resistance take several weeks. The assay is more sensitive for detecting TB than the standard sputum-smear microscopy to. Additionally, it is much faster for detecting TB and MDR-TB than standard tests involving bacterial growth in laboratory cultures.

The ability of Xpert to detect TB rapidly in patients in whom bacteria cannot be seen with a microscope (as is common for persons co-infected with HIV) also provides a significant advantage over microscopy. Because the test is based on a fully automated system that requires minimal handling of infectious sputum, biosafety requirements are minimal; however, the need for a continuous power



Xpert training in Bangladesh

supply and cost of the machine and test kits are two significant barriers to widespread implementation. When used optimally, Xpert is expected to result in earlier diagnosis of TB (especially among those who are HIV infected) and MDR-TB, thereby allowing earlier initiation of appropriate treatment, which will reduce the amount of time patients are infectious and decrease transmission.

Basic research, discovery, and advanced product development: NIAID provided support for key steps in the development of the Xpert test, including funding for research to create the unique molecular beacon technology used in the assay, development of a process to disinfect the samples, and simplification of Cepheid's original Gene Xpert platform that allows for rapid, direct testing of sputum samples with minimal staff effort and biosafety risk. NIAID continues to support research to adapt this technology, for example, by sponsoring development of a second-generation test that can be used to detect XDR-TB and studies to determine whether Xpert can be used to detect other infectious diseases.

Global technical leadership: The USG supports the GLI to develop global policy guidance, norms, and standards for Xpert implementation. With USAID and PEPFAR funds, an intensified approach to Xpert introduction was developed and piloted in Nigeria, Vietnam, and Indonesia that addresses laboratory, clinical, and programmatic issues. This approach has been used in a number of other countries and is being developed into a global model for implementation. For example, CDC is utilizing a similar approach in collaboration with the Ministry of Health of Botswana to introduce the technology at 22 HIV care and treatment clinics. CDC, State/OGAC, and USAID jointly develop policy and technical approaches for USG country projects including operational research and impact measurement. Importantly, this interagency commitment has yielded standard tools and guidance across USG projects.

Country roll-out of Xpert: By the end of FY12, the USG purchased 156 Xpert machines in 25 countries, including 84 with USAID funds and 72 with PEPFAR funds. Procurement of additional instruments and cartridges with FY11 and FY12 PEPFAR funds is in process. In FY13, the USG will continue to provide financial resources and technical assistance to expand the use of Xpert, including an \$11 million PEPFAR project that will cover approximately 150 additional machines, cartridges, and technical assistance to 14



Laboratory supervisor preparing GeneXpert instrument for annual calibration, Nigeria

Credit: Manuela Rehr, TB CARE I, KNCV

countries focusing on the detection of HIV-associated TB. In an effort to maximize impact, these projects support not only machine and test kit procurement, but also support comprehensive technical assistance to Ministries of Health for operational and programmatic implementation and a monitoring and evaluation framework to measure the impact of Xpert roll-out. NIAID has also supported the use of Xpert machines to facilitate research studies in their AIDS clinical trials network sites.

Commodity market shaping: In August 2012, PEPFAR and USAID partnered with the Bill & Melinda Gates Foundation and UNITAID in an innovative public-private partnership to ensure a 10-year price reduction in the cost of Xpert test cartridges from \$16.86 to \$9.98 in 145 high-burden and developing countries. This joint action significantly accelerates access to this cutting-edge technology.

THE USG'S EFFORTS IN SOUTH AFRICA TO ADDRESS THE CARE OF MDR-TB PATIENTS

South Africa has the highest burden of TB and MDR-TB in sub-Saharan Africa, and one of the highest in the world. HIV/AIDS has further exacerbated the TB epidemic, and 65 percent of patients with TB also have HIV. Although the country has made progress in creating a unified public health system and improving access to both TB and HIV services, there is still room for improvement in both the quality and scope of services to ensure people with TB are effectively diagnosed, properly treated, and receive support to complete their treatment. South Africa's treatment success rate remains at 79 percent, lagging behind the USG and WHO goal of 85 percent. XDR-TB was first reported in South Africa in 2006 in an internationally publicized outbreak at a hospital in KwaZulu-Natal, and is an ongoing concern for the program.

Last year, the Government of South Africa announced its commitment to achieving zero new TB infections and preventable deaths in the next 20 years, a commitment demonstrated by robust, integrated TB/HIV services, aggressive improvements in diagnosis and treatment of drug resistance, and collaborative efforts to improve pediatric TB case-finding and treatment. USG support is aligned with the new National Strategic Plan and lays the foundation for a sustainable and country-owned response. The USG is supporting a number of activities to improve TB diagnosis and treatment services in South Africa, drawing on each agency's comparative advantage and in alignment with their unique mandates, drawing on long-standing relationships with local partners and their presence in South Africa.

MDR-TB Case Management: An Integrated USG Approach to Decentralization

Until recently, patients with MDR-TB completed a six-month intensive phase of treatment at national or regional TB referral hospitals in South Africa before being released to continue treatment at clinics closer to their home. With the growing number of MDR-TB patients and limited availability of hospitals to provide inpatient MDR-TB treatment, the National Department of Health (NDOH) and USG partners identified alternative approaches to case management. USAID, PEPFAR, NIAID, and CDC have been working collaboratively with the NDOH to develop and test models for decentralized MDR-TB care, identify ways to scale-up proven strategies, and strengthen program management.

Developing and Scaling-up a Model for Decentralization

NIAID has established a pilot research project in rural KwaZulu-Natal to evaluate the efficacy of an integrated home-based pilot treatment program for MDR-TB and HIV. Patients are administered oral TB and antiretroviral drugs at home and intensively monitored for side effects. Education on treatment and adherence support is an essential component of the research study. This mentored research project will follow a cohort of 100 patients enrolled in the project to examine the feasibility, efficacy, and safety of this approach to MDR-TB and HIV treatment. Specifically, the study will: assess the feasibility of the home-based model, including completion of home visits, injections, adverse event monitoring, and laboratory testing; compare mortality and treatment outcomes to patients treated in a traditional inpatient program; describe side effects and serious adverse events; and identify predictors of survival among the cohort. Early findings in this study have helped inform a national plan for decentralized MDR-TB treatment.

Capitalizing on its strength in implementation, USAID and its partners have been working in KwaZulu-Natal and seven other provinces to scale-up the community-based model for MDR-TB care. USAID is providing technical assistance and training to decentralized project sites in 16 districts. In addition, USAID has conducted workshops on planning and budgeting for comprehensive community-based MDR-TB programs at provincial, district, and sub-district levels. As a result, over 570 provincial, district, and sub-district managers have been trained. The model utilizes a holistic approach to patient care by providing a range of services to affected households. For example, staff provide at-home injections of TB drugs to patients during the intensive phase and treatment support during the continuation phase; screen household members for TB symptoms, referring them, when appropriate, for further evaluation; and educate patients on TB, MDR-TB, and treatment adherence.

THE FIVE "I'S" FOR TB/HIV PROGRAM

Intensified case management

Isoniazid Preventive Treatment (IPT)

Infection control

Integrated TB/HIV approach

Intensified treatment

To encourage completion of therapy, alleviate demand on hospitals, and address patients' calls for close-to-home options, South Africa has formally adopted a model of decentralized MDR-TB care, utilizing, in part, the model developed in partnership with the USG. This model represents a policy shift at the national level as well as within USG-supported programs paired with robust training programs.

Supporting the Decentralization Effort

In 2012, PEPFAR signed a five year South Africa–U.S. Partnership Framework fully supporting the National Strategic Plan (NSP) and transitioning PEPFAR engagement in South Africa from emergency response to a sustainable and country-owned approach. Over the next two years, PEPFAR will focus on aligning its activities with the NSP. A primary challenge confronting both TB and HIV service platforms is the emergence of drug-resistant TB.

PEPFAR implementing partners, particularly USAID and CDC, are helping the NDOH develop policies and implement programs across South Africa to prevent the development and spread of drug-resistant TB, including early diagnosis and treatment of susceptible and MDR-TB, scale-up of Gene-Xpert MTB/RIF for rapid diagnosis, ensuring a consistent drug supply, and strengthening TB infection control. A major component of PEPFAR's efforts is supporting scale-up of the decentralized model. Unique contributions building on PEPFAR's strengths include accelerated implementation of the five "I"s, and improved recording and reporting to monitor the impact of this new policy on health systems and patient outcomes.

Identifying Factors Associated with Drug Resistance

CDC, Ministries of Health, and local partners in nine countries spearheaded the Preserving Effective TB Treatment Study (PETTS), which prospectively evaluated the development and consequences of resistance to second-line drugs among 1278 patients treated for MDR-TB. South Africa was the largest study site, including many participants from KwaZulu-Natal.

PETTS found that nearly half of all patients were resistant to at least one of the drugs in their anti-TB regimen, highlighting the need for rapid and accurate diagnostic tests so patients are started on the right drug regimen. Minimizing treatment interruption and ensuring treatment completion both for susceptible and drug-resistant TB are important strategies for preventing resistance. CDC, in collaboration with PEPFAR, is supporting the MOH to implement these



strategies and improve access to rapid diagnostics and quality treatment. Findings from this study informed WHO's New Global framework for providing support to build quality drug-resistant TB programs.

Building Support for the Management of MDR-TB among Children

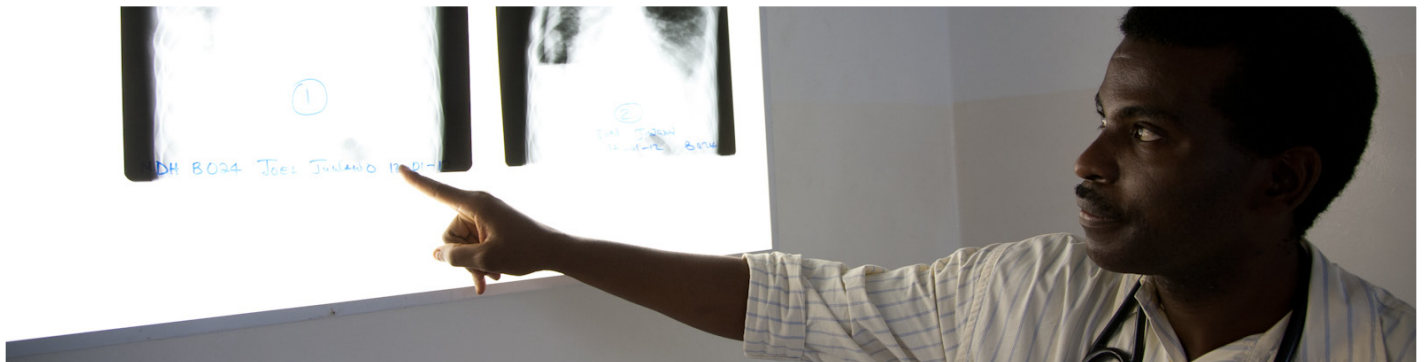
Very little is known about MDR-TB -TB in children, except that it is on the rise globally, especially in countries with a high HIV burden. In South Africa, CDC is conducting the largest study of MDR-TB among children in history, including more than 1,000 children, to describe risk factors associated with pediatric MDR-TB, methods of diagnosis and treatment, and patient outcomes. In collaboration with the NDOH and the Medical Research Council (MRC), CDC convened an expert consultation of key stakeholders in South Africa to identify challenges in finding, diagnosing, and treating children to inform a research and policy agenda for addressing these challenges. This consultation considered the effect of decentralization on management of children with drug-resistant TB, given the additional complexities of their treatment, and ways to apply the model to best serve children.

Efforts in South Africa to address drug-resistant TB illustrate the USG's interagency approach: utilizing each agency's comparative advantages to move from research to implementation at scale while continually monitoring progress and incorporating new knowledge and approaches into existing strategies.

PARTNERING WITH THE GLOBAL FUND

The Global Fund and USAID are the two largest sources of external funding for TB prevention, diagnosis, and treatment services in high burden countries. The Global Fund's TB grants finance all components of implementation of the WHO Stop TB Strategy. USG TB bilateral funds play an important role in contributing to the WHO Stop TB Strategy primarily through global leadership, global research, and technical assistance to countries, which are not usually supported by Global Fund resources. The Global Fund does not have in-country presence or broad disease technical expertise on its staff and relies on partners for this support.

The Global Fund grants and USAID bilateral TB work plans are developed to fill the financing gaps identified in the national TB strategic plans. This approach ensures country ownership, promotes NTP management capacity, enables coordination of external and national TB resources, and maximizes outcomes. In the countries supported by the USG, most of the TB technical assistance to the Ministry of Health's NTP is funded through USAID TB programs by trained national, regional, and international experts.



CONCLUSION

There has been progress in TB prevention, care, and treatment, but challenges remain. TB, MDR-TB, and TB/HIV threaten the economic productivity of developing countries, and threaten the well-being of the population. WHO estimates that the global community is not diagnosing a third of all TB cases, and only one in five of the estimated MDR-TB cases globally were reported to have been enrolled on treatment. Continued efforts are needed to find these cases, to expand access to services, and secure universal access, especially by extending the delivery of quality services provided by the private sector and reaching poor and vulnerable populations. In addition, intensified efforts are needed to address TB/HIV co-infection, and develop additional diagnostic tools, drugs, and a TB vaccine. The USG needs to continue to focus on these efforts to ensure that the achievements endure, and that progress continues to be accelerated.

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