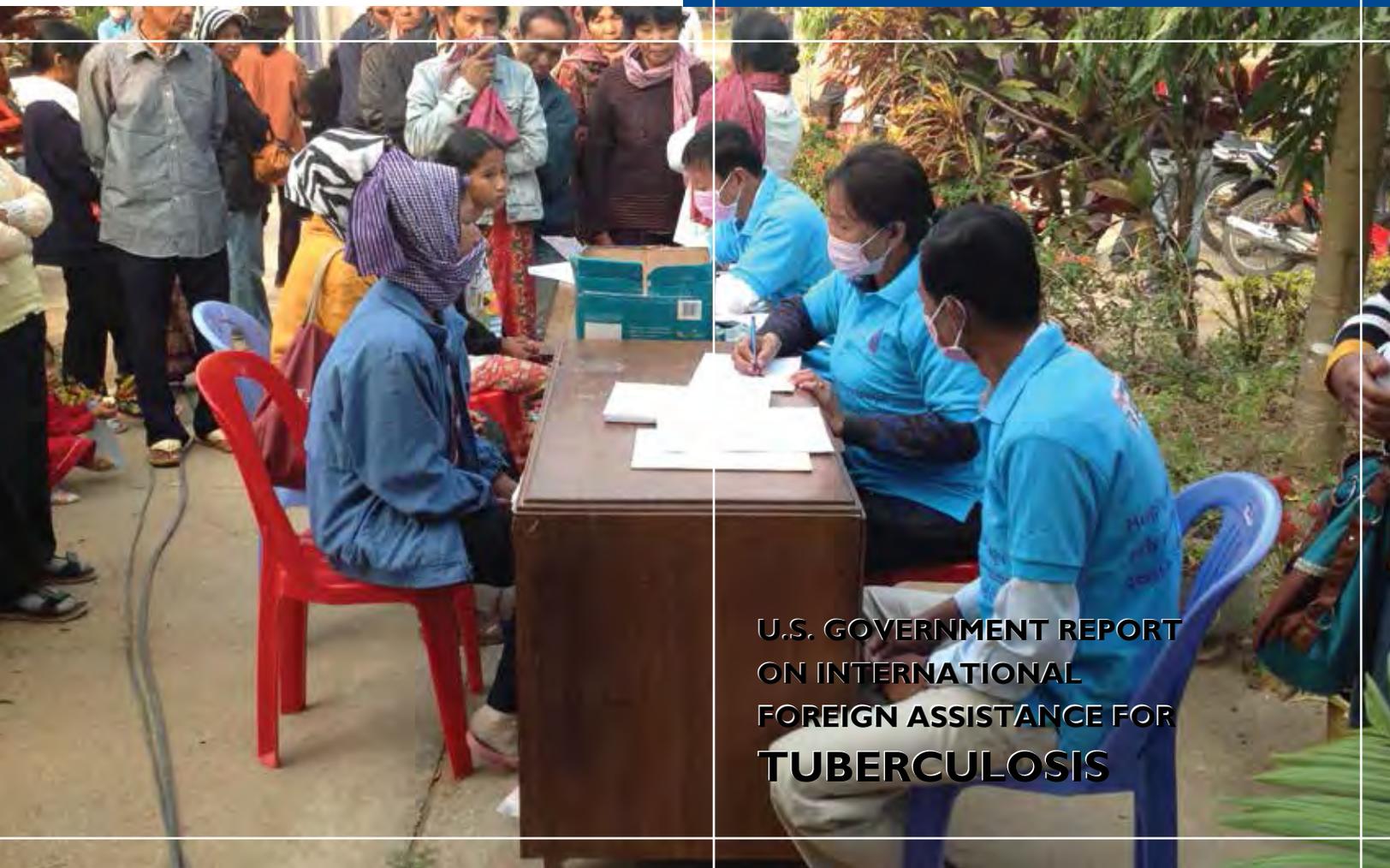


IMPACT AND LEADERSHIP



U.S. GOVERNMENT REPORT ON INTERNATIONAL FOREIGN ASSISTANCE FOR TUBERCULOSIS

FISCAL YEAR 2013



USAID
FROM THE AMERICAN PEOPLE



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



National Institute of
Allergy and
Infectious Diseases



An aid worker reviews an X-ray for signs of tuberculosis. (Photo by RESULTS)



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(COVER) Active tuberculosis case-finding among the elderly in Cambodia. (Photo by Rajendra Yadav)



Executive Summary

For too long, tuberculosis (TB) has inflicted a burden of suffering on mankind, especially among the most poor and vulnerable populations. TB is a contagious airborne disease that killed approximately 1.3 million people in 2012, the majority of whom were in the lowest income quintile. TB knows no boundaries or borders, making it a global health emergency that must be addressed with immediate and aggressive action.

Despite the availability of effective regimens and efficient strategies to deliver treatment, the efforts to control TB worldwide are impeded by the complications of TB-HIV co-infection, multidrug-resistant TB (MDR-TB), poor quality services or limited access to TB services. Conditions that weaken the immune system, particularly HIV and AIDS, place people at higher risk for TB. Failure to complete TB treatment or the mismanagement of TB drugs can result in the development of deadly MDR-TB. TB prevention and care also continue to be hampered by the lack of more effective diagnostic tools to detect TB and MDR-TB in both adults and children, as well as the lack of more effective, less toxic drug regimens that can shorten and improve treatment outcomes and vaccines to prevent new cases.

Strong national TB diagnostics and treatment – and, ultimately, prevention programs – are essential in reducing the transmission of the disease and saving lives. The U.S. Government is a global leader in providing assistance to countries for the fight against TB with a well-coordinated strategy that supports proven interventions and builds on lessons learned from global and country-specific experiences. U.S. Government's global TB program is implemented through USAID as the lead agency, in collaboration and coordination with the U.S. Centers for Disease Control and Prevention (CDC), the Office of the Global AIDS Coordinator (OGAC) at the Department of State, the National Institute of Allergy and Infectious Diseases (NIAID) within the National Institutes of Health (NIH) and the Department of Defense (DoD). The missions of U.S.

Government agencies working on TB are aligned and cover all aspects of biomedical, operational, domestic, and international public health research and implementation. OGAC is the lead for the U.S. Government response to TB-HIV co-infection as part of the President's Emergency Plan for AIDS Relief (PEPFAR). CDC is the lead agency for domestic TB prevention and control efforts and provides international technical support for TB care and treatment in collaboration with USAID and OGAC. While it does not provide foreign assistance of any kind, including for TB control, the NIH, working with CDC, leads U.S. Government research efforts for the development of new TB diagnostics, drugs and vaccines. Finally, DoD has laboratories in numerous priority countries to monitor the quality of TB diagnostic services and conduct operational research.

U.S. Government efforts in TB program implementation and research are coordinated through the U.S. Federal TB Task Force, particularly the working group on international TB. U.S. Government agencies involved in TB program implementation and research – each using its comparative advantage – work to improve understanding of the disease; develop and implement new tools for diagnosis, prevention, care and treatment; and ensure programmatic efficiencies.

USAID supports countries with high burdens of TB to implement high-quality prevention, diagnosis and treatment services. The U.S. Government is the largest bilateral donor for TB and provides one-third of all contributions to the Global Fund to Fight AIDS, Tuberculosis and Malaria. The U.S. Government works closely with the Global Fund to formulate policies, provide technical assistance and promote country coordination to ensure the best and financially strategic use of Global Fund resources. Over the past year, USAID has led efforts to address significant grant bottleneck issues at the country level and improve Global Fund grant performance.

USAID supports the four key intervention areas outlined in the U.S. Government TB strategy for foreign assistance: accelerated detection and treatment of TB; scaled-up prevention and treatment of MDR-TB; expanded coverage for interventions for TB-HIV; and improvements in the health system through strengthening country-owned and generated approaches. During the FY 2013 reporting period, TB deaths in the 27 USAID-supported countries decreased by 41 percent, and TB prevalence decreased by 40 percent. Further, nearly 1.32 million people with TB were successfully treated, and more than 45,000 people with multidrug-resistant TB were put on treatment. USAID bilateral funds focus on interventions that will diagnose and treat people at highest risk for TB and MDR-TB.

Each year an estimated 3 million TB cases go undetected – and therefore undiagnosed and untreated. USAID is supporting efforts to find and treat people with TB through the development of new strategies and approaches; through in-country implementation of new diagnostics, treatments and technologies; and through contributions to the implementation of clinical trials. With USAID’s support, community TB interventions are identifying local solutions to be more effective in the fight against TB, including engagement with the private sector and prison systems to improve the care of patients. CDC, USAID and global partners launched the *Roadmap for Childhood TB: Towards Zero Deaths*, the first-ever action plan developed specifically on TB and children, aimed at increasing the detection and diagnosis of children with TB.

In FY 2013, the U.S. Government continued to invest in the scale-up of Xpert® MTB/RIF (Xpert), a technology to better diagnose drug-sensitive and drug-resistant TB, including TB associated with HIV infection. Through PEPFAR, USAID and CDC are supporting the procurement and placement of more than 250 Xpert instruments in countries with high rates of TB-HIV co-infection. The U.S. Government, through USAID and CDC in-country teams, is providing critical technical assistance to assure that systems are in place to realize the benefits of this new diagnostic technology. Initial data from USAID-supported projects show that use of the technology can significantly decrease the time for diagnosis and treatment initiation of TB and MDR-TB.

The growing MDR-TB epidemic is one of the major threats to progress made so far in controlling TB. USAID’s investment in MDR-TB aims to improve the prevention, detection and treatment of MDR-TB through global- and country-level development and implementation of policies, guidelines, scale-up plans and treatment support. During the current reporting period, USAID supported more than 17 countries in the scale-up of programmatic management of MDR-TB. In addition to technical assistance, USAID support included strengthening laboratory capacity to increase diagnostic capability as well as socioeconomic support to patients to increase their adherence to treatment.

Current MDR-TB treatment regimens come with debilitating side effects and require daily medications for up to 24 months, posing serious challenges to both providers and patients. In FY 2013, USAID, in collaboration with U.S. Government partners, continued to support clinical studies to shorten TB regimens, especially for MDR-TB. Early results show that several new drugs can be used in combination to shorten treatment, but their positive impact on patient adherence and clinical outcomes needs to be determined. Additionally, USAID is working to improve the quality and cost of drugs for MDR-TB by working with existing and new pharmaceutical suppliers. Due to these efforts, USAID has significantly improved the number of manufacturers producing second line drugs, and the price for regimens has been cut by more than 25 percent. The U.S. Government’s work directly impacts lives as described by Azmara Ashenafi in her story on page 23.

Despite the progress in prevention, detection and treatment, TB remains a formidable global health challenge. If we are to achieve the post-2015 global goal of a world free of TB, continued efforts are needed. Further, aggressive investments in research must continue so we can bring new tools and diagnostics in the fight against TB and encourage rapid uptake of these tools as they become available. The U.S. Government will continue its collaboration with partners to scale up all components of the Stop TB Strategy and maintain its leadership role in addressing and reducing the global TB burden so that achievements continue and millions of lives are saved.

This report presents the global TB context; outlines USAID’s achievements in TB prevention, diagnosis and treatment at the global and country level under the framework of the Lantos-Hyde Reauthorization Act; and explains the coordinated U.S. Government approach. Other U.S. Government agencies involved in Global TB Research and Development are mentioned in specific areas to highlight broader U.S. Government contributions.



Tuberculosis is a public health emergency and the leading cause of death in communities with high levels of HIV. South Africa faces one of the world's most devastating TB epidemics. (Photo by USAID)

The Global TB Context

Tuberculosis is an enormous global public health problem. Worldwide, 2 billion people are estimated to be infected with *Mycobacterium tuberculosis* (MTB), and a significant proportion of these are at risk of developing TB. In fact, more people die of TB each year than of any other curable infectious disease. In 2012, there were an estimated 8.6 million new cases of TB and 1.3 million deaths due to the disease. Every hour, more than 200 people die from this curable disease.

TB disproportionately affects vulnerable populations, such as people living in poverty or experiencing crowded living conditions with poor ventilation – such as miners and prisoners. HIV and AIDS, diabetes, malnutrition, and other health factors further affect a person's vulnerability to TB. The rise in global urbanization is leading to densely populated, overcrowded urban centers that could negatively contribute to the increase in the TB epidemic. By 2030, urban areas worldwide will house an additional 1.4 billion people, with the vast majority of this growth occurring in developing and transitioning countries, where 95 percent of the global burden of TB is concentrated. Such urbanization creates the perfect environment for the spread of TB. Many TB patients in urban and poor settings are from underserved and difficult-to-reach communities that face barriers to accessing TB services, which may contribute to delays in diagnosis and poor treatment outcomes.

More people die of TB each year than of any other curable infectious disease.

TB can also be socioeconomically devastating for families, households and communities, particularly those already suffering from poverty. For many families, just the cost of transportation to seek health care is prohibitive, compounded by the need for multiple visits due to inaccurate diagnosis or treatment follow-up. Even when diagnosis and treatment services are available free of charge, the cost of accessing that care can sap families of their income



TB Infection Control Coordinators from TB and sentinel surveillance services, guided by a WHO specialist, start assessment at a TB lab in Bukhara, Uzbekistan. (Photo source: <http://www.tbcare1.org/countries/car/uzb>)

and savings. Besides the immediate impact on people who have TB, in terms of lost income and savings, other members of the family may be forced to leave work or school to care for the affected individual. If the bread winner becomes ill with TB, the family is often compelled to take desperate measures, such as taking out high-interest loans or asking their children to work, affecting the next generation and perpetuating the vicious cycle of poverty.

The U.S. Government is a global leader in the international fight against TB and has made significant contributions to global and national efforts to reduce illness and death associated with the disease. In FY 2013, USAID bilateral funds provided technical assistance to 27 countries with a high burden of TB. All USAID-supported countries have developed National TB Strategic Plans (NSPs) that are aligned with the internationally recommended Stop TB Strategy and focus on improving the quality of prevention, care and treatment services. In addition to leading public sector TB services, National TB Programs (NTPs) are collaborating with pharmacists, private sector clinics, traditional healers and other community providers to properly screen and refer people with symptoms, and in the case of private physicians, correctly diagnose and treat TB.

Despite these efforts, challenges remain in meeting some of the Millennium Development Goals. The world is on track to meet the 2015 goal of reducing incidence by 50 percent from 1990 rates, but there is still considerable

work to be done to decrease the mortality rate, particularly in certain regions of the world. In addition, there are still many people globally without access to TB diagnosis and treatment.

Worldwide, notifications of TB cases have stabilized and, in some countries, the number of diagnosed TB cases has decreased in recent years. However, according to global TB burden estimates, approximately 3 million people with TB – one third of the total estimated burden – have not been identified by NTPs. Although there are ongoing efforts to develop better TB diagnostics, new drugs and a vaccine, these efforts need to be accelerated to bring new tools to the fight against TB and better employ existing ones. There is also a strong need for improved TB case detection at the community level. These 3 million missing cases are a risk to their community if they continue to spread the disease. If these patients are inappropriately treated, they run a high risk of developing multidrug-resistant TB (MDR-TB), a form of TB resistant to the two most powerful antibiotics used to cure TB. Clearly, these missing cases must be reached to drive down ongoing TB transmission and illness and to avoid more deaths. Reaching the 3 million requires reducing barriers to care and expanding access to quality testing and care services through all major public and private sectors, including hospitals, prisons and nongovernmental organizations (NGOs).

There are now indicators of alarming increases in drug-resistant TB cases in countries that have trailed behind in implementing high-quality TB programs. Initially, the failure to appropriately manage first-line TB drugs

***The U.S. Government
is a global leader in the
international fight
against TB.***

drives the development of drug-resistant strains, but once those strains begin circulating in the community, the rates of drug-resistant TB among new cases also begin to rise. This trend threatens to reverse progress in halting the spread of the disease and increases the risk of further antimicrobial resistance. Strengthening underlying TB control programs to provide high-quality treatment and patient support to prevent development of resistance and finding and treating existing drug-resistant TB cases can help in addressing this situation.

It is difficult to diagnose MDR-TB since the available laboratory tests are slow to produce results, and central laboratories are often located far from many patients. MDR-TB also requires up to 24 months of treatment with toxic and expensive drugs, including daily injections during the first two months of treatment. Many of these drugs have severe side effects, including hearing loss, psychiatric disorders, gastrointestinal disturbance and epileptic seizures. Better, faster tools are needed to fight MDR-TB. Fortunately, in the past few years, new diagnostic tools have been introduced and scaled up in many countries with the highest burden of TB. Many countries, however, still lack the capacity to effectively treat MDR-TB once a diagnosis has been made. After nearly 50 years without a new class of TB drugs, two new drugs have joined the arsenal to treat MDR-TB. Bedaquiline, approved by the Food and Drug

Administration (FDA) and by Europe for the treatment of MDR-TB, and delamanid, recently approved in Europe, could offer new hope and treatment options to many individuals living with MDR-TB and for whom no other treatment options exist, although it is still not proven whether either of these will shorten or improve treatment. While many countries now have the capability to find additional MDR-TB cases, they often lack the capacity or adequate supply of drugs to effectively treat MDR-TB once a diagnosis has been made. The newest drugs are out of reach for many countries, but so are the standard second-line drugs needed to treat these cases.

Globally, there are approximately 600,000 people with MDR-TB, many of them undiagnosed and untreated.* Greater efforts to find and treat existing cases and develop innovative new tools and approaches to address MDR-TB are required to maintain progress against TB.

Finally, the HIV epidemic continues to thwart efforts to prevent the spread of TB. At least one third of the 35 million people living with HIV and AIDS (PLHIV) are infected with the disease, and the overwhelming majority of these people live in sub-Saharan Africa. In these HIV-prevalent

settings, the number of new TB cases remains high with alarming death rates among persons co-infected with TB and HIV. PLHIV often have different TB symptoms than patients not infected with HIV and are more difficult to diagnose. They may require visits to separate facilities in order to receive care for each illness. Persons diagnosed with TB likewise require access to HIV services. A package of interventions to prevent, diagnose and treat TB in PLHIV has been defined by WHO. These interventions include clearly articulating the mechanisms of collaboration between TB and HIV programs to deliver integrated services, testing TB patients for HIV and assuring linkage to HIV care and treatment, regular screening for TB as well as preventative treatment among PLHIV, and assuring infection control activities are in place to prevent ongoing TB transmission to highly susceptible persons.

Globally in 2012, 46 percent of TB patients knew their HIV status, up from 40 percent in 2011. Coverage of HIV testing was particularly high in the African region, where 74 percent of reported patients were tested. Screening for TB among PLHIV has also improved; 4.1 million people enrolled in HIV care were screened in 2012, up from 3.5 million in 2011. Rates of antiretroviral therapy (ART) for TB-HIV patients are improving, now at 57 percent, but more work needs to be done to ensure early ART for all co-infected patients.

*WHO estimated prevalence for MDR-TB in 2012.



U.S. Ambassador to Ukraine Geoffrey Pyatt visits Dnipropetrovsk oblast TB dispensary for an update on USAID's long-term cooperation on TB case-finding. (Photo by USAID Ukraine)

U.S. Government's Strategic Global TB Approach: Increasing Access to TB Care, Prevention and Treatment

The U.S. Government collaborates with international partners and the Global Fund to ensure that resources for TB foreign assistance are deployed to support evidence-based strategies. With the current U.S. Government TB strategy (2009–2014) for use of appropriated funds for TB foreign assistance – developed in response to the Lantos-Hyde Reauthorization Act of 2008 – coming to an end this year, the formulation of a new strategy for 2015–2019 is underway. In tandem, WHO and the global community are also in the process of finalizing post-2015 targets and strategy. The U.S. Government strategy will align closely with the global post-2015 TB goal of a world free of tuberculosis.

The Federal TB Task Force is a coalition of U.S. Government agencies working together to address the domestic and global challenge of TB. The international working group of the TB Task Force is comprised of USAID, CDC, NIH, OGAC and DoD, where each agency brings specific technical expertise and/or country presence to the global TB response.

USAID is the U.S. Government 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 27 countries and many others through regional platforms and targeted technical assistance. USAID is one of the major implementers of PEPFAR-funded TB-HIV programs, along with CDC. USAID also supported community-based approaches, operational research to improve the effectiveness and efficiency of TB diagnosis and treatment services, and engagement of all providers, including the private sector, to improve access to TB care.

OGAC coordinates the U.S. Government response to HIV and AIDS across federal agencies and **leads the U.S. Government'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 investments are based on science that will save lives and target populations where HIV is found. Ending HIV-associated TB among people living with HIV and AIDS is possible through a combination of widespread standard ART, 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 December 2012 PEPFAR Blueprint, “Creating an AIDS-free Generation.”

CDC leads domestic TB control efforts and the U.S. Government's international laboratory efforts and also provides critical technical support to ministries of health. CDC's efforts aim to strengthen laboratory networks and surveillance systems, improve clinical and program management through mentorship, and improve TB program practice and policy through operational research. Along with USAID, CDC is a major implementer of PEPFAR's TB-HIV programs. CDC conducts clinical and operational research to evaluate promising diagnostic and treatment strategies for the management of TB, TB-HIV, MDR-TB, and pediatric TB. CDC leads 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 and latent TB infection.

NIH leads U.S. Government efforts in TB biomedical basic and translational research by conducting and supporting research and product development domestically and internationally. NIH-funded science is focused on improving the fundamental understanding of TB and TB-HIV in adults and children 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. NIH does not provide foreign assistance for the care of TB. **Within NIH, NIAID is the lead institute for TB research.** However, other institutes and centers, such as the National Heart, Lung and Blood Institute (NHLBI) and the Fogarty International Center (FIC) contribute to TB research. The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), through its general mission of clinical research in infants, children, adolescents and pregnant/lactating women, also supports studies of TB and TB-HIV in these important special populations.

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 to support efforts to ensure adequate TB services in those challenging circumstances.

**International Working Group of the Federal TB Task Force:
U.S. Government Agencies Involved in TB Programs**

AGENCY	LEADERSHIP ROLE / COMPARATIVE STRENGTHS	KEY ACHIEVEMENTS / ILLUSTRATIVE CONTRIBUTIONS IN 2012-2013
U.S. Agency for International Development (USAID)	Lead for international TB efforts covering 27 countries, and many others, through regional platforms and focused technical assistance to ensure universal access to TB diagnosis and treatment, MDR-TB, and laboratory strengthening; implementer for OGAC-funded TB-HIV programs	<ul style="list-style-type: none"> • More than 1.3 million smear-positive TB patients successfully treated in 2012 in USAID’s priority countries • More than 45,000 people with MDR-TB were enrolled in treatment through U.S. Government-supported programs <p><i>Additional USAID achievements highlighted on page 14</i></p>
Department of State Office of the U.S. Global AIDS Coordinator (OGAC) President’s Emergency Plan for AIDS Relief (PEPFAR)	Lead for activities to address TB-HIV co-infection	<ul style="list-style-type: none"> • Increasing rates of HIV testing among TB patients in many countries where PEPFAR works. Percentage of TB patients in the African region aware of their HIV status rose from 69% in 2011 to 74% in 2012 • Contributed to improved rates of ART coverage among TB-HIV patients globally, from 49% in 2011 to 57% in 2012; accelerating the uptake of early ART for all co-infected patients is an urgent priority
U.S. Centers for Disease Control and Prevention (CDC)	Lead for domestic TB program and international lab support with operational research; provider of technical support to ministries of health; implementer for OGAC-funded TB-HIV programs	<ul style="list-style-type: none"> • Led development of <i>Roadmap for Childhood TB: Towards Zero Deaths</i>, outlining immediate actions to accelerate progress against deadly disease in children • Provided technical support and training for laboratory staff in 13 countries. Assisted two national laboratory systems in achieving regional and international laboratory accreditation • Strengthened disease surveillance systems in 14 countries, while working with the World Health Organization (WHO) to develop a global framework for evaluating and improving systems worldwide to enable countries to use national data for continuous program improvement
National Institutes of Health, National Institute of Allergy and Infectious Diseases (NIAID)	Lead for biomedical and translational research; facilitator of development of new drugs, vaccines, and diagnostics for TB; support agency for the U.S. biomedical research enterprise to study all aspects of TB disease	<ul style="list-style-type: none"> • Critical contributor to the development of Cepheid Xpert® MTB/RIF assay • Invested in biomedical basic, translational and clinical research contributing to numerous diagnostics, two thirds of drug and one half of vaccine candidates as part of the current global clinical product pipeline • Supported clinical trials to study the co-management of TB and HIV and AIDS

Xpert® MTB/RIF Development Timeline

The U.S. Government continues to play a lead role in supporting the roll-out of a rapid diagnostic test, Cepheid Xpert® MTB/RIF assay (Xpert). Xpert is a revolutionary diagnostic tool that can rapidly and accurately detect TB resistance to rifampin, one of the most potent drugs used in the treatment of TB. Greater access to this test boosts health care workers' ability to diagnose TB quickly and help reduce TB transmission, the development of TB disease and premature TB deaths.



“Molecular beacon” assay, the science behind the test, developed and patented by Rutgers State University of New Jersey with contributions by a NIAID grant to detect TB and RIF resistance.

NIAID awards grant to Rutgers and Cepheid to develop MTB/RIF cartridge for the Xpert system.



FIND conducts multicenter evaluation studies in four countries: Azerbaijan, India, Peru and South Africa.

1994-2000

2002

2008-2009

2000s

2000

2006

2009

Collaboration starts between Rutgers and Cepheid Inc. to develop “field-friendly” assay for high-burden TB countries.

Foundation for Innovative New Diagnostics (FIND) signs agreement with Rutgers and Cepheid and negotiates a significantly reduced pricing model for high-burden TB countries.

NIAID awards grant to Rutgers to expand utility of Xpert beyond detection of RIF resistance.





Assistant Secretary of State Dr. Kerri-Ann Jones visits the laboratory where U.S. technology has cut drug-resistant tuberculosis diagnosis from days to hours. The microbiological research laboratory is housed at the University of Indonesia. (Photo by USAID)



FIND examines the operational feasibility, accuracy and effectiveness of Xpert implementation. It conducts this work in collaboration with the Centers for Disease Control and Prevention (CDC) in six countries: Azerbaijan, India, Peru, South Africa, Philippines and Uganda.

2009-2010



A coordinated U.S. Government response involving USAID, CDC and PEPFAR develops policy and technical approaches for Xpert country projects. These resources include standard tools and guidance for implementation, operational research and impact measurement.

2010-PRESENT

PEPFAR and USAID partner with the Bill & Melinda Gates Foundation and UNITAID in an innovative public-private partnership to ensure a 40% reduction in the cost of Xpert test cartridges from \$16.86 to \$9.98 in high-TB burden countries.

2012



2010

The World Health Organization (WHO) endorses and recommends Xpert MTB/RIF assay for use as the initial diagnostic test for adults thought to have multidrug-resistant TB or HIV-associated TB.

2011-PRESENT



USAID and PEPFAR funded partners roll out and/or scale up Xpert implementation in more than 30 countries, procuring Xpert instruments and cartridges and using a comprehensive technical approach.

2013

WHO endorses and recommends that Xpert assay should be used as the initial diagnostic test in children suspected of MDR-TB or HIV-associated TB and as the initial diagnostic test in testing cerebrospinal fluid specimens from patients presumed to have TB meningitis.

Joint Agency Collaboration in Lab Strengthening, Childhood TB and TB-HIV Activities

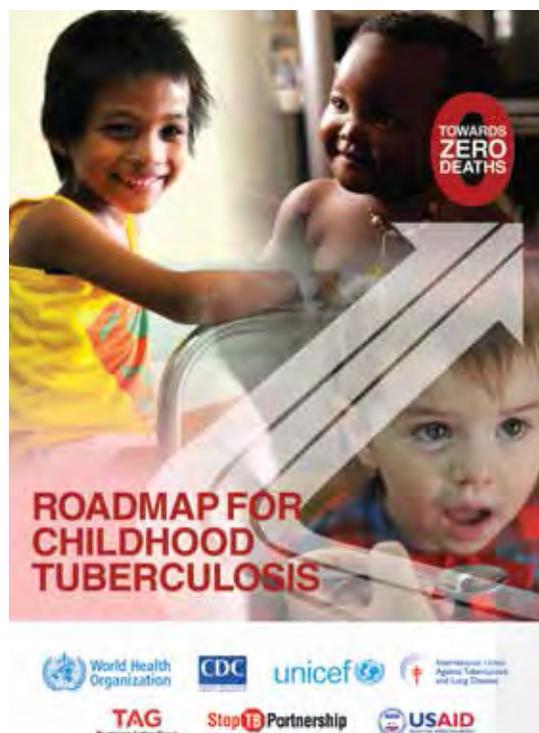
During FY 2013, different combinations of U.S. Government agencies continued collaboration to maximize comparative advantages and strengths related to global efforts for TB care, prevention and treatment. Below are highlights of interagency partnership indicating the agencies involved in each project.



New Supranational Reference Laboratory in Kampala, Uganda. (Photo by Tristan Bayly)

USAID and CDC Supported National TB Laboratory Receives Supranational Reference Status from WHO

In April 2013, following six years of investment and support from USAID, and more recently from CDC, the National Tuberculosis Reference Laboratory (NTRL) of Uganda became the first TB laboratory in East Africa to acquire Supranational Reference Laboratory (SRL) status from WHO. The Uganda SRL, located in Kampala, is currently supporting laboratory services in Burundi, Kenya, Rwanda, Somalia, South Sudan, Tanzania and Zambia. Support from the SRL to these countries will enhance and accelerate laboratory capacity to better diagnose TB and drug-resistant TB in the region.



Roadmap for Childhood TB: Towards Zero Deaths

On October 1, 2013, CDC, USAID and global partners launched the first-ever action plan developed specifically on TB and children: *Roadmap for Childhood TB: Towards Zero Deaths*. The deaths of more than 74,000 children from tuberculosis could be prevented each year through measures outlined in the Roadmap, which include building the capacity of health care workers to look for TB among children through training and access to existing tools, integrating TB screening into family and community health services, tracing children exposed to TB and providing preventive therapy, and closing the funding gap for childhood TB. Every day, more than 200 children die needlessly from TB. The World Health Organization estimates that one in 10 TB patients worldwide is a child. The actual burden is likely higher, because diagnosing TB in children is challenging and is a low priority in low-resource settings.



MDR-TB education exercise
on treatment support, Nigeria.
(Photo by FHI)

USAID, CDC and other partners have been working with ministries of health in 16 countries to develop innovative approaches to diagnosing and treating TB in children while making the best use of available tools to reach children at risk for TB. The U.S. Government is partnering with communities and health care workers to improve TB case-finding and patient outcomes through training and tailoring available tools to meet community needs. A community-wide approach to TB prevention, case-finding and supportive care is essential to ensure all children with TB receive effective diagnosis and treatment so that we can ultimately eliminate TB deaths among children.

Improving Access to TB-HIV Diagnosis, Care and Treatment

TB remains the main cause of death among people living with HIV (PLHIV). PLHIV who are infected with *Mycobacterium tuberculosis* (MTB) are much more likely to develop active TB disease than those who are HIV negative. Since 2004, WHO recommendations have guided efforts to reduce the burden of TB among PLHIV. Collectively, these interventions are known as collaborative TB-HIV activities. They include establishing and strengthening coordination mechanisms for delivery of integrated TB and HIV services, intensifying TB case-finding among PLHIV, provision of isoniazid preventive therapy (IPT) to PLHIV who do not have active TB, early initiation of ART for co-infected patients, and controlling the spread of TB infection in health care and congregate settings such as prisons. These activities are referred to as the Three I's for TB-HIV. Since December 2010, the rapid molecular test, Xpert, has been recommended as the primary TB diagnostic test for PLHIV who have TB symptoms.

The progress to date in reducing the TB burden among PLHIV, however, has been slow. Although in 2012 there was an increase in screening for TB among PLHIV – 4.1 million in 2012 compared to 3.5 million in 2011 – a large number of PLHIV in care do not receive consistent TB screening. Similarly, with IPT, the coverage needs to be increased; of the 1.6 million PLHIV who were newly enrolled in care in 2012, only 520,000 received

preventive therapy, according to WHO's *Global Tuberculosis Report 2013*.

Scale-Up of the Three I's in Zambia

With some of the highest TB-HIV co-infection rates in the world, Zambia is addressing the issue by scaling up implementation of the Three I's (supported with PEP-FAR funding). In this initiative, Xpert is featured as a pillar of the project design of intensified case-finding and enhanced TB screening. A district "hub and satellite" model is being implemented with the Xpert platform. To expand the reach of the laboratories, the satellite facilities transport specimens to the "hub" to fast-track access to this new diagnostic. Four provinces with high co-infection rates were selected for implementation of activities, including IPT provision and infection control measures. A total of 29 health care facilities, 14 laboratories and 8 prisons in 11 administrative districts implement these intensified activities. In some districts, prison screening has been established, and specimens enter into the "hub" model from each prison satellite facility. Courier systems between the hub and satellite facilities for delivering specimens and reporting patient results have been strengthened as a result of implementation activities. Facility baseline assessments for infection control and Xpert installation, conducting extensive trainings, and development of robust monitoring and evaluation measures underpin the systematic approach to scaled-up implementation. Preliminary screening numbers from only half of the implementation sites in Zambia (for only two months) already point to early successes. For example, out of the 1,600 PLHIV screened with Xpert, 207 had active TB and started on treatment. Thirty-seven were resistant to rifampicin, one of the more potent anti-TB drugs, most often a marker of MDR-TB.

Although countries are still in the early implementation phase, some initial lessons learned are being documented. These include the importance of strong collaboration between the TB and HIV programs, as well as active engagement and country ownership required for delivery of these essential services. U.S. Government-supported, targeted and focused technical assistance was instrumental for these early successes.

Impact and Leadership: USAID's Response to TB in FY 2013

The U.S. Government TB Strategy for TB foreign assistance provides a blueprint for expanded TB treatment and care through our investments. USAID, CDC and PEPFAR are committed to working with host country governments to contribute to halving TB prevalence and mortality through successful treatment of 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 2015. In cooperation with partners at global, national, and local levels, USAID is supporting TB programs to accelerate detection and treatment of TB for all people, scaling up TB-HIV integration, expanding prevention and treatment of MDR-TB, and assisting with overall strengthening of health care systems.

USAID's work on TB prevention and care focuses on countries with lower income, the greatest burden of TB and HIV and AIDS, rates of MDR-TB, and challenges in detecting and treating TB cases. 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 National TB Programs (NTPs). USAID reduced the number of countries with national scale programs from 40 to 27 countries, although there are regional platforms and targeted technical assistance in others. The data in Figure 1 reflects the 27 countries to measure USAID's national level contribution to the global TB goals, compared to the 40 countries.

During the FY 2013 reporting period, the mortality and prevalence of TB in the 27 USAID-supported countries decreased by 41 percent and 40 percent, respectively, since 1990. Nearly 1.32 million sputum smear-positive TB patients were successfully treated during the reporting period, and the quality of treatment has been maintained in these countries with an 87 percent treatment success rate. The number of MDR-TB patients enrolled in treatment nearly doubled from 26,000 last year (without Russia) to more than 45,000 cases in FY 2013. This increase is largely a result of USAID's intensified MDR-TB case-finding and expansion of access to care since many of these countries did not have the capacity to diagnose, treat or care for people with MDR-TB. Despite these achievements, challenges remain to reaching global and national targets for MDR-TB. Availability of quicker and point-of-

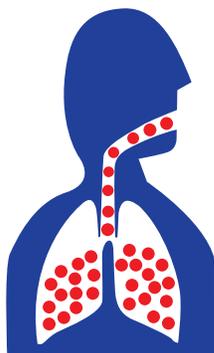
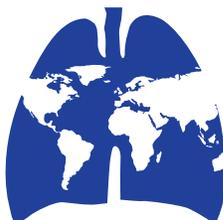
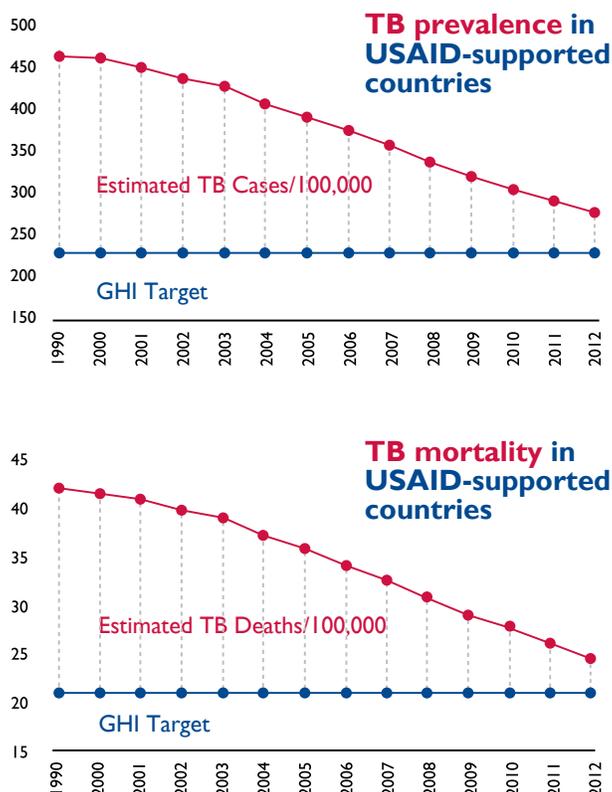


Figure 1. Trends in TB prevalence and mortality in USAID-supported countries



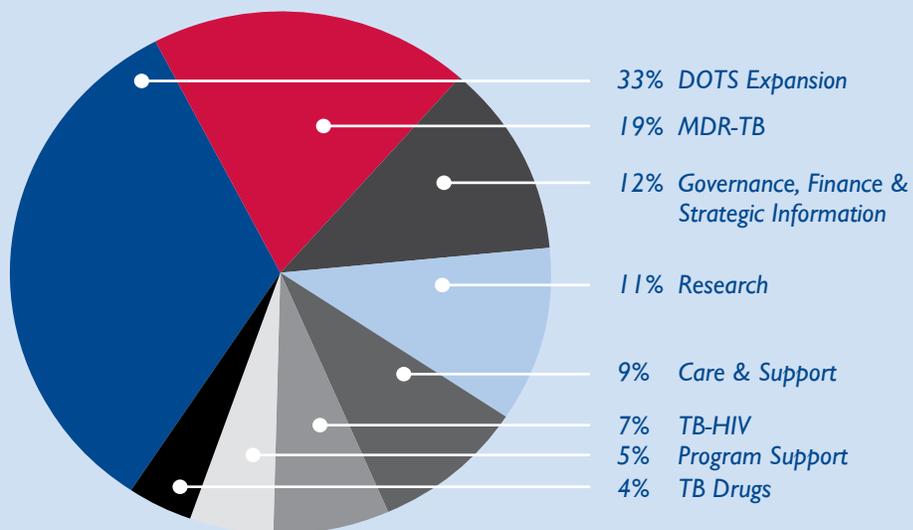
^a =TB prevalence is defined as the number of existing cases per 100,000 population as of July 1 for each year (the mid-year point). TB mortality is defined as the number of TB deaths per 100,000 population as of July 1 for each year. Prevalence and mortality estimates are taken from the WHO Global TB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

use diagnostics, as well as better-tolerated drugs are desperately needed to reduce adverse drug reactions, cure patients, and thus limit transmission. In addition, aggressive scale-up of new and innovative interventions is urgently needed to bring services closer to patients and adequately support them while they are on treatment so that advances in TB and MDR-TB treatment made over past decades continue to be accelerated.

Investing for Maximum Impact

USAID focuses its technical support on areas and interventions that will have the greatest impact on improving TB prevention, diagnosis and treatment services. In FY 2013, \$236 million was appropriated through the Global Health Programs account to USAID to support TB programs worldwide. As shown in Figure 2, 83 percent of USAID's TB resources were programmed to directly support patient services for Directly Observed Therapy Short-course (DOTS) expansion, MDR-TB, TB-HIV, TB drugs and care and social support for TB patients. Eleven percent of the budget was invested in operational and implementation research.

Figure 2. USAID TB expenditures in FY 2013



X-ray training in Cambodia.
(Photo by Seak Kunrath)

Strengthening Country-Owned and Generated Approaches

TB services are primarily implemented through existing country health systems. Therefore, the development of these systems is critical for TB care and treatment. USAID's bilateral funds support countries to develop country-owned and generated approaches to develop the skills required to sustain efforts.

The global TB community has lagged in the development and introduction of new approaches, technologies and research. In order to sustain efforts and truly develop country-level capacity, effective methods for promoting locally generated and innovative solutions to existing challenges are necessary for meeting country and global goals. As countries progress and develop, they will need to adapt country-specific solutions that are innovative and address key TB challenges, including stagnating case detection, low treatment success, high mortality and default rates and low private sector engagement. New technologies to improve diagnosis and treatment of TB, specifically in low-resource settings, will also be critical to addressing these challenges and will have to be developed by countries with the appropriate biomedical and clinical research infrastructure to contribute to overall global TB research efforts. Examples of new technologies include Xpert, new or improved treatment regimens and mHealth. In addition, there is a need for comprehensive technical approaches and monitoring and evaluation frameworks to roll out and assess their utility, optimal implementation and create medical evidence of the effectiveness of any new technologies and tools. The best practices and lessons learned from these activities would in turn inform country and global policies to contribute to the achievement of improvements in patient care and health outcomes.

U.S. Government* Accomplishments in FY 2013:

18	countries had in-depth reviews of their national TB programs
10	countries finalized their national strategic plans
6	countries completed fieldwork for a drug resistance survey
18	countries received technical support for the implementation of their Global Fund grants
31	countries received technical assistance to strengthen their laboratory network
30	countries were supported in scaling up the programmatic management of MDR-TB
4	countries developed national TB infection control guidelines
25	countries received training for health care providers on pediatric TB

**Includes contributions from other U.S. Government agencies*

Community health worker helps a TB patient taking her daily pills in Afghanistan.
(Photo by Mostafa Shefa)



A lab technician tests tuberculosis samples at a lab in Bandung's Public Health Laboratory. Indonesia is ranked 4th out of 22 countries with the highest burden of TB cases in the world and 8th for multidrug-resistant (MDR-TB). Indonesia also has the world's highest number of confirmed human infections with H5N1. (Photo by USAID)



USAID works closely with countries to assist them with the successful development and implementation of robust National TB Strategic Plans (NSPs) and provides mentorship opportunities for countries through hands-on workshops and in-country technical assistance where countries are led through the process of identifying the key elements that are needed to strengthen their plans. Although USAID and partners have been supporting countries in the development of NSPs, the Global Fund has made the development of a strong NSP a requirement in the new funding model. This will build on the basis of USAID's previous work with National TB Programs (NTPs), assisting in the standardization and improvement of strategic planning.

USAID works closely with NTPs and the Global Fund to ensure that bilateral funds and other donor funding is not duplicative and that TB activities are aligned with the NSP, filling strategically important financial, human resource, and programmatic gaps. USAID also works to ensure that its program is fully supporting the NTP and not establishing a parallel program. Technical assistance is provided in a coordinated manner among partners to ensure that Global Fund grants are successfully implemented so that countries can access this much-needed funding.

The U.S. Government is the main supporter of global technical TB policy and implementation, as well as programmatic tool development, mainly through support to WHO and country-level strategic guidance with other partners. The comparative advantage of USAID's bilateral funds is the ability to implement TB programs at scale; pilot innovative approaches in field settings; monitor, document, and use results; and work directly with ministries of health to build national and local capacity to implement their TB care and treatment programs. USAID uses country implementation experience to inform global policy and guidance and vice versa. It is the main donor working in TB with both field and development experience.



USAID's Technical Assistance Model

In response to the development of the Global Fund's new funding model and the need to accelerate TB care activities, USAID has developed a technical assistance model to ensure that Global Fund grants are successfully implemented to improve coordination among partners, to build country capacity, and to ensure that the greatest challenges in TB prevention and care are met. The goal of this model is to build country capacity and significantly decrease the amount of "fly-in/fly-out technical assistance," in which several different consultants travel to countries to provide technical assistance at different times, leaving behind recommendations that countries often do not have the capacity to implement. Instead, USAID is focusing on a combination of coordinated long-term, short-term, and multi-partner technical assistance, where several partners provide technical assistance that is aligned at the country level to resolve issues. This coordination will ensure that USAID resources are used in the most efficient manner.

Leveraging Resources and Collaborating with the Global Fund

The U.S. Government is a major donor to the Global Fund, which in turn is the largest global donor for TB care and treatment. The USAID works closely with the Global Fund on formulating policies, the provision of technical assistance, and country coordination to maximize public health outcomes. Since the Global Fund does not offer in-country presence or broad technical expertise within its Secretariat, the organization often relies on USAID-supported technical assistance and its model described to the left.

Over the past year, USAID led the U.S. Government's coordination efforts to address significant Global Fund grant bottleneck issues at the country level and improve grant performance. USAID has prioritized its technical assistance support for countries with the largest Global Fund TB investments and bilateral TB funds so that these resources are maximized and used in the most efficient manner. USAID has led the efforts on coordinating the roll-out of the Global Fund's new funding model, including a mapping of technical assistance providers who are supporting activities in specific countries to ensure there is no duplication of efforts. USAID has been mobilizing support for national TB epidemiological assessments, the development of TB NSPs, and the development of Global Fund concept notes. This has included working closely with the "5% Initiative" and the "BACKUP Initiative," which are technical assistance initiatives funded by the French and German governments respectively, to support Global Fund grant implementation. USAID is also contributing its technical expertise to support the new Global Fund mandate that countries with a high burden of co-infection with TB and HIV shall submit a single concept note that presents integrated and joint programming of the two diseases.



A DOTS patient collects sputum at Guarulhos Parque CECAP Health Unit funded by USAID, in Sao Paulo, Brazil. DOTS (directly observed treatment, short-course), the tuberculosis control strategy recommended by the World Health Organization, has five components: political commitment with increased and sustained financing, case detection through quality-assured bacteriology, standardized treatment with supervision and patient support, an effective drug supply and management system, and monitoring and evaluation system and impact measurement. (Photo by Ricardo Funari)

USAID funds the active search for potential tuberculosis patients by trainee nurses in Guarulhos CECAP Health Unit in Sao Paulo, Brazil. (Photo by Ricardo Funari)



Leveraging Local Resources to Improve TB Control in Urban Centers in Latin America

In Latin America, where 80 percent of the population lives in cities, the urban population tends to have higher rates of poverty and TB. This is due to the increased population density, crowded living conditions and poor access to health services. The combination of these social determinants creates concentrated pockets of TB in urban slums, where, as the population continues to grow, living conditions continue to worsen.

In an effort to leverage existing local resources and social protection programs and increase access to health services and TB treatment to the urban poor of Latin America, USAID partnered with the Pan American Health Organization (PAHO) to address TB in urban centers. Focusing on municipalities with a high burden of TB, the project works with city governments and local health authorities to identify vulnerable populations living in their jurisdictions, address barriers that impede these individuals from accessing health services and develop strategies to improve TB diagnosis and treatment among these populations.

This USAID-supported project has already seen tremendous success in Guarulhos, a large city in the metropolitan area of Sao Paulo, Brazil, and has been welcomed with strong commitment from local authorities. A situational analysis was completed at the beginning of the project to provide the city government and health authorities with key data needed to inform their decisions and strengthen TB control in their communities. Most importantly, at the local government level, analyses were completed to find ways to incorporate TB activities and funding in strategic plans at the national and local levels.

The modest investment by USAID has led to significantly increased collaboration and partnership with civil society groups, other areas of the health sectors, and an informed local government with a strong commitment for TB control. Given this success, Brazil's NTP has expanded this approach to 12 other cities with their domestic funding of approximately US\$6.8 million to improve access to TB diagnosis and treatment for the urban poor.

Intensified Case-Finding: Access to Quality Treatment for All People

Without the right interventions to prevent transmission, infection and disease and without intensified efforts to find and treat the most vulnerable people with TB, the global community will not be able to achieve the goal of reducing burden and death from the disease.

According to recent WHO estimates, each year, approximately 3 million people – or one-third of all new TB cases – are not diagnosed or reported to country health systems, contributing to stagnating TB case notifications. Weak links in the TB care chain (a chain that includes detection, treatment and care) are at the heart of this challenge and lead to such people being missed. Further compounding the problem is the fact that TB programs often do not have the capacity to find and care for people who are “hard to reach” or served outside the formal or local health system.

The expansion of global urbanization will also impact case-finding, access to diagnosis and treatment and TB treatment outcomes. TB disproportionately affects those dwelling in urban areas due to overcrowding and links to poverty. In countries with large, urban areas, local challenges to accessing TB services and keeping people on appropriate treatment are even more critical than in other areas. Deliberate strategies for assessing the situation and evaluating interventions for best practices and scale-up need to be developed to tackle urbanization in a systematic and sustainable manner.

The prevention and reduction of the number of infections for high-risk populations and settings are other critical components of case-finding and are necessary to achieve a significant reduction in the number of TB cases. Persons and children living with individuals who have drug-sensitive or resistant active TB; people with HIV and AIDS, diabetes or other conditions that weaken their immune system; and people living in congregate settings, such as prisons, are all considered at high-risk of developing TB. Many countries lack the resources and expertise to support key interventions that would help strengthen infection control and transmission prevention within their health care systems. USAID’s country-level approach involves collaborating with ministries of health and other key partners to provide in-country training, supervision and mentorship activities so that countries can increase their knowledge and expertise and develop a comprehensive approach to infection control.

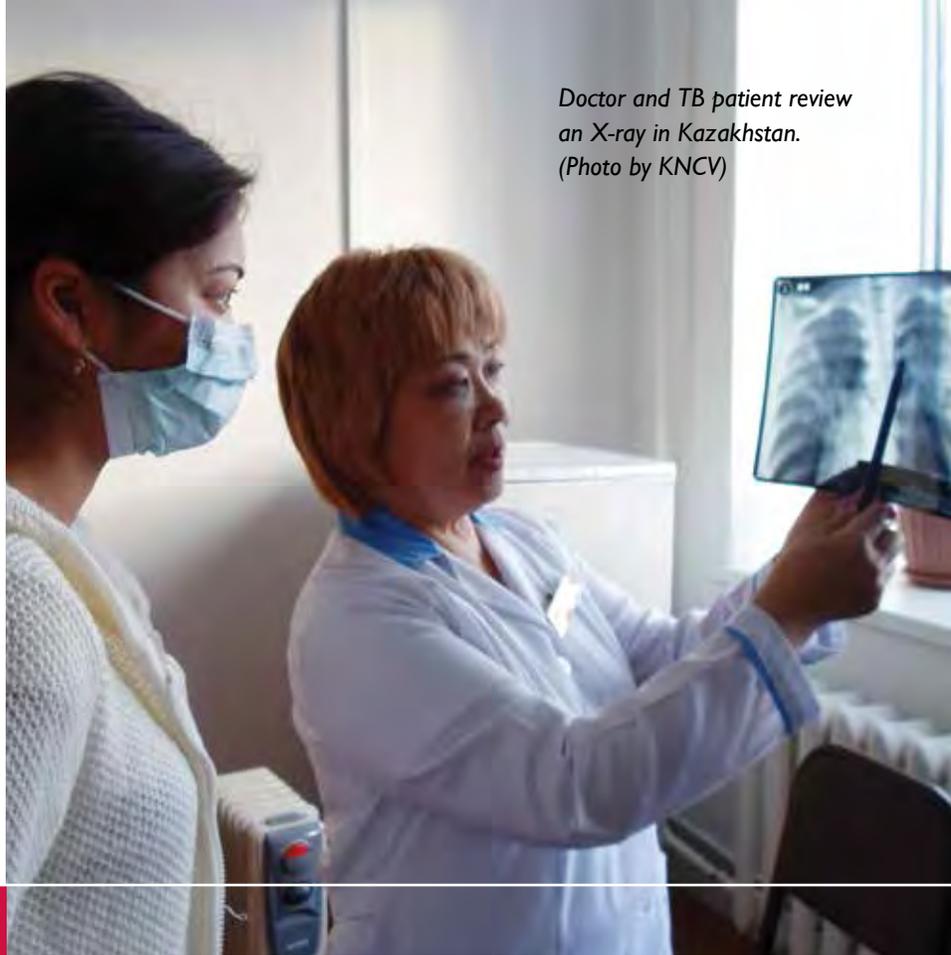
In the **Kyrgyz Republic**, weak infection control in TB facilities posed a major problem in preventing transmission of TB and MDR-TB. USAID technical assistance developed new National TB Infection Control Guidelines and advocated for their adoption and implementation. The support included the roll-out of the guidelines through a pilot test at seven hospitals providing TB treatment services. As a result of these interventions, both the NTP and program partners observed significant improvements in infection control at all seven facilities. Activities undertaken

USAID’s Patient-Centered Approach to TB Care and Treatment

Putting the needs of a patient first and treating the patient as a partner rather than just a recipient of care is at the heart of a patient-centered approach. The four elements of USAID’s patient-centered LIFE model, which is tailored by country, include:

- Leadership in the country to ensure there are policy and guidelines to involve patients and communities in TB service delivery
- Involvement of all stakeholders and building partnerships to support patients
- Fostering a better relationship between the patient and the provider
- Empowering patients and promoting patients’ rights

by the hospitals in support of infection control have included timely diagnosis of TB, proper separation of drug-resistant and susceptible TB patients, installation of secure sputum collection rooms, and improved individual protection practices for patients and health workers. All pilot facilities in the Kyrgyz Republic are now equipped to measure the effectiveness of their infection control practices and to ensure that new standards are being met.



Doctor and TB patient review an X-ray in Kazakhstan. (Photo by KNCV)

Smartphones as Case Detection Tools in Nigeria

In Nigeria, health workers are using smartphones at more than 500 facilities to more accurately diagnose and treat TB as a result of a successful pilot program to integrate mobile technology into the TB supervision process.

This project is part of an effort by the National TB and Leprosy Control Program (NTBLCP) to tap into mobile technology to provide more supportive supervision and improve health services, especially in areas with high defaulter rates, drug stock outs and TB-HIV services integration.

By using smartphones on their facility visits to collect TB data, supervisors and health care workers have eliminated the need for printed forms, minimized human error in data entry, reduced the lag time for getting data to policymakers and managers and helped pinpoint ways to improve the quality of care. Results from Lagos and Abia States show impressive clinical impact.

- In Abia pilot sites, the percent of TB-HIV co-infected patients on co-trimoxazole preventive treatment (CPT) jumped from 34 percent to 100 percent in one year.
- In Lagos pilot sites, the number of TB-HIV co-infected patients on ART increased from 26 percent to 72 percent in the same year. Defaulter rates in both states have also declined considerably.

Every individual has the right to access quality TB diagnosis, care and treatment. Between 2012 and 2013, USAID continued to scale up its five-pronged approach to intensify case-finding and improve universal access to TB care and will continue to innovate case-finding to identify the 3 million not currently notified through national TB programs (NTPs).

Bangladesh is a

TB endemic country with approximately 337,000 new TB cases and 64,000 TB-related deaths annually. Diabetes is also a big threat for Bangladesh, with an estimated 8.4 million people between the ages of 20–79 living with diabetes. USAID is helping initiate a partnership with the Diabetic Association of Bangladesh (DAB) to reach large numbers of diabetes patients with TB services. Presently in Bangladesh, opportunities for detection of TB cases among diabetes patients are few. The majority of people with diabetes and TB remain undiagnosed or are diagnosed too late. The partnership will address this critical service delivery gap, contribute to early detection of TB, and improve care and control of both diseases. USAID is also helping provide technical assistance through training doctors and nurses to develop capacity for TB screening and management of co-morbidities, strengthening quality and capacity for diagnosis, and improving infection control.

TB AND DIABETES

- Research has established that diabetic patients are two to three times more likely to contract TB than others.
- The risk of death is also higher among diabetic patients with TB.
- Globally, about 10 percent of TB cases are linked to diabetes.

01

Actively finding TB cases through contact investigation, co-morbidities and health service integration

ACTIVE CASE-FINDING

EXPANDED ACCESS TO SERVICES
USAID'S FIVE PRONGED APPROACH

PRIVATE SECTOR INVOLVEMENT

02

Ensuring the private sector adheres to proper diagnosis, care and treatment for TB according to public health guidelines

USAID has continued to support the implementation of Public Private Mix (PPM) activities in countries such as Cambodia, Indonesia, Kenya, Namibia, Nigeria and Indonesia. In **Indonesia**, USAID supported the establishment of PPM teams in 25 districts located in seven provinces. These teams are improving coordination and ensuring networking between provincial health services, hospitals, private providers, professional societies, prison departments, laboratories and workplaces. An increased number of TB patients were notified in public and private hospitals in four project-supported provinces. This contributed to 13,434 (13 percent) out of 104,515 cases notified in 2012.

Ensuring that laboratories have the equipment, training and procedures in place to diagnose TB, including drug-resistant forms, is critical to helping people access lifesaving treatment as quickly as possible. During FY 2013, USAID played a pivotal role in infrastructure upgrades in five central laboratories across **India** to allow for the introduction of the line probe assay (LPA), a rapid molecular TB diagnostic test that allows for the detection of TB and MDR-TB by looking at the most common genetic mutations associated with resistance to two most potent TB drugs, rifampicin and isoniazid. Prior to these laboratory upgrades, MDR-TB diagnosis was not available in many parts of the country. Once certified, these five upgraded laboratories will provide MDR-TB diagnostic services for 30 million persons.



05 Improving the quality and performance of TB laboratories

USAID continued to make significant investments in community-based DOTS activities at various levels in countries that it is supporting, working through subcontracts with local NGOs focusing on TB and HIV. Most of these countries have successfully moved past the pilot phase of community-based DOTS and built the capacity of community health workers (CHWs) needed to deliver TB care. In the **Democratic Republic of Congo (DRC)**, early identification and treatment of individuals with TB is one of the most important strategies to stop ongoing transmission of TB in the community. In DRC, Club des Amis Damien (CAD), a community-based organization composed of former TB patients, was supported by USAID to expand its activity to seven sub-provinces. Through this expansion, 80 community-based groups comprised of former TB patients were formed and trained to identify and refer individuals with TB symptoms to TB clinics for early diagnosis and treatment. During FY 2013, members of the CAD referred 3,082 presumptive TB cases to a TB health facility, out of which 52 percent were confirmed as TB patients. Without the CAD's involvement, these cases could have gone undetected and continued to transmit TB in the community.

04 Providing TB diagnosis, care and treatment in communities, beyond the health care facilities

03 Developing quality TB diagnosis, care and treatment programs in prisons

Prisons are often high-risk environments for TB transmission because of severe overcrowding, poor nutrition, poor ventilation and limited access to often insufficient health care. According to WHO, the prevalence of TB in prisons is up to 100 times higher than in the civilian population. USAID is working in several countries to address the growing public health problem of TB in correctional settings. In **Vietnam**, for instance, USAID supported the development of a multi-sectoral plan for TB, HIV and MDR-TB in prisons in collaboration with the Global Fund. This plan includes a model of care and social support for prisoners once they are released to ensure that they finish their treatment. In **Tajikistan**, USAID-supported programs target improving communication between the administrative and medical prison departments to ensure effective discharge planning and linkages with civilian TB control so that released inmates with active TB can continue their treatment once they are out of prison.

Quality MDR-TB Scale-Up: Strengthening Programmatic Management of Multidrug-Resistant TB

The growing MDR-TB epidemic is one of the major threats to progress made so far in controlling TB. Drug-resistant TB cases have grown steadily over the past decade, and globally there are about 600,000 estimated existing cases of MDR-TB. This is largely a result of countries not adopting international standards of TB care early enough, resulting in clinical and programmatic mismanagement, including provision of poor quality drugs, providers not prescribing the proper regimen and patients not receiving the support they need to complete the full course of treatment. With the rapid scale-up of Xpert and the projected increase in case detection in many high burden countries, there is risk that globally MDR-TB diagnosis will outpace treatment.

USAID's investments in MDR-TB aim to improve the prevention, detection and treatment of MDR-TB through global and country-level development and implementation of policies, guidelines, scale-up plans and treatment support. The implementation of a successful MDR-TB program is a complex and labor-intensive process and the consequences of a poorly performing MDR-TB program can pose a significant challenge to governments, communities and families. USAID provides technical assistance to countries to develop effective plans for the programmatic management of drug-resistant TB (PMDT) among their population. These plans include strategies for increasing the rapid detection of drug-resistant TB, improving treatment capacity through better and more adaptive models that involve communities, increased domestic resources for MDR-TB services and a strategy to secure the needed finances. In addition to technical assistance, USAID supports the training of health care workers for the management of MDR-TB through web-based teaching, mentoring and on-the-job training. During the current reporting period, USAID

continued to provide assistance to more than 17 countries that are expanding their MDR-TB program. In addition to training and mentoring, technical support was provided, including strengthening laboratory capacity to increase diagnostic capacity and socioeconomic support for patients to increase their adherence to treatment.

USAID's technical assistance, coupled with support from the Global Fund, assisted the **Kazakhstan** NTP in notifying 86 percent and initiating treatment for 82

percent of estimated MDR-TB patients nationally. With the USAID-supported quality improvement model, MDR-TB treatment completion improved from 25 percent to 85 percent in the USAID pilot site.

In **Indonesia**, with USAID support, the NTP succeeded in halting the increase of initial default and mortality rates of notified MDR-TB cases. To improve patient adherence, USAID supported the NTP with the decentralization of MDR-TB management services to the nearest health facility, improvement of patient support, and establishment of peer

educators for MDR-TB. By the end of 2013, more than 300 PMDT satellite health centers were functional in the country.

In FY 2013, USAID provided support to 30 countries in scaling up programmatic 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. In **Tanzania**, USAID reinforced programmatic management of MDR-TB by supporting quarterly expert panel and cohort review meetings where various cohorts of MDR-TB patients were reviewed for status at 6 months, 12 months, and when treatment ends at 24 months. Through these meetings, 40 patients were evaluated for their final

MDR-TB PROGRAM EXPANSION IN ETHIOPIA

USAID has supported MDR-TB program expansion in Ethiopia since late 2009/early 2010. The program initially started with two treatment centers and by FY 2013 there were more than 10 MDR-TB treatment centers in six regions throughout the country, with enrollment of more than 1,000 MDR-TB patients through sustained supply of SLDs and rollout of ambulatory care. In addition to expanding MDR-TB treatment programs, USAID is providing technical and financial support, patient care and treatment guidance, TB infection control, as well as provision of lab equipment and supplies.

Timely Intervention: A Young Ethiopian Mother and Her Three-Year-Old Get a New Lease on Life

For three years, Azmara Ashenafi had been losing weight and suffering from a recurrent cough and frequent fevers. Although the local health facility had diagnosed Azmara with TB, the six months of TB treatment had failed to alleviate her symptoms. Fearing she would soon be too ill to care for her three young children, Azmara left her village to seek better care at the health center in Muja, where a USAID-trained health officer suspected that Azmara might have MDR-TB, and sent a sputum sample and drug sensitivity test to the nearest reference laboratory.

Azmara's sputum culture proved that she indeed had MDR-TB. The health center organized an ambulance and sent Azmara to an MDR-TB treatment center at Boru Meda Hospital, where a USAID-supported program had recently helped renovate a 20-bed treatment center and trained physicians, nurses and lab professionals on MDR-TB treatment and follow-up. Azmara was one of the first patients admitted in the new MDR-TB treatment center.

The MDR-TB physician also screened Azmara's family since the likelihood of MDR-TB transmission is high among those in close contact with anyone with an active infection. The physician was able to identify that Azmara's three-year-old son, Fesseha, also had MDR-TB symptoms, and the little boy was also put on treatment immediately. After two months of hospitalization, Azmara's first sputum microscopic test was negative, her health, as well as that of her little boy, improved quickly, and she was discharged from the hospital to continue her two-year course of MDR-TB treatment under direct observation at the nearest health center. At their one year follow-up visit this year, Azmara and Fesseha were considered in good health and are continuing with their treatment.

"I thank the Muja Health Center and Boru Meda Hospital staff for diagnosing the disease and initiating free MDR-TB treatment as well as the regular follow-ups to save mine and my child's life," says Azmara.

Since the USAID-supported project began in 2011, three new MDR-TB treatment hospitals have been renovated in Ethiopia and more than 5,000 health workers have been trained on TB and MDR-TB identification, including staff at the Muja Health Center, where Azmara was treated. As of September 2013, 211 new MDR-TB patients have initiated treatment through the project's support. With the additional use of Xpert, the diagnosis of MDR-TB was able to occur more rapidly.



Azmara and her son Fesseha.
(Photo from USAID Ethiopia)

treatment outcomes. Treatment success rates for the two years were impressive, with 80 percent for the 2009 cohort and 78.2 percent for the 2010 cohort.

USAID also helped finance social support programs for MDR-TB patients in 11 countries, thus increasing the chances that these patients will complete the long, difficult treatment regimen. This support includes food, hospitalization fees, biochemical tests to monitor treatment side effects and transportation costs to health facilities.

Comprehensive MDR-TB control is also dependent on the uninterrupted availability of Internationally Quality Assured (IQA) TB drugs at affordable prices. USAID is working to address the ways countries can ensure patients have

No MDR-TB Waiting Lists in Pakistan

Pakistan, one of 27 High-burden MDR-TB countries in the world, became the first country to be awarded funding under the Global Fund's new funding model, and received an additional \$8 million in their existing TB GF grant. USAID was actively engaged in the preparations for the Phase 2 renewal for this grant in November 2012 and worked closely with TBTEAM and the GDF to use USAID funding to advance-purchase the SLDs needed for already diagnosed MDR-TB patients waiting for access to free quality assured drugs. This allowed the grant to jump-start its scale up of the MDR-TB program between the end of Phase 1 and the signing of Phase 2. This advance-purchase enabled Pakistan to provide timely and life-saving treatment to thousands of MDR-TB cases, by placing all patients on treatment in 15 sites throughout the country.

access to quality medicines when they are needed. While the cost of a complete drug regimen to treat drug-sensitive TB is the equivalent of \$22, treating MDR-TB with the currently recommended regimen can cost on average 100 times more. This high cost is driven by the limited market for high-quality second-line drugs (SLDs), making them orphan-like drugs. Because of the limited capacity to diagnose and treat MDR-TB in many countries, the demand for SLDs per country is limited and does not provide sufficient incentive to manufacturers. To improve the availability of high quality SLDs and influence market forces, USAID is working with the Global Drug Facility (GDF) and other partners through an initiative to encourage manufacturers to produce quality and sufficient amounts of the four most expensive MDR-TB drugs. Through this work, GDF's registered price for a standardized SLD regimen has decreased by 26 percent, the cost of pediatric formulations has decreased by 30 percent, and the cost of isoniazid has decreased by 43 percent. USAID also facilitates drug purchases by country governments through GDF's flexible funding mechanism, which allows for advance drug purchases to be made in the event a country has funding delays from the Global Fund or domestic resources. This intervention prevents the risk of drug "stock-outs" that can interrupt the treatment of patients and cause further resistance.

Research and Innovation: Accelerating the Development of New Tools and Diagnostics

Despite advances in TB prevention and treatment, progress in controlling and eliminating TB continues to be hampered by the unavailability of a simple point-of-care test that can quickly detect TB and MDR-TB, the lack of effective, short and well-tolerated treatments for drug-sensitive and drug-resistant forms of TB, and the absence of a vaccine to prevent new TB cases. The U.S. Government's global leadership in all aspects of research, through the missions of USAID, CDC and NIH, involves continued investment in biomedical, operational and implementation research that contributes to the development of new diagnostics and assures that necessary interventions are appropriately integrated into global TB treatment and care programs.

USAID, CDC and PEPFAR have been working closely with ministries of health to train public health professionals to identify TB challenges, design research studies to investigate potential solutions, and translate

findings into policy and practice. This approach builds the skills needed to use local data to improve program performance and solve challenges unique to each program. Featuring a series of courses on operational and implementation research design and data collection and analysis, this approach requires sustained training and mentorship over several years. Ultimately, participants are able to conduct operational and implementation research independently, providing opportunities for personal growth while building the technical capacity of ministries of health.

USAID's approach to TB operational and implementation research focuses on investing in new approaches that are less labor-intensive, more cost-effective, of greater efficacy, and can be delivered easily to patients. To accelerate TB diagnosis, USAID, in collaboration with U.S. Government partners, supported and guided studies in FY 2013 to assess the real-world

performance of revolutionary diagnostic tools such as Xpert and the Line Probe Assay. Discovery and development of novel drugs and regimens is a major focus of TB biomedical research and also supported by NIH/NIAID funds. USAID supported the evaluation of new regimens that may shorten and simplify TB treatment by using novel TB drugs. One such treatment regimen, including the experimental drug PA 824 in combination with the approved drugs moxifloxacin and pyrazinamide (PAMZ), has proven to be safe and effective for the treatment of TB in a small number of patients and trials to evaluate in a large cohort are scheduled to start during the first quarter of FY 15. PA-824's preclinical and clinical development also received support from NIH/NIAID. (See www.clinicaltrials.gov: NCT01674218 and NCT01571414.)

USAID is also supporting the STREAM study,* an evaluation of a short-course regimen for the treatment of MDR-TB that will be free from injectable drugs, usually associated with severe side effects and high default rate in patients. If successful, the results of this study could positively influence the scale-up of MDR-TB

**Additional information on the STREAM study is available at: http://www.ctu.mrc.ac.uk/research_areas/study_details.aspx?s=117*



Xpert at Kariadi Lab in Indonesia

programs, improve treatment outcomes, and eventually be used as a reference regimen when evaluating new MDR-TB treatments, thus reducing costs associated with development of MDR-TB drugs. Additionally, USAID is supporting an evaluation of the newly FDA approved TB drug, bedaquiline (TMC 207), as part of the STREAM study. Bedaquiline's interaction with other drugs is also being evaluated through NIH/NIAID support. (See www.clinicaltrials.gov: NCT01341184 and NCT00992069.)

Conclusion

Since 1990, the world has made progress toward meeting global targets for reducing the number of TB cases and deaths, and we are on track to meet the global target of a 50-percent reduction in mortality by 2015. Still, TB remains a global threat. MDR-TB and TB-HIV pose a serious threat to the economic productivity of developing countries and the well-being of their populations. WHO estimates that the global community is not diagnosing one third of all TB cases, and only one in five of the estimated MDR-TB cases globally was reported to have treatment. Although the proportion of TB patients who know their HIV status continues to increase and reached 74 percent in the African region, access to ART remains weak; in 2012, fewer than 60 percent of HIV-positive TB patients were on ART. Furthermore, private sector engagement in TB care remains challenging, as the private sector is large, unregulated and growing in many countries and often provides services not in line with international standards of TB care.

As the U.S. Government revises its TB foreign assistance strategy to align with the global post-2015 TB goal of a world free of TB, the U.S. Government's focus will be on responding to both current challenges and future priorities. The new strategy will be ambitious and will require a dramatic scale-up of TB diagnosis and treatment, especially in vulnerable and poor populations. It will require advances in universal health coverage, economic development and poverty reduction; substantial investment in research and development to accelerate the availability of new TB tools; and widespread uptake of these new tools as they become available.

As we look to the future, sustained leadership at the global and country levels is necessary to achieve maximum impact. A sustained, robust U.S. Government response to the TB epidemic will be essential to achieving a world with zero TB deaths.

FY 2013 Highlights by Country

1 Afghanistan
USAID has focused its efforts on active case-finding through a variety of methods. Due to this support to the national program, the DOTS coverage increased from 21% in 2009 to 65.7% in 2013. Also, notification of all forms of TB cases improved by 76%. More importantly, TSR improved remarkably from 49% in 2009 to 91% in 2012.

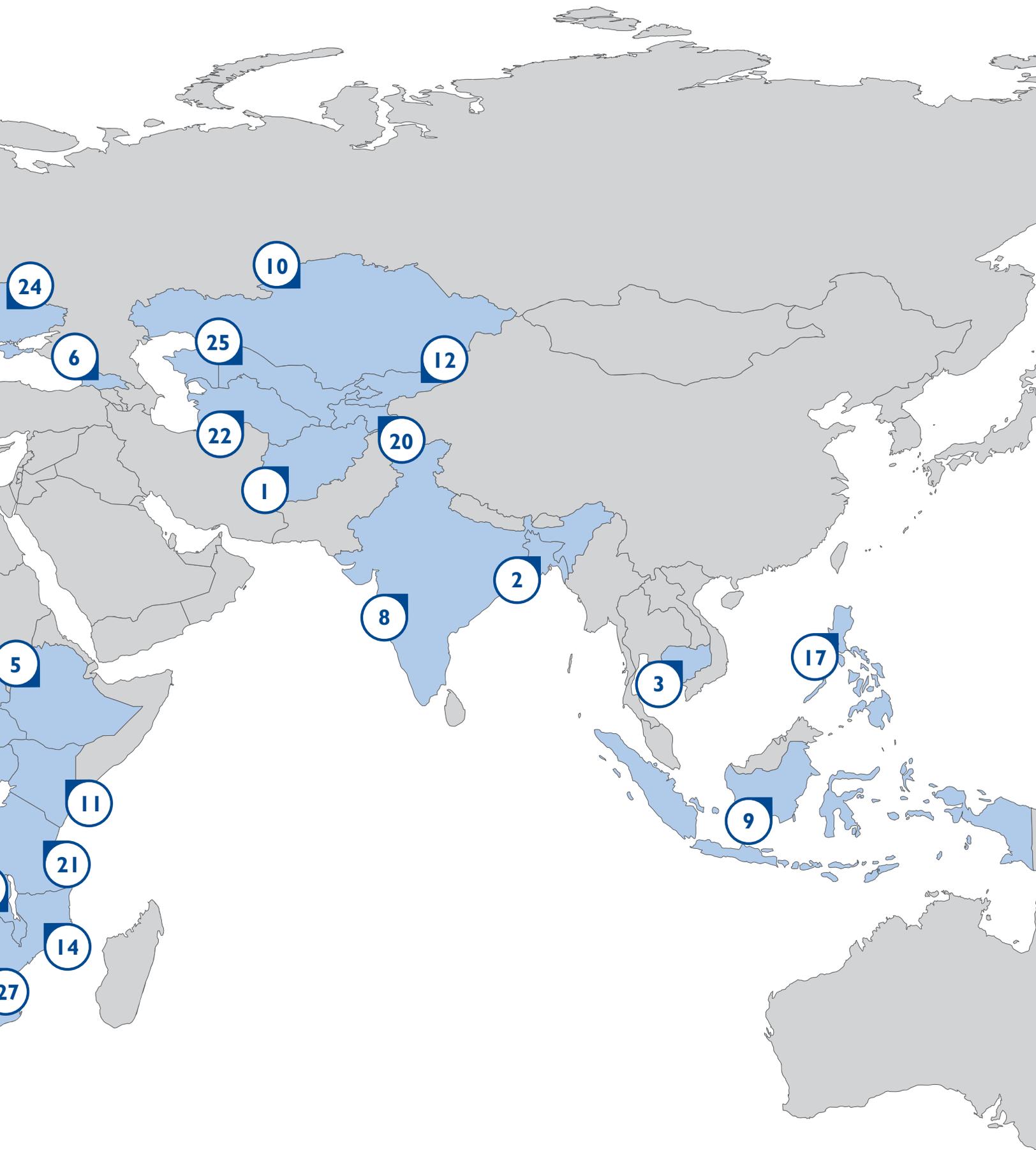
2 Bangladesh
In FY 2012, the number of TB cases notified increased by 16% with support from USAID's project. Also, 18 Xpert machines were successfully installed in strategic locations throughout the country, more than doubling the capacity of the country to better diagnose TB and DR-TB. These machines already identified 753 DR-TB cases.

3 Cambodia
Following intensive efforts to improve screening of MDR-TB patients with Xpert, 117 MDR-TB patients were diagnosed in 2012, a doubling in one year from only 56 MDR-TB cases diagnosed in 2011. 94% (110/117) of the MDR-TB patients diagnosed in 2012 were put on treatment.

4 DR Congo
During FY 2013, TB-HIV integrated activities were scaled up from 14 to 70 sites. As a result, 97% of the new TB patients were counseled for HIV testing, of whom 87% were tested for HIV. In these sites, 75% of the confirmed HIV-positive cases were placed on co-trimoxazole treatment, and 60% received ART.

5 Ethiopia
In the past three years, there has been a huge expansion in the availability of MDR-TB treatment centers. By FY 2013, more than 10 MDR-TB treatment centers were opened in six regions of the country. Enrollment has increased to more than 1,000 MDR-TB patients through sustained supply of second line drugs (SLD) and rollout of ambulatory care.





FY 2013 Highlights by Country

6

Georgia

As outpatient treatment for TB is introduced, it is critical to build up the capacity for early detection of TB patients. USAID has provided training to more than 1,000 primary care physicians and nurses in active and early TB detection, representing four regions and 38% of the population. The training resulted in increasing the TB referral rate from 6% in 2012 to 13% in 2013 in the target regions.

7

Ghana

In 2012, an assessment of the implementation of hospital TB case detection activities using USAID-supported standard operating procedures (SOPs) for TB case detection was conducted. The results showed that in USAID-supported hospitals there was a 46% increase in the number of TB cases detected and a 37% decline in deaths relative to the 2011 baseline.

8

India

By early 2013, all 692 districts in India could provide MDR-TB services and drug sensitivity testing for all smear-positive re-treatment cases with USAID-supported capacity-building efforts. In addition, USAID supported the roll-out of Xpert, resulting in a 36.5% increase in overall TB case detection in pilot sites and a MDR-TB detection rate 13 times greater than it had been.

9

Indonesia

In the areas where USAID introduced Xpert, the number of tests for DR-TB increased by almost 50% in FY 2012 and TB detection increased by 15%. Additionally, public and private hospitals newly engaged in FY 2012 contributed 13% of TB notifications in four major provinces of the country.

10

Kazakhstan

USAID's technical assistance, coupled with support from the Global Fund, has assisted the NTP in notifying and initiating treatment for 86% of estimated MDR-TB patients nationally. With the USAID-supported quality improvement model, MDR-TB treatment completion improved from 25% to 85% in the USAID pilot site.

11

Kenya

USAID-supported activities to increase participation of all care providers in TB care and treatment have shown major results. By 2013, the number of private treatment facilities providing TB services increased by 34% and 61% for diagnostic centers. In three years, with USAID support, private sector notifications contributed 10% of the national case-finding.

12

Kyrgyz Republic

In collaboration with partners, USAID assisted in closing the treatment gap for about 400 MDR-TB patients who were diagnosed but did not have access to second-line medicines. As MDR-TB services are expanded to outpatient facilities, referrals of TB patients in USAID pilots increased from 19% to 30%.

13

Malawi

USAID supported the expansion of TB treatment sites from 11 in 2010 to 73 in 2013 to increase access and improve TB detection. As a result, USAID-supported districts now account for 35% of all TB cases, up from 14% in 2010.

14

Mozambique

In FY 2012, USAID-supported community-based TB services expanded to cover almost 40% of the districts. Among the more than 28,000 symptomatic individuals referred by community-based volunteers to DOTS facilities, more than 15% were diagnosed with TB and started treatment, often with the support of the volunteer who provided the referral.

15

Namibia

To address the rise in drug-resistant TB in the country, USAID supported the development and implementation of a new case notification system. Due to this effort, 100% of all identified cases with any form of drug-resistant TB were initiated on treatment.

16

Nigeria

In FY 2013, USAID supported the establishment of 248 new TB DOTS clinics and 130 microscopy laboratories. Approximately 9,000 patients suspected to have TB have accessed TB diagnostic services through the U.S. Government's network of Xpert instruments, which detected more than 3,000 cases of TB.

17 Philippines
Through USAID support, the Philippines developed a MDR-TB training course to strengthen management of DR-TB in the Laguna region. Three months from workshop completion, the Satellite Treatment Center reported a significant increase in the number of referrals. The number of cases referred to the center each month increased six-fold in the first month. This approach helped the center detect more cases and enroll them immediately on treatment.

18 South Africa
USAID supported the government's effort to increase the number of MDR-TB treatment sites from 11 in 2009 to 45 in 2013. In addition, decentralization of care contributed to elimination of MDR-TB treatment waiting lists.

19 South Sudan
The number of health facilities providing TB services increased from 34 in 2008 to 82 in 2012, greatly improving access to TB services. There was a more than 25% increase in notified TB cases from 2008 to 2012. The average treatment enrollment time for TB patients in Juba City decreased from 12 to 3 days.

20 Tajikistan
With USAID support, more than 96% of PLHIV were screened for TB. The number of MDR-TB patients enrolled in USAID pilot sites increased by 2.5 times.

21 Tanzania
MDR-TB case notification more than doubled from 2012 to 2013. In addition, the introduction of Xpert in two USAID-supported sites contributed to detection of nearly half of the MDR-TB cases diagnosed and initiated on treatment.

22 Turkmenistan
USAID supported the development of an electronic database and a distance e-learning tool for TB care and treatment. Twelve distance learning training courses covering all aspects of TB were developed and will soon be available online.

23 Uganda
In September 2012, USAID operationalized two Xpert machines. As a result, a total of 4,028 specimens were processed in one year.

24 Ukraine
Through USAID support, the pilot phase of Ukraine's first ever TB Drug Resistance Survey (DRS) was completed. The full-scale DRS will be implemented in 2014 and will be able to accurately estimate levels of drug resistance among new and retreatment cases, not just at the country level, but also for regions and big cities.

25 Uzbekistan
With USAID support, a voucher referral system was successfully implemented for PLHIV and other key populations, and a national TB-HIV plan and guidelines for screening, testing, and treatment were developed.

26 Zambia
With USAID and PEPFAR support, a successful Three I's project was initiated in selected districts of the country. The Three I's is a comprehensive strategy targeting reduction of the TB burden among people living with HIV and has resulted in a strategic implementation of Xpert.

27 Zimbabwe
Diagnosis of drug-sensitive and drug-resistant TB was strengthened through training, support supervision, and introduction of Xpert, which made it possible to diagnose drug-resistant TB in a timely manner to prevent further spread in the community. In FY 2013, USAID procured 10 of the country's 36 Xpert machines, leading to the identification of 149 cases of MDR-TB, an increase from the 118 cases previously diagnosed.



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