Protecting the United States from the Health Security Risk of Global Tuberculosis

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A Report of the CSIS GLOBAL HEALTH POLICY CENTER
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Acknowledgments

From March to April 2017, CSIS convened a series of working group discussions with domestic and global TB experts on the greatest pressing issues in TB control, financing, research, and product development. This report resulted from those consultations. I am grateful to the working group and reviewers for their time and expertise. I also appreciate the input of CSIS colleagues, including research intern Oladeji Oloko for assistance with research and analysis.

This work was made possible by the generous support of the Bill & Melinda Gates Foundation.

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Audrey Jackson

Executive Summary

Tuberculosis (TB), an airborne infectious disease caused by the bacterium *Mycobacterium tuberculosis*, is the number one infectious disease killer in the world and among the top 10 causes of death worldwide. Moreover, numbers of drug-resistant forms of TB, currently 5 percent of global TB cases, are rapidly rising, posing a health security threat to the United States and the world. Cases of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) are difficult and costly to treat, and are often fatal. Epidemics of MDR-TB and XDR-TB can originate within U.S. communities or spread from other countries. To be effective in protecting Americans from a costly and potentially deadly disease, the U.S. government must address TB and drug-resistant TB both domestically and globally.

TB, including drug-resistant TB, is a growing global problem and world leaders are beginning to grasp the magnitude of the health threat, but have not yet committed the political will and resources to adequately address it. According to the World Health Organization (WHO), there were 10.4 million new cases of TB and 1.8 million deaths worldwide in 2015. Globally, HIV is the leading illness or condition that triggers the progression from inactive (i.e., latent) to active TB disease. Approximately 10 percent of TB patients globally are also infected with HIV, although the percentage of TB/HIV coinfection is as high as 60–70 percent in parts of sub-Saharan Africa. Each year there are approximately 600,000 new cases of MDR-TB and XDR-TB. Globally, only 20 percent of patients with drug-resistant TB receive treatment, and only half of those are treated successfully, meaning that the vast majority of patients with drug-resistant TB are continuing to spread disease until they die. If this situation persists globally, it is only a matter of time before the rising number of drug-resistant TB cases threatens Americans. The United States is not insulated from the rest of the world, and cannot afford to be complacent until it is too late.

It is more cost-effective for the U.S. government to invest in preventing the development and spread of drug-resistant TB epidemics globally than to respond to an epidemic in the United States. While the number of TB cases in the United States is currently relatively low, these

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1 Audrey Jackson is a senior fellow with the CSIS Global Health Policy Center in Washington, DC.
3 Ibid. MDR-TB is defined as TB that is resistant to rifampicin and isoniazid, the two most common TB drugs. XDR-TB is defined as TB that is resistant to all or nearly all first-line and second-line TB drugs. The figure of 600,000 also includes cases that are only resistant to rifampicin but must be treated with the same drugs as MDR-TB.
cases are costly financially and in terms of human suffering. Financial costs are often borne by the public health system, and an outbreak of MDR-TB or even a single case of XDR-TB can bankrupt the public health budget of a city or locality. There are about 10,000 cases of TB and roughly 100 cases of drug-resistant TB annually in the United States. Treatment of a typical patient in the United States with drug-sensitive TB costs about $18,000, an average case of MDR-TB costs $154,000, and an average case of XDR-TB costs $494,000. If there were an epidemic of drug-resistant TB, these costs could quickly add up. In the 1990s, a resurgence of TB linked to the rise of HIV/AIDS led to outbreaks of MDR-TB in New York City and other major cities. The extensive public health efforts required to control outbreaks in New York City alone cost at least $1 billion.

It is in the national interest of the U.S. government to invest resources wisely to prevent, detect, and treat TB cases at home and abroad. Several factors are coalescing to make this a possible turning point in the fight against global TB. Recent scientific and technological advances have brought forth new drugs, diagnostics, and service delivery technologies for TB care. Increased U.S. programmatic investments and technical advice at this moment can have a great impact on the global TB epidemic by helping to deploy these new tools more quickly to affected populations. U.S. scientific ingenuity is leading the way in TB research and product development, and there are promising new drugs, diagnostic technologies, and vaccine candidates in the pipeline. Internationally, world leaders are recognizing the impact of TB on their populations. It is a particularly opportune time for the United States to capitalize on the forward momentum and advance U.S. leadership on global TB control by working together with donor and affected countries to coordinate and amplify the impact of TB investments.

Yet the Trump administration’s budget proposal for Fiscal Year (FY) 2018 includes cuts to all the agencies and programs that are involved in addressing TB domestically and globally, including the U.S. Centers for Disease Control and Prevention (CDC), the U.S. Agency for International Development (USAID), the President’s Emergency Plan for AIDS Relief (PEPFAR), and the National Institutes of Health (NIH). The administration’s budget reduces the USAID bilateral TB program by 26 percent, the PEPFAR program by 18 percent, and the U.S. contribution to the multilateral Global Fund for AIDS, TB, and Malaria by 17 percent. It also cuts CDC’s domestic TB division by 8 percent and CDC’s global health funding by 20 percent. CDC does not receive direct funds for global TB and it leverages PEPFAR and other global health funding for its global TB activities. It is critical for Congress to work on a bipartisan basis with the administration on a negotiated FY 2018 budget and a forward-looking strategy that aligns with the health security challenges of TB.

To make the most of the newly available medical countermeasures, innovative scientific thinking, and burgeoning international political will, the time is ripe for a heightened U.S. focus on the global TB epidemic. We call for the U.S. government to invest strategically in

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domestic and global TB programs and research and development (R&D) that will contribute to ending the TB epidemic. In the short-term, there are existing and newly emerging treatments and diagnostics that can be deployed effectively to reduce the impact of TB in the United States and globally. Innovations in service delivery can enhance treatment outcomes and prevent the development and spread of MDR-TB and XDR-TB. Immediate and ongoing investments in R&D are also needed to stimulate new treatments, diagnostics, and ultimately a vaccine to end the global TB epidemic.

We recommend that the U.S. government take the following priority actions:

- Expand screening and treatment of inactive (or latent) TB in high-risk individuals in the United States, to reduce the pool of Americans who may develop TB or drug-resistant TB in the future

- Accelerate TB control in 10–15 countries of strategic importance to the United States by deploying increased resources and technical assistance, and rigorously monitoring the impact of interventions over a determined time period. Country selection should be based on criteria such as: high level of TB, TB/HIV, and MDR-TB burden, greatest sources of TB cases to the United States, demonstrated engagement on TB by political leadership, and demonstrated ability to partner with donors in implementing health programs. Based on demonstrated success, the U.S. government should then invest even more resources and expand this program into a presidential-level priority initiative similar to PEPFAR.

- Stimulate greater domestic investments for TB control in middle-income countries by engaging with national governments and by working with the World Bank and regional banks on additional financing mechanisms

- Support research and product development for the prevention, detection, and treatment of TB and drug-resistant TB

To support these actions, Congress should, through the budget and appropriations process, fulfill the U.S. commitment to the Global Fund, and increase funding, or at a minimum maintain level funding, in domestic, global, and R&D funding. In particular, we support the call for $450 million in FY 2018 for bilateral global TB control activities.

Introduction

Tuberculosis (TB), an airborne infectious disease caused by the bacterium *Mycobacterium tuberculosis*, is the number one infectious disease killer in the world and among the top 10 causes of death worldwide. Moreover, numbers of drug-resistant forms of TB, currently 5 percent of global TB cases, are rapidly rising, posing a health security threat to the United States and the world.

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According to the World Health Organization (WHO), there were 10.4 million new cases of TB and 1.8 million TB deaths globally in 2015. Case numbers of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) are rapidly rising, with approximately 600,000 new cases added every year.\(^9\) Treatment of MDR-TB and XDR-TB is more difficult than for drug-sensitive TB—usually requiring more medicines for a longer period; causes more significant side effects for patients; and more often fails, resulting in patient death. Globally, only 20 percent of patients with drug-resistant TB receive treatment, and only half of those are treated successfully,\(^10\) meaning that the vast majority of patients with drug-resistant TB are continuing to spread disease until they die. If this situation persists globally, it is only a matter of time before an epidemic threatens Americans.

An epidemic of drug-resistant TB that is primarily transmitted from person to person poses a threat to U.S. and global health security. Drug-resistant TB arises in one of two ways. When TB treatment is not effective or patients do not successfully complete a course of treatment, drug-resistant TB strains can grow and multiply in the patient, leading to “acquired” drug-resistant TB. Drug-resistant TB bacteria can also be transmitted directly from an infected person to someone who has never been treated for TB. Multiple studies have shown that as an epidemic takes hold in a region, more patients get MDR-TB or XDR-TB directly through airborne transmission.\(^11\) Recent studies suggest that the majority of drug-resistant TB cases are now due to person-to-person transmission of a drug-resistant infection, and that the burden of drug-resistant TB will continue to grow.\(^12\)

To be effective in protecting Americans from a costly and potentially deadly disease, the U.S. government must simultaneously address TB domestically and globally because epidemics of MDR-TB and XDR-TB can originate within U.S. communities or spread from other countries. In the short term, there are existing and newly emerging treatments and diagnostics that can be deployed effectively to reduce the impact of TB in the United States and globally. Innovations in service delivery can enhance treatment outcomes and prevent the development and spread of MDR-TB and XDR-TB. Immediate and ongoing investments in R&D are also needed to stimulate new treatments, diagnostics, and ultimately a vaccine to end the global TB epidemic.

**Tuberculosis and U.S. Health Security**

It is more cost-effective for the U.S. government to invest in preventing the development and spread of drug-resistant TB epidemics globally than to respond to an epidemic in the United States.\(^13\)

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\(^9\) Ibid.
\(^10\) Ibid.

States. While the number of MDR-TB and XDR-TB cases in the United States is relatively low—89 patients in 2015—these cases are costly financially and in terms of human suffering. Financial costs are often borne by the public health system, and an outbreak of MDR-TB or even a single case of XDR-TB can bankrupt the public health budget of a city or locality. If there were an epidemic of drug-resistant TB, these costs could quickly add up. In the 1990s, a resurgence of TB linked to the rise of HIV/AIDS led to outbreaks of MDR-TB in New York City and other major cities. The extensive public health efforts required to control outbreaks in New York City alone cost at least $1 billion.\footnote{13}

TB in the United States exerts a toll on patients and the health care system through medical costs, loss of income, and impact on quality of life. Curative treatment of a typical patient with drug-sensitive TB requires a 6-month regimen of four drugs and costs about $18,000 in the United States. Patients diagnosed with MDR-TB are usually treated with a more complicated treatment regimen for 18–24 months, and an average case in the United States costs $154,000. A patient with XDR-TB requires a much longer treatment regimen and longer hospitalization, costing on average $494,000 per case. Furthermore, when additional costs are tallied, including the loss of productive working time and loss due to untimely death, the estimated societal cost of TB in the United States is $450 million per year.\footnote{14}

Outbreaks of TB and drug-resistant TB in the United States often arise in schools, health care facilities, correctional facilities, and homeless shelters. Children and adults who receive services or work in these settings can be at risk of contracting TB. Americans who were born in, have lived in, or traveled to a high-TB-burden country are also at risk of having been infected abroad. For example, 2.3 million Americans travel every year to India and China, two of the 30 countries on the WHO list of TB high-burden countries.\footnote{15} Americans have ongoing ties to other high-burden countries, including through business ties, trade, tourism, family relationships, and other connections. Isolationist rhetoric and policies, including any attempts to close national borders in the event of a transnational epidemic, would not be effective for disease control. Indeed, such actions would be detrimental to multiple U.S. goals, including trade, health, and scientific relationships.

Through the diligent work of health care workers and public health professionals in state, local, and territorial TB control programs, with federal support from the U.S. Centers for Disease Control and Prevention (CDC), there are now fewer than 10,000 TB cases annually in the United States.\footnote{16} The number of TB cases in the United States had been steadily falling every year since 1992, but has leveled out in the last few years.

When an individual encounters someone with active TB and becomes infected, he may become sick relatively quickly or his immune system might be able to hold the bacteria in check. Approximately one-quarter of the world’s population is infected by inactive, or latent, TB, but only a small number—10 percent—will ever progress to active TB disease. People with latent TB do not have symptoms and cannot infect others. Because there are currently no medical tests to predict which people with latent TB will progress to active TB, most people in the world with latent TB do not get tested and treated. However, it is known that some people with latent TB are at higher risk of progressing to active TB. Many of those who develop active TB disease have another illness or condition that stresses their immune system, such as HIV/AIDS, diabetes, or smoking.

In a low-TB-burden country such as the United States, a program of screening and treating latent TB in high-risk populations is necessary to eliminate TB and prevent the rise of drug-resistant TB. High-risk populations include health care workers, correctional facility workers, and immigrants from high-burden countries. Current screening programs for immigrants and refugees entering the United States are effective in the identification and treatment of those with active cases of TB, but the program can be expanded. The expanded screening and treatment should be carefully conducted based on medical and public health evidence, in order not to provoke anti-immigrant sentiments. Such sentiments would heighten fear among the immigrant population and would be detrimental to public health disease control goals. Furthermore, recent data from the CDC demonstrate that most immigrant Americans who are sick with TB today did not enter the United States sick, but may have come to the United States 10 or more years ago with latent TB. Screening and treatment of latent TB in high-risk populations in the United States will prevent the development of active TB later in life, as recommended by the U.S. Preventive Services Task Force.

As the United States learned from the 2014 Ebola epidemic, the best way to protect Americans is to reduce the health security threat both at home and globally. In addition to expanding screening and treatment, the U.S. government should engage with the governments of countries that are the biggest source of TB cases in the United States on

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**Kenni’s Story**

Kenni, a Texas resident, dental hygienist, and mother of two, became very sick in 2012. After numerous misdiagnoses, she finally learned she had TB. Several weeks after her initial symptoms, she began TB treatment. She continued her treatment regimen for 9 months with a nurse assigned to observe her take her pills daily. Kenni finished her treatment and has been TB free. She doesn’t know where or how she became infected with TB but she regrets that it took so long for a diagnosis. “I wanted to tell my story so others can see that TB still happens in this country, and can happen to anyone,” says Kenni. “The good news is that once you get a correct diagnosis and get on the right treatment, you will start to get better.”

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strategies to control TB in those countries. For the lower-middle-income countries in this category (e.g., Philippines), the United States should provide direct assistance and technical support. For the upper-middle-income countries in this category (e.g., Mexico), the United States should use high-level diplomacy to persuade these governments to expend more domestic resources on TB, and U.S. officials should work with their counterparts to help develop TB control and research plans with feasible targets.

U.S. Leadership in Tuberculosis Control Policy and Programming

To reduce the health security threat to the United States from drug-resistant TB, the U.S. government should strengthen its leadership role in improving the detection, treatment, and prevention of both drug-resistant and drug-sensitive TB globally. As the number one infectious disease killer in the world, TB was responsible for the death of 1.8 million people in 2015, as noted earlier. The tragedy of this statistic is that there are existing and newly emerging medical products available to diagnose and cure TB, including drug-resistant TB. The global TB epidemic can be impacted in the short term by the deployment of emerging innovations in medical products and technology, and ended in the long term with new tools as a result of continued R&D.

U.S. scientists and developers in the academic, pharmaceutical, product development partnership, and public sectors have led the way in developing the latest diagnostics, medicines, and technology for TB. The U.S. government can display American expertise and leadership by aiding in the delivery of the medicines, diagnostics, and technologies to populations where they will have the greatest impact on the TB epidemic. By doing so, the government will also provide an enabling environment for companies and public-private partnerships to continue engaging in the development of new medical products and technologies.

In addition to reducing a health security threat and promoting U.S. leadership in health innovations, the United States would see additional benefits from playing a strong role in ending the TB epidemic globally. As a global economic leader, the United States has often acted on a moral imperative to assist in humanitarian causes and ease suffering and illness when possible. TB is an age-old disease that has long been underfunded and that afflicts the poorest populations, limiting their ability to engage in their own economic development. Many high-burden countries are important trading partners for the United States, and ultimately the United States would benefit from the gains in health and economic development that occur in these countries. Moreover, countries with healthy populations and a growing economy also tend to be more stable politically.

There are several challenges to global TB control, including lack of funding, weak health systems, outdated tools, unavailable or poor-quality drugs, and lack of awareness among political leaders and the general public of the impact of TB. In 2015, an estimated 10.4 million people developed a new case of active TB worldwide. Only 60 percent of these people were

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20 The figure of 1.8 million deaths includes 400,000 deaths of persons who were coinfected with HIV and TB.
accurately diagnosed and reported to their national public health system, which is critical for tracking important public health threats such as TB. To end the epidemic by 2035, the WHO and Stop TB Partnership have declared that 90 percent of those with TB need to be accurately diagnosed and reported.21 In many high-burden settings, finding and diagnosing people with TB is a major hurdle. Treatment completion rates must also be improved. In 2014, 83 percent of TB patients completed treatment, and the WHO and Stop TB Partnership have set a global goal of 90 percent treatment completion. Despite the resources committed by national governments of high-burden TB countries, donor governments, nongovernmental organizations, and other sources, a significant global financing gap remains, currently estimated to be an annual gap of $2 billion. In the current era of limited resources, it is important to think about new ways of doing business that will support the efficient use of resources.

The U.S. government plays a significant role in global TB control, in partnership with host-country governments, other donors, and multilateral organizations like the Global Fund to Fight AIDS, Tuberculosis, and Malaria (Global Fund). The U.S. Agency for International Development (USAID) leads U.S. global TB activities and the Office of the U.S. Global AIDS Coordinator (OGAC) leads activities related to TB/HIV coinfection as part of the President’s Emergency Plan for AIDS Relief (PEPFAR).22 USAID supports the Global Drug Facility at the Stop TB Partnership to facilitate access to quality-assured anti-TB drugs globally. CDC provides technical expertise on laboratory networks, surveillance systems, infection control, and capacity development. The National Institute of Allergy and Infectious Diseases (NIAID) leads U.S. TB research activities and collaborates with other components of the National Institutes of Health (NIH), including the Fogarty International Center, to support international research and training for TB. Other agencies also play a role in TB activities, including the Department of Defense (DOD) though its overseas laboratories. Each of the U.S. government agencies involved in the international response to TB contributes uniquely with its particular set of core competencies, and should strengthen efforts to work in an integrated, whole-of-government approach to end the TB pandemic.

U.S. funding for global TB and TB/HIV programs is primarily appropriated to USAID and to OGAC for PEPFAR and the Global Fund. NIH is appropriated funding for research and spending on TB research is determined at the level of the Institute. In FY 2017, USAID received $241 million for TB activities, a slight increase of $5 million to a budget that has generally remained flat since 2010. Indeed, in each of the last three budget cycles, the administration proposed a 19 percent reduction in the USAID bilateral TB budget and congressional lawmakers rejected the cut, resulting in flat funding. PEPFAR allocated $118 million in FY 2016 to TB/HIV-related programs, which are implemented primarily through CDC, USAID, and DOD.23 CDC does not receive direct funding for global TB activities, but

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utilizes funding from various other U.S. government programs, including USAID bilateral funding, PEPFAR, and the Global Health Security Agenda (GHSA). NIH funding for TB research amounted to $302 million in FY 2016, primarily from NIAID.24

The United States has pledged $4.3 billion to the Global Fund for the period 2017–2019, subject to congressional appropriations, and Congress approved $1.35 billion for FY 2017. The Global Fund serves as the largest donor program for TB services globally. The Global Fund spends approximately 18 percent of pledged contributions on TB programs, and there are important synergies realized between Global Fund activities and U.S. TB and TB/HIV programs. For example, in many high-burden countries, grants from the Global Fund support the procurement and distribution of drugs for TB and MDR-TB while U.S.-funded bilateral programs support community and clinic-based management of TB patients, procurement and operation of diagnostic instruments, and technical assistance such as guidance on laboratory services. U.S. funding to the Global Fund stimulates spending from other donors and from host governments. The United States incentivizes additional donations to the Global Fund by requiring other donors to invest $2 for every $1 of U.S. investment. The Global Fund also requires grantee governments to spend a minimum proportion of their domestic budget on health. Through these policies, everyone does their part to contribute to improving TB control. The Global Fund has recently received positive ratings by independent organizations assessing its organizational effectiveness and impact.25 Data from the Global Fund illustrates that every $100 million invested provides TB treatment and care for 153,000 people; provides MDR-TB treatment for 4,300 people; and spurs domestic health investment of $300 million, among other outcomes. The United States should continue to fulfill its commitment to the Global Fund with FY 2018 appropriations of $1.45 billion.

The Trump administration’s budget proposal for FY 2018 includes cuts to all the agencies and programs that are involved in addressing TB domestically and globally, including CDC, USAID, PEPFAR, and NIH.26 The administration’s budget reduces the USAID bilateral TB program by 26 percent, the PEPFAR program by 18 percent, and the U.S. contribution to the multilateral Global Fund for AIDS, TB, and Malaria by 17 percent. It also cuts CDC’s domestic TB division by 8 percent and CDC’s global health funding by 20 percent. It is critical for Congress to work on a bipartisan basis with the administration on a negotiated FY 2018 budget and a forward-looking strategy that aligns with the health security challenges of TB.

We propose that the U.S. government scale up global TB program activities in a core set of prioritized countries to accelerate the fight against TB in those countries. Currently USAID

supports activities primarily in 23 prioritized low-income and lower-middle-income countries, and additional support from USAID, CDC, and other agencies reaches a total of approximately 50 countries. According to USAID, new TB cases have decreased 19 percent and deaths due to TB have decreased 30 percent in supported countries since 2000. If the U.S. government wants to contribute to ending the global TB epidemic by 2035, it must be able to show greater reductions in TB cases and deaths more quickly. We believe that the United States can effect greater impact by scaling up activities in approximately 10 to 15 priority focus countries, deploying new tools in a targeted manner, innovating programs and service delivery, and rigorously tracking spending and outcomes to demonstrate the return on investment. Recently, congressional leaders asked their colleagues to support appropriations of $450 million for bilateral TB activities. This additional funding would enable agencies to begin scaling up activities in selected countries, while maintaining current activities in the remaining countries.

U.S. government agencies, including USAID, CDC, and OGAC, should collectively develop a strategy that includes selecting these high-priority countries based on several criteria, including high level of TB, TB/HIV, and MDR-TB burden, greatest source of TB cases to the United States, demonstrated engagement on TB by political leadership, and capacity to be strong partners in implementing donor-funded programs. In the prioritized low-income and lower-middle-income countries, current activities should be expanded and intensified. Specific interventions will be tailored by country need, but will cover activities such as detection and treatment of TB, including drug-resistant TB; infection control to prevent the spread of TB and drug-resistant TB; preventive TB therapy for persons living with HIV; integration of services for patients with TB and HIV; and innovations in service delivery, including greater use of adherence technology and community management of drug-resistant TB. In prioritized upper-middle-income countries like South Africa, which are already financing 87 percent of their TB control programs, U.S. activities should focus on high-level diplomacy, technical advice, and sustainable financing mechanisms.

A recent report from CSIS examined opportunities for strengthening the effectiveness of U.S. global TB programs.\textsuperscript{27} The authors identified a number of critical requirements for an effective government-wide program: a coherent and inclusive strategy, sufficient funding, visible high-level leadership, coordination of policy and program implementation, and periodic external program evaluations. They recommend 1) the appointment of a focal person to lead “whole-of-government” U.S. government global TB efforts; 2) increased funding for global TB control to USAID and CDC; and 3) an external, independent evaluation of the entirety of the U.S. government global TB enterprise. We endorse these recommendations and agree that greater effectiveness in global TB control will require a higher level of commitment and focus from the U.S. government. We recommend that the first step be to scale up resources and intensify the fight against TB in 10–15 countries, while rigorously monitoring the impact of the focused resources. Demonstrated success in these countries will provide Congress with the evidence and rationale to increase resources further and expand program implementation. Ultimately, ending the global TB epidemic will require

bold new vision, leadership, and multiyear commitment, such as a presidential-level initiative with strong legislative and budgetary authorities as exist for PEPFAR and the President’s Malaria Initiative (PMI).

Toward Sustainable Global Financing for Tuberculosis Control

Global TB control has been recognized by economic experts as a best buy in global public health and worthy of investment even given limited resources. Economists have long argued that TB treatment, particularly treatment of drug-sensitive TB, is relatively inexpensive and very effective. On average it can give an individual 20 additional years of productive life, providing substantial benefits in terms of health and economic productivity. Yet global TB control remains underfunded. To end the epidemic by 2035, as outlined in the WHO End TB Strategy and endorsed by member states at the World Health Assembly, significantly more resources are needed from both domestic and international sources. Multiple sources estimate that there is a gap of approximately $2 billion annually between the current funds available for TB control and the funds needed to meet the 90 percent diagnosis and treatment outcome targets in the End TB Strategy.

In *The Global Plan to End TB 2016–2020*, the Stop TB Partnership presented modeling estimates demonstrating that $65 billion invested over that five-year period would result in 90 percent of people with TB diagnosed and started on treatment, with 90 percent treatment success by the year 2020. If the global community can marshal those resources, 29 million people will be treated, 45 million cases of TB will be prevented, and 9.5 million lives will be saved. The average return on investment is projected to be $85 for each dollar invested.

High-burden TB countries can be thought of roughly in two categories: upper-middle-income countries that are largely financing their own TB programs, and the poorer countries that will continue to need international assistance to fight TB. The single largest source of international TB financing is the Global Fund. Figure 1 shows how the $65 billion would be invested—14 percent ($9 billion) in R&D and the remainder on TB control activities (e.g., diagnosis, treatment, and prevention). Fifty-four percent of the expenditures ($35 billion) would occur in high-income and upper-middle-income countries, including most of the BRICS (i.e., Brazil, Russian Federation, China, and South Africa; India is a lower-middle-income country). These countries already finance almost all of their TB control programs and it should be a U.S. diplomatic priority to urge their governments to increase domestic health spending on TB until the health system can diagnose and successfully treat 90 percent of those with TB. The United States and other donor countries should work with the World Bank and regional banks to develop new financing mechanisms particularly for upper-middle-income countries that cannot benefit from Global Fund and other donor programs. The remaining 33 percent ($21 billion) would be needed for program implementation in low-

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income and lower-middle-income countries, which rely almost exclusively on international sources for financing of TB control programs.

In addition to scaling up U.S. government investments in TB control as outlined in the previous section, the United States now has an opportunity to help lead the international community in an unprecedented coordinated assault on TB, which has the promise of significantly reducing the impact of TB globally. In the past few years there has been increasing engagement in the fight against TB by the governments of several countries and most recently by the collective international community through the United Nations. South Africa’s Minister of Health Aaron Motsoaledi, who chairs the Stop TB Partnership Coordinating Board, has pressed for increased investments and engagement from his own government, from other high-burden countries, and from the international community. Last year he led a call for the United Nations to convene a High-level Meeting on TB, which will be held in 2018. In the lead-up to the UN High-level Meeting on TB, the WHO is cohosting a global ministerial conference on TB to be held in Moscow in November 2017. The global ministerial conference will be an opportunity for representatives of high-burden countries and other governments to engage in dialogue and make commitments to actions that are needed for progress in the fight against TB.

Other countries are also stepping up efforts. India, the only lower-middle-income BRICS country, has made significant strides in the past few years, starting with the development of more accurate estimates of TB cases in the country and efforts to expand diagnosis and treatment of drug-sensitive and drug-resistant TB. In early 2017, the government of India committed to eliminate TB in India by 2025. Traditional donor countries such as the United Kingdom and Canada are also expressing interest in increasing their TB control investments and collaborating with other governments to maximize their contributions. The United States

![Figure 1: Investments Needed to Impact the Global TB Epidemic, 2016–2020 ($B)](image_url)
could partner with the United Kingdom and Canada in a new alignment on TB that would leverage each country’s resources.

Private-sector engagement should be prioritized and expanded. The private sector plays a key role in research and product development, which is highlighted in the next section. In addition, the private sector can play greater roles in developing and implementing innovative health care delivery solutions; workplace health programs; communication and community outreach; and financing solutions, among other areas.

There is clearly a momentum of political will building internationally, and this is an ideal moment for governments, the private sector, and other stakeholders to amplify and expand TB control efforts. At this critical moment, the United States should continue and even expand its leadership in global TB control. The U.S. government can maximize the return on U.S. investments by engaging productively with the governments of high-burden countries such as India and South Africa, working collaboratively with other international donors such as the United Kingdom, and through effective multilateral instruments such as the Global Fund, WHO, and the Stop TB Partnership.

U.S. Leadership in Scientific Innovation and Research and Development for Tuberculosis

Although TB research has been chronically underfunded, scientific and medical progress has been made recently through funding from the public and private sectors, which has enabled the diligent work and collaboration of academic researchers, product development partnerships, biotechnology, and pharmaceutical companies. The first new classes of TB drugs in decades were approved in 2012 and 2014 to be included in combination treatment regimens for MDR-TB patients. Faster and more accurate TB diagnostic tests have been endorsed by the WHO and are being procured and implemented in many country settings. National TB control programs are adopting novel treatment regimens for MDR-TB that shorten treatment from approximately 20 months to 9 months. Innovations in service delivery, such as expanded community management of MDR-TB patients, have enabled patients to spend less time hospitalized and have freed up hospital beds for additional patients. Yet many challenges remain that require new advances in product development and service delivery.

Continued support is needed for treatment R&D and policies designed to improve the availability of new drugs to patients in need. Current treatment regimens for TB and drug-resistant TB are still of long duration, can be accompanied by serious side effects such as hearing loss, and for drug-resistant TB include some period of hospitalization, which increases treatment costs and relies on weak health systems in many parts of the world. Combination therapies are required to treat TB, but the clinical development and regulatory approval for combination treatment regimens is more complicated than for a single therapy. Recent trials of novel combinations and repurposed old drugs are promising, and would benefit from increased funding. There is also an opportunity to develop safer, faster-acting, longer-acting drugs for the treatment of latent TB, which could be used more widely than current therapies for latent TB and would contribute to turning off the tap of new active TB
cases. Although two new TB drugs, bedaquiline and delamanid, were conditionally approved in the past five years based on interim clinical trial data, there has been poor availability to patients. Barriers to availability include lack of a regulatory license for the drug in LMICs, financial cost, fears of drug resistance, and lack of clear guidelines for patient use.

Innovations in technology and service delivery are needed to improve diagnosis and patient management for both drug-sensitive TB and drug-resistant TB. Diagnostic testing for TB generally takes from two to seven days and depends on a number of factors, including the testing methodology used and the availability of health care personnel to obtain patient samples, deliver samples to a testing facility, run the testing load in a given facility, and relay results back to the treating clinician. New diagnostics are needed that shorten the testing time and are suited for low-resource settings. With the support of donor funds and technical assistance, many national TB control programs are deploying advanced molecular diagnostic tests such as GeneXpert that enable identification of TB and drug-resistant TB. However, in addition to the cost of the GeneXpert machine, each test requires a $10 cartridge and additional consumable supplies, such as gloves and testing solutions. A consistent and reliable power source is also needed, which is a challenge in many low-resource settings. Finally, new diagnostic tests can have the maximum impact on TB control if test results can be quickly linked to patient treatment. For example, if a test result identifies MDR-TB, there must also be a hospital bed available for the patient to begin treatment.

Early diagnosis and rapid treatment of TB help prevent TB transmission, but additional prevention efforts are needed. The only available TB vaccine, BCG, is only effective in children and its effectiveness diminishes over time. An effective vaccine that provides lifelong immunity could be a game-changer in controlling and ultimately ending the epidemic. The development and dissemination of better infection control guidelines is critical to preventing the spread of TB and drug-resistant TB among patients and health care workers in health facilities.

Additional research needs to include a significant focus on pediatric research and greater investment into operational and implementation science. Operational and implementation research are growing and important fields that provides data on how medical products and technologies can be scaled up and integrated within a real-world health care system. This research helps the health community utilize medical products and technologies for maximum impact on disease.

Research spending also provides benefits beyond specific product development for TB. For example, the scientific knowledge gained from understanding how the immune system functions can have benefits for other diseases. Conducting research and clinical trials outside of the United States, where most TB patients reside, helps build capacity in these countries for research on TB and other global health diseases. Finally, investing in laboratory and surveillance networks is critical to global health security. Better global surveillance on drug-resistant TB is a key component of protecting the United States from a transnational MDR/XDR-TB epidemic.
The nongovernmental organization Treatment Action Group has tracked global funding for TB R&D since 2005.\textsuperscript{31} From 2011–2015, funders invested $3.29 billion in TB R&D, only one-third of the $9 billion needed, as estimated by the Stop TB Partnership. In 2015, they report that funding for TB R&D fell to $621 million, the lowest level since 2008. In order to achieve any of the research and product development goals outlined here, the trajectory of funding research must be turned around. Increased commitment from the public and private sector is needed to save lives, ease suffering, and end the global TB epidemic. Continuous investment is critical for the best research outcomes because research studies build on prior studies and can take unexpected turns. If the United States and the global community waits until a disease outbreak to invest in research, the needed medical products will not materialize overnight.

The U.S. government is the major funder of TB R&D, with most funding support coming from NIH, including NIAID, and to a lesser extent USAID and CDC. Continued and increased appropriations from Congress will enable U.S. government agencies to fund needed TB research and product development. American nonprofits and private-sector companies are also playing a leading role in funding and conducting research. There is an opportunity for the United States to expand its leadership role in R&D and innovation, stimulate new involvement from the private sector, and increase collaborations with partners in affected countries, particularly in the BRICS and other middle-income countries.

**Recommended U.S. Government Actions to Protect the United States from the Health Security Risk of Tuberculosis**

**Domestic U.S. TB Programs**

- Expand TB screening by CDC of various visa holders from high-burden countries, including immigrants, refugees, long-term visitors, workers, and students\textsuperscript{32}

- Screen and treat latent TB in high-risk individuals, including those who were residents of high-burden TB countries\textsuperscript{33}

**Global Programs**

- USAID and CDC, working with OGAC and other relevant agencies, should select 10–15 priority countries for scale-up of global TB activities based on criteria such as: high level of TB, TB/HIV, and MDR-TB burden, greatest sources of TB cases to the United States, demonstrated engagement on TB by political leadership, and demonstrated ability to partner with donors in implementing health programs


• Strategically deploy additional resources and technical assistance in select countries and rigorously monitor the impact of interventions
  
  - Increase diagnosis through active case-finding, expanded community interventions, and greater use of molecular diagnostic testing
  
  - Analyze the diagnosis and treatment cascade in each setting to understand how, where, and when patients access diagnosis and treatment, and identify interventions to optimize services
  
  - Deploy human resources (e.g., doctors, nurses, community health workers) and technology (e.g., information communication technology for adherence) to address identified gaps in patient-centered care
  
  - Provide technical assistance to improve infection control protocols
  
  - Support health information systems to improve data-gathering and utilization
  
  - Support capacity-building of laboratories and surveillance networks
  
  - Integrate TB and HIV control programs more fully at all levels, from local health facilities to national programs
  
  - Conduct routine screening for TB in all persons living with HIV, with immediate TB treatment for those who test positive and TB preventive therapy for those who test negative
  
  - Support the use of appropriate diagnosis and treatment guidelines in both the private and public sectors, and improve systems to ensure that cases identified in the private sector are reported to and incorporated into national surveillance systems
  
  - Work to eliminate out-of-pocket costs for patients for TB diagnosis and treatment

• Prioritize activities designed to prevent, diagnose, and treat MDR-TB
  
  - Support the widespread adoption of the WHO-approved nine-month treatment regimen for MDR-TB
  
  - Support the expansion of community-based MDR-TB care
  
  - Improve infection control measures and provide technical assistance to prevent the spread of MDR/XDR-TB
  
  - Train health care workers to conduct contact investigations to identify, evaluate, and monitor MDR-TB contacts
o Support the uptake of next-generation diagnostic tools that are faster and better suited for low- and middle-income country settings

- Elevate TB as a priority at the highest levels of the government, and organize internally to combat global TB more efficiently
  
  o The executive branch and the U.S. Congress should appoint a single focal person with full responsibility for leading U.S. global TB efforts. For long-term success of U.S. global TB activities, the leader should be supported by a presidential-level initiative and with legislative authorities similar to those provided by Congress for the leadership of PEPFAR and the President’s Malaria Initiative, including budget authority for the entirety of the program.

  o Congress or the executive branch should request and fund an independent program evaluation of all U.S. government activities that relate to global TB and the linkage of global TB to TB in the United States. The scope of this evaluation should include specific recommendations for an administrative and leadership structure.

Financing and International Leadership

- Avoid backsliding on U.S. government investments for global TB control, and provide robust resources through USAID, CDC, PEPFAR, and other relevant agencies and programs
  
  o Congress should, through the budget and appropriations process, increase funding to USAID and CDC for global TB control activities to at least $450 million annually

  o Fulfill the U.S. commitment to the Global Fund for 2017–2019

- Advance U.S. leadership on global TB control through enhanced collaboration with other donor countries to coordinate and amplify the impact of TB investments

- Develop desired outcomes for the 2018 U.N. High-level Meeting on TB through the U.S. government interagency process and by engaging with external stakeholders

- Raise the importance of global TB control and financing at international forums such as the G-7 and G-20 Summits

- Stimulate greater domestic investments for TB control in middle-income countries by engaging with national governments and by working with the World Bank and regional banks on new financing mechanisms

- In coordination with country leadership, urge prioritization of TB as a focus of global health security activities, including building surveillance and laboratory capacity
• Continue to integrate TB into national and global AMR policy priorities, including ongoing outcomes from the United Nations High-level Meeting on AMR in 2016

Research and Product Development

• Provide robust resources to support research and product development funding at NIAID, CDC, USAID, the NIH Fogarty International Center, and other relevant agencies
• Advance R&D of novel vaccines
• Support the development of new tools and approaches for detection of drug-sensitive and drug-resistant TB
• Improve surveillance and analysis of the country-specific drivers of TB transmission globally
• Support research to identify biological markers to help detect latent TB and progression to active TB
• Support the development of novel drugs and shorter treatment regimens for drug-sensitive, drug-resistant, and latent TB
• Work with the pharmaceutical sector, national medicines regulatory authorities, and relevant international organizations and nongovernmental organizations to approve new treatment regimens for MDR/XDR-TB and to promote access to new drugs
• Increase capacity to conduct biomedical and clinical research on TB in TB-endemic countries through training and technical assistance
• Promote domestic resource mobilization by affected countries in research through high-level diplomacy
• Promote the inclusion of TB in U.S. government R&D initiatives for antimicrobial resistance, including at the Biomedical Advanced Research and Development Authority
• Improve support for pediatric TB R&D, including new drug formulations and better diagnostics
• Support research on improved infection control and other prevention methods
Protecting the United States from the Health Security Risk of Global Tuberculosis

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