Tackling Tuberculosis Abroad

The Key to TB Elimination in the United States

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A Report of the CSIS Global Health Policy Center

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Global Burden of TB

Tuberculosis is the second-leading cause of death from infectious disease and the leading cause of death among people living with HIV (PLHIV). Ambitious global targets set nearly 15 years ago called for the elimination of TB as a public health threat by 2050, which was defined as reducing cases below one per million population. Meeting this target would require 20 percent annual reduction in TB incidence globally. Today, the annual rate of decline is approximately 1 percent.\(^2\)

Since 2003, a renewed global commitment to expand access to care has supported the development of new tools, medicines, and strategies to prevent and control TB. Between 2001 and 2011, bilateral U.S. government support for global TB control nearly quadrupled to $238 million, while multilateral assistance was also increasing dramatically through contributions to the Global Fund to Fight AIDS, TB, and Malaria (GFATM). Growing U.S. government support paired with cost reductions of drugs, commodities, and new diagnostics have made it possible to scale up TB control activities in countries hit hardest by TB. Due to expanded global TB efforts, 56 million people have been successfully treated and 22 million lives saved since 1995.\(^3\)

Despite these achievements, TB remains an urgent global health challenge. The World Health Organization (WHO) estimates that nearly one in three people has latent TB

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\(^3\) Ibid.
infection. In 2012, 8.6 million people developed active TB disease, and 1.3 million people died from TB. Each year, nearly 3 million of those with active TB disease are not diagnosed. Some regions of the world will not meet Millennium Development Goals to reduce the number of TB cases and deaths. Many of the hardest-hit countries struggle to address HIV-associated TB (TB/HIV) and the rise of drug-resistant TB.

TB programs in the highest burden countries often face funding gaps and technical challenges, limiting the ability to diagnose and successfully treat cases or invest in strategies to prevent transmission. Further, countries with emerging economies and high TB burdens are now struggling with how to involve the private and informal health sectors in TB control efforts. These providers offer opportunities for access to care for people with TB, but they may undermine fundamental TB control principles and fuel drug resistance through inadequate or inappropriate case management and treatment practices. International travel and migration are changing the epidemiology of TB in low-incidence countries like the United States. The reality is that TB anywhere is TB everywhere—which is why the challenges of addressing TB in high-burden countries must be met with a coordinated and focused global response.

**Active TB Disease**

Some people develop TB disease within weeks of becoming infected before their immune system can fight off the bacteria. Other people may get sick years later when their immune system becomes weak for another reason. The TB bacteria multiply, causing the person to become sick, contagious, and develop TB signs and symptoms. TB disease is diagnosed through a combination of clinical examination, chest radiograph, and microbiological techniques (e.g., smear microscopy, culture). Depending on the type of TB diagnosed, treatment of TB requires combination therapy with at least four anti-TB drugs for between six months and two years (if the bacterium is resistant to certain drugs).

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**TB in the United States: A Reflection of the Global Burden**

TB was once the leading cause of death in the United States. But with general improvements in health systems and the introduction of effective TB drugs in the 1940s, TB began declining in the United States and Europe by more than 10 percent per year. In the mid-1990s, TB resurged in the United States, fueled by sharp declines in funding for TB control, the emergence of HIV/AIDS, growing drug resistance, and extensive outbreaks in health care and correctional facilities. The United States stopped this resurgence with reinvestment in the infrastructure for TB prevention and control and intensive efforts to stop transmission combined with implementation of new screening and treatment approaches.

In 2012, the United States marked the twentieth consecutive year of declining TB incidence, which fell below 10,000 TB cases for the first time (Figure 1). However, rates of TB remain higher among certain vulnerable U.S.-born populations and among foreign-born populations. While TB incidence declined 61 percent among all U.S.-born

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4 Ibid.
7 Ibid.
individuals since 2000, it has fallen more slowly among certain U.S.-born groups and by less than 18 percent among foreign-born individuals.\(^8\)

**TB among Vulnerable U.S.-born Populations**

TB incidence among certain groups declined more slowly than among the general population, concentrating the epidemic in these populations. These vulnerable populations, such as individuals recently incarcerated, experiencing homelessness, using substances, or abusing alcohol, are at high-risk for infection and progressing from infection to disease. In addition, they face barriers to successful care and treatment. Combined, these groups now account for 36 percent of U.S.-born TB cases.\(^9\) TB programs often prioritize interventions to identify active TB cases and test their contacts for TB and latent TB infection (LTBI) to detect and stop recent transmission. This strategy is most effective among contacts of U.S.-born TB cases, particularly in these vulnerable groups, because recent transmission is a more common factor among these populations than among other U.S.-born and foreign-born TB cases.\(^{10}\)

**TB among the Foreign-born Population**

Comparing TB rates between U.S.-born and foreign-born individuals living in the United States reveal dramatic differences in progress against TB. By 2012, the TB incidence rate among foreign-born persons in the United States was 11.5 times higher than the rate among U.S.-born persons. In 2012, 63 percent of TB cases and 86 percent of multidrug-resistant TB (MDR TB) cases in the United States occurred among foreign-born individuals. TB among this group rose substantially as a proportion of all TB cases in the United States while the actual number of cases among foreign-born persons declined slightly (Figure 2). This reflects the steep decline in TB cases among

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\(^9\) CDC, *Reported Tuberculosis in the United States, 2011*.

U.S.-born individuals (61 percent) compared to the slight decline (18 percent) among foreign-born individuals.\textsuperscript{11} Children of foreign-born parents are also at greater risk of developing TB disease than children of U.S.-born parents. Children account for nearly 10 percent (approximately 1,000) of all TB cases in the United States, and nearly 90 percent of these are among U.S.-born children.\textsuperscript{12} However, two recent studies have shown that between half\textsuperscript{13} and two-thirds\textsuperscript{14} of U.S.-born children with TB have at least one foreign-born parent. Compared with TB rates among U.S.-born children with U.S.-born parents, rates were 32 times higher in foreign-born children and 6 times higher in U.S.-born children with foreign-born parents.\textsuperscript{15}

Characteristics of TB among Foreign-Born Individuals

Understanding the demographics of patients and the clinical characteristics of TB among foreign-born individuals in the United States is essential to selecting optimal approaches for addressing it. Table 1 summarizes and compares the top 22 countries of origin for U.S. foreign-born TB cases, U.S. immigrant visa admissions, and WHO high TB burden countries. Each index is ranked according to magnitude. Overall, more than half of all foreign-born persons with TB were born in five countries (Mexico, the Philippines, India, Vietnam, and China). Further, there is considerable

\begin{figure}
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\caption{Trends in TB Cases among Foreign-born Persons in the United States, 1992–2012}
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11 CDC, \textit{Reported Tuberculosis in the United States, 2011}.
15 Moonan et al., “Using genotyping and geospatial scanning to estimate recent \textit{Mycobacterium tuberculosis} transmission.”
overlap among ranked countries across the three indices. Seven of the top 12 countries of origin for U.S.-bound immigrants are also WHO high TB burden countries and major contributors to foreign-born TB cases diagnosed within the United States.


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The rate of TB disease among individuals who have recently entered the United States (entry within two years) is three to seven times higher than the rate among non-recent arrivals (entry more than two years ago). However, 70 percent of TB cases among foreign-born persons occur among non-recent arrivals. The majority of foreign-born individuals in the United States with TB disease were infected with TB prior to arrival, immigrated to the United States with latent TB infection, and developed active TB disease after arriving in the United States. While TB among the U.S.-born is often due to recent transmission, TB among the foreign-born in the United States is due to past infection that develops into disease when the immune system is compromised. TB among children of foreign-born individuals is related to exposure to a parent or visitor with TB disease. Contact investigations will continue to play an important role in identifying children who may have been exposed to enable appropriate treatment. The methods used to identify and treat active TB disease differ from those of other transmission settings.

17 Moonan et al., “Using genotyping and geospatial scanning to estimate recent *Mycobacterium tuberculosis* transmission.”
used to identify and treat latent TB infection, but both are essential to combatting TB in the United States \(^\text{18}\) (see text box for more information).

The impact of the global burden on the U.S. TB burden is clear: the majority of TB and MDR TB cases in the United States originate from abroad. While the global burden of TB remains high and cross-border travel and migration continue, the U.S. TB program cannot eliminate TB from the United States.

**A New Strategy for Fighting TB at Home—and Abroad**

Targeted interventions in high TB burden countries that contribute to U.S. TB burden could impact both U.S. domestic TB-control efforts as well as contribute toward global efforts.

Two interdependent strategies should be considered for a comprehensive U.S. government approach to reducing TB among foreign-born individuals:

1. Strengthened overseas TB screening for both active TB disease and latent TB infection paired with post-entry follow-up; and
2. Strategic investment to strengthen TB control in high-burden TB countries and countries contributing substantially to the U.S. TB burden.

The most appropriate approach and priorities for U.S. investment will depend on TB epidemiology and TB control efforts in each country as well as migration patterns and pathways to the United States.

**Strengthened Overseas TB Screening and Post-Entry Follow-up**

An estimated 164 million individuals legally enter the United States each year, including 163 million nonimmigrant visa applicants, more than one million immigrants, and 60,000 to 80,000 refugees. Considering these numbers, screening all entrants to the United States for active or latent TB infection is not feasible. Current screening requirements focus on identifying and treating active TB disease in persons seeking permanent U.S. residence (i.e., U.S.-bound immigrants and refugees). Overseas TB screening for active TB disease is implemented by the United States through physicians in 151 countries. The overall screening program consists of two integrated components: 1) screening for and treating TB disease overseas prior to entering the United States, and 2) establishing a process for follow-up evaluations for individuals either diagnosed with or suspected of TB after arrival in the United States.

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States. This intervention has been shown to reduce the importation of infectious TB cases.

From 2001 through 2008, approximately 15 percent of TB cases each year were among foreign-born persons in the United States arriving within the last year. Based on modeled estimates, the top three foreign-born populations with the highest TB incidence rates within one year of arrival were 1) immigrants and refugees from high TB burden countries, 2) students and temporary workers from high TB burden countries, and 3) immigrants and refugees from medium TB burden countries. Nearly 60 percent of foreign-born cases diagnosed within one year of arrival were among nonimmigrant visitors that had not been screened for TB overseas through the screening process because screening is not required for this population.

Strengthening Screening Protocols: Expanding Screening for Active Disease and Latent Infection

These findings suggest that enhanced, targeted overseas TB screening and treatment among U.S.-bound immigrants, refugees, and other entrants from countries with a high TB burden may reduce TB in the United States. Addressing only active TB disease and focusing on recent transmission among the foreign-born population may result in missed opportunities to address latent TB infection and prevent development of active TB disease. Enhanced efforts to reduce the incidence of TB in newly arrived foreign-born individuals could include screening for active TB disease and latent TB infection among nonimmigrant visitors if they are 1) from a high-burden country, and 2) intend to stay in the United States for an extended period of time. Post-arrival follow-up evaluations of students and temporary workers with suspected TB may be feasible because the average length of stay in the United States is 18 months, allowing adequate opportunity for follow-up and completion of treatment for TB or LTBI, if warranted.

While TB screening overseas is a necessary and high-yield intervention, recent modeling has suggested it is insufficient to address TB among the foreign-born. Thus, to further reduce and prevent TB, the U.S. government should consider diagnosis and treatment of latent TB infection among U.S.-bound immigrants and refugees from high-burden countries. Further study is needed to determine the feasibility and optimal point during migration for such expanded screening, whether at the point of origin or at the post-migration destination. In addition, strategies should be considered to ensure foreign-born individuals in the United States at high risk for progression to TB disease have better access to LTBI diagnosis and treatment after entry.

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19 Liu et al., “Overseas screening for tuberculosis in U.S.-bound immigrants and refugees.”
22 Ibid.
23 CDC, “Recommendations for Use of an Isoniazid-Rifapentine Regimen.”
24 Liu et al., “Overseas Screening for tuberculosis in U.S.-bound immigrants and refugees.”
Strategic Investment in High TB Burden Countries

By the end of the century, current TB elimination efforts are likely to succeed among the U.S.-born population. But elimination of TB among the foreign-born appears out of reach, even with increased testing and treatment pre- and post-entry. That is why screening and treatment must be coupled with investments in TB control in moderate- and high-burden countries. Modeling of this joint approach has shown it would save more than $130 million over 20 years for interventions in just three countries while reducing TB in the United States.26

The U.S. government is a leader in strengthening local capacity through technical assistance, building the global evidence base through research, and translating research into practice. The U.S. government also has unique expertise in the primary technical areas for TB control, which have traditionally included surveillance systems and impact measurement, laboratory networks and diagnostics, TB infection control, TB case-finding, and diagnosis and management of HIV-associated TB and drug-resistant TB. The U.S. government provides bilateral support to partner governments for TB control programs and multilateral assistance through the Global Fund to Fight AIDS, TB, and Malaria to purchase commodities and medicines. Historically, however, bilateral and multilateral aid has not supported long-term technical assistance or substantial support to countries of origin for U.S. TB cases. Additional efforts in these areas are needed to address TB beyond our borders. This need has been recognized by the WHO’s Executive Board, which recently released a resolution calling for an ambitious global strategy and targets for TB prevention, care, and control after 2015.27

Meaningful Partnerships with Host Governments

TB control is primarily funded and managed by ministries of health, as opposed to other disease-control programs that have significant private or nonprofit infrastructures separate from partner governments. In fact, two-thirds of current funding for TB control worldwide comes from host-country financing, not external aid.28 Improving TB control in high TB burden countries can benefit long-term partnerships with ministries of health to address key knowledge and capacity gaps across public health competencies. Long-term partnerships and U.S. government investment can enable ministries of health to optimize basic TB program functions, identify priority at-risk populations, deploy high-quality interventions, and monitor impact of the TB program. Any long-term partnership could tailor research, policy, and technical assistance plans to the needs of a particular country across the primary technical areas. In addition, health-systems strengthening could be a component to any such partnership, focused on five broadly defined areas:

• **Surveillance-Systems Strengthening:** Accurate, comprehensive, and timely surveillance systems are the bedrock of any disease control program. Strong surveillance systems enable the assessment of disease burden, identify hot spots and risk factors, and measure program impact. Strengthening these systems would be a priority for any comprehensive support to priority countries.

• **Laboratory Networks:** Laboratory networks that are quality-assured and adequately staffed by trained laboratory scientists are critical to scaling up access to diagnosis and care. Strengthening such networks requires implementation of biosafety measures and development of laboratory strategic plans and management systems to achieve global and regional laboratory accreditation. Such networks must be supported through training laboratory staff to perform specific diagnostic tests and monitor quality assurance. Adequate supplies of laboratory equipment and commodities are required, and can be supported through multilateral programs.

• **Infection Control:** Appropriate biosafety and infection-control measures, especially in health care and congregate settings, are the first line of defense in stopping transmission and preventing TB. Strengthening policies and protocols related to infection control, paired with staff training and health care worker TB screening, can help reduce transmission and protect the health care workforce.

• **Treatment Capacity:** As laboratory capacity grows, infrastructure to deliver quality-assured treatment must expand to effectively treat additional cases diagnosed through more aggressive case-finding approaches. Expanded treatment capacity requires adequate access to and effective management of quality-assured drugs. Once a stable supply chain in established, these medications must be delivered to patients using proven techniques (e.g., directly observed therapy short-course [DOTS] and DOTS-Plus for MDR TB treatment). This infrastructure can be strengthened through staff training on supply chain logistics and case management and operations research to identify solutions to program challenges. Multilateral institutions would continue to play a critical role in providing access to medications.

• **Clinical and Operational Research Capacity:** An independent, effective TB program should be able to identify knowledge gaps, conduct clinical and operational research to answer key questions, and use data to improve practice. Developing and maintaining research partnerships and training programs in-country can help build this infrastructure. Such partnerships could also include training for clinical, laboratory, and program staff on evidence-based methods for preventing, diagnosing, and treating TB relevant to that country’s TB epidemiology.

Future interventions should be monitored and evaluated for their impact on increasing TB case detection and treatment success rates and reducing TB incidence and prevalence. Interventions not meeting these goals should be modified to enable demonstrable benefit to TB control efforts.
Building the Evidence Base

The United States should continue its leadership role in basic science and clinical and programmatic research to identify new and improved methods for TB prevention, diagnosis, and treatment while committing to translate these findings into practice. Recent advances from such investments have included a faster TB diagnostic test (Xpert MTB/RIF®), which diagnoses TB and drug resistance in hours instead of weeks,29 and a new 12-dose drug regimen for treating LTBI, which shortens treatment by six months and cuts the pill burden by nearly 75 percent.30 In addition, several vaccine candidates and shorter treatment regimens for TB and drug-resistant TB are currently under study, which may simplify prevention and treatment. Several U.S. government-supported studies are underway to identify improved methods for screening and diagnosing TB from clinical, laboratory, and programmatic angles to improve programs on the ground. These advances could inform and improve the technical guidance provided to partner ministries of health and ensure innovation reaches health centers and the people who need it most.

Continued Multilateral Assistance for Equipment and Commodities

Strengthening technical capacity alone is not sufficient to achieve the desired impact. TB programs will still require assistance to purchase equipment, commodities, and quality-assured drugs. As stronger TB programs find more TB and drug-resistant TB cases, support will be needed to ensure patients receive appropriate, complete courses of treatment. The U.S. government should maintain and strengthen partnerships with multilateral institutions and ministries of health to enable this continued support. Working together, these partners can build sustainable health systems infrastructure and treatment capacity, including uninterrupted access to anti-TB drugs used to treat TB and drug-resistant TB.

Conclusion

TB elimination in the United States is not possible without also addressing TB beyond our borders. Strengthened and expanded screening efforts to address TB among the foreign-born are needed to have a sustainable impact on TB morbidity and mortality in the United States. These efforts should be paired with greater U.S. government engagement in global TB control through strategic investment and research to accelerate global progress against TB.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

30 CDC, “Recommendations for Use of an Isoniazid-Rifapentine Regimen.”
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