DGHT
Division of Global HIV & TB

FINDING THE MISSING 4 MILLION:

THE ROLE OF ENHANCED DIAGNOSTICS AND CASE-FINDING IN REACHING ALL PEOPLE WITH TB

OVERVIEW

Each year, it is estimated that 10.4 million people develop active TB disease, but 4.3 million of these individuals are "missed" each year by health systems and do not get the TB care they need and deserve. More than 75 percent of missed cases are concentrated in just ten countries. Among these cases are an estimated 600,000 children with TB and 400,000 people with drug-resistant forms of the disease. Without proper treatment, up to two thirds of people ill with TB will die. In addition, people who are ill with TB can infect up to 10 to 15 people with whom they are in close contact in a single year. This means that each missed case can expand the current TB burden which compounds the challenge to end TB.

Many of the "missing 4 million" are among vulnerable or underserved populations that are hard to reach or have difficulty accessing public health services, such as children, people living with HIV (PLHIV), migrants, refugees, and miners, among others. Diagnosis of TB is more challenging for certain groups, such as children and PLHIV, because traditional diagnostics – like sputum smear microscopy – do not perform as well and can fail to diagnose TB even when it is present. Another challenge is the growing private and informal health sectors in many countries. These sectors often do not have access to or utilize quality-assured diagnostics or the anti-TB drugs needed to appropriately diagnose and cure patients, which can lead to under-diagnosis or inappropriate treatment which can cause drug resistance.

Finding these missing cases and breaking the cycle of transmission is a major priority in the global efforts to end TB. This requires a strong health care system, a public health workforce that can reach those who need care, the laboratory capacity to quickly and effectively diagnose the disease, and innovative approaches to meet people where they receive care and expand access to TB diagnostic and treatment services.

CDC'S ROLE

CDC's role in finding these missing cases revolves around four distinct but related streams of work:

- Building the evidence base to improve case-finding approaches and diagnostic algorithms;
- Scaling-up access to TB screening and diagnosis among PLHIV;
- Providing guidance and technical support for implementing and evaluating new TB diagnostic tools, assuring quality laboratory services, and developing laboratory strategic plans with ministries of health to ensure the right diagnostic tools are in the right place; and
- Strengthening national surveillance systems to document the burden of TB disease and identify gaps in case-finding efforts.

ACCOMPLISHMENTS / RESULTS

Building the evidence base to improve case-finding and diagnostic algorithms

- The U.S. Centers for Disease Control and Prevention (CDC) led a cross-sectional study in Southeast Asia that identified a simplified approach to screening PLHIV for TB. This screening approach found three times as many cases of TB than the standard at the time. Because of the sensitivity of the algorithm and improved confidence that patients who screened negative did not have disease, the algorithm called for providing isoniazid preventive therapy (IPT) to all PLHIV who screened negative to prevent them from developing active TB disease. This study laid the foundation for a dramatic shift in the World Health Organization (WHO) international guidelines for how to both prevent and diagnose TB disease among PLHIV in 2011.
    - After the change in these guidelines, CDC evaluated the implementation and performance of these screening algorithms to both evaluate the diagnostic yield and outcomes of those screened, and to determine the appropriate frequency for screening. This study found a prevalence of TB among PLHIV nearly 57 times greater than in the general population, and suggests that repeated screening is useful for diagnosing TB as well as initiating preventive therapy for eligible patients.
    - In 2015, the WHO stated that the total number of people started on preventive treatment globally was 910,124, more than 10 times higher than in 2010. WHO attributed much of this progress to the changed algorithm in 2011.

Scaling-up TB Screening among PLHIV

- CDC has been working closely with the ministries of health to incorporate and scale-up systematic TB symptom screening among PLHIV in U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and national HIV programs. TB screening among PLHIV has improved dramatically since the new guidelines were released, with more than 85 countries reporting systematic TB screening for PLHIV in 2015. In 2015, more than 70 percent of PLHIV in PEPFAR-supported care and treatment programs were systematically screened for TB.

- CDC continues to provide technical and program support to PEPFAR-supported programs to improve TB/HIV service integration and facilitate ART uptake among PLHIV diagnosed with TB. In 2015, 79 percent of HIV-positive TB patients were receiving ART in PEPFAR-supported countries.

Strengthening laboratory capacity

- CDC played a critical role in the global effort to rollout Xpert MTB/RIF®, a rapid molecular diagnostic test endorsed by WHO in 2010. This test can diagnose TB and rifampicin-resistant TB in a matter of hours (compared to days or weeks for traditional diagnostics) and shows vastly improved performance in diagnosing TB among PLHIV and children.

- Since 2010, more than 10 million tests have been delivered to high-burden countries worldwide. U.S. Government was the lead donor for scale-up of Xpert MTB/RIF®, with PEPFAR and CDC playing major roles in providing the guidance, training, technical assistance, and monitoring and evaluation support needed to implement this test.

- CDC continues to build the evidence base for improved global guidance on implementation and provide intensive support to in-country partners to calibrate, validate, and implement Xpert.

- Since the global rollout of Xpert, diagnoses of MDR TB have nearly doubled and the number of PLHIV systematically screened for TB has more than doubled.

Measuring the burden

- The global burden of TB and the proportion of cases that are missed each year were revised upward in 2016 because, as global and national surveillance systems improve, so does our understanding of the burden of TB disease and the gaps and weaknesses in the surveillance system itself. Improving disease burden estimates gives us a better understanding of where we are making progress and how far we still have to go to reach global TB targets.

- CDC has been working closely with the WHO to establish surveillance standards and benchmarks, assist with surveys of TB prevalence to document burden of disease, provide technical support to strengthen national surveillance systems, and conduct inventory studies to understand how many patients are actually diagnosed and/or started on TB treatment, but are unknown to the national TB program.

FUTURE EFFORTS

CDC will continue to lead operational and programmatic research to identify innovative approaches to case-finding, scale-up screening for TB, optimize the use of diagnostic tools, and improve surveillance systems.

Improving screening approaches and diagnostic algorithms

- CDC is currently leading a multi-year study to develop a diagnostic algorithm to diagnose TB among children and establish a new gold standard for diagnosis.

- CDC is working with multiple partners in southern Africa to identify approaches to screen and diagnose TB among miners, who are at increased risk of TB and often have limited access to TB diagnostic and screening services. This project will identify optimal screening modalities as well as approaches to ensure treatment and continuity of care as miners travel from mining camps back to their home communities.

Scaling-Up Screening and Diagnosis among PLHIV

- CDC continues to work with our partners in PEPFAR countries to mainstream and scale-up TB screening among PLHIV and ensure clients diagnosed with TB are promptly linked to care and treatment.

- CDC is demonstrating the impact of combined TB and HIV case-finding, treatment and prevention interventions as a model program to accelerate the decline in TB incidence and reduce mortality due to HIV and TB.

- Children who have been exposed to TB, especially children living with HIV, can move rapidly from infection to disease and develop more severe forms of TB more quickly. CDC is implementing a model for comprehensive screening at the household level through a family-centered care model which could identify children at risk of TB more quickly, prevent development of active disease, and ensure rapid diagnosis and initiation of therapy.

Quality-Assured Laboratory Services and Surveillance Systems

- CDC continues to work with partners to develop global guidance on the use of new and existing diagnostic tools and strengthen laboratory networks through technical support, implementation of continuous quality improvement systems, and training for laboratory staff.

- Strengthening surveillance systems in-country through assessments and technical support and informing global guidance and tools remain a critical priority for CDC.