



Treatment Action Group

The TB Research Engine That Could: Sustaining the Success of TBTC Research in Turbulent Times

New public health innovations in tuberculosis (TB) prevention, diagnosis, and treatment have accelerated in recent years, due in large part to United States' leadership and investment in research and development (R&D). One of the most critical leaders of this advancement lies within the U.S. Centers for Disease Control and Prevention (CDC) Division of TB Elimination (DTBE), at the Tuberculosis Trials Consortium (TBTC). This small research network has carried the weight of a sector where new tools are needed more than ever. The TBTC is a unique research network formed by partnerships between CDC, academic institutions, and public health departments. The TBTC has produced cutting-edge clinical trials to address TB, the world's deadliest infectious disease second only to COVID-19.

TBTC's structure enables it to conduct research that is relevant to state and local health departments supported by the DTBE and international TB programs alike. By sponsoring academic research institutions in partnership with health departments and trial sites in the United States and around the world, TBTC studies reflect the on-the-ground realities that TB programs face both domestically and abroad. In practical terms, this means that programs are able to communicate their needs directly to the researchers who are best positioned to address them. In turn, the innovations produced by TBTC research can be implemented by public health programs. The TBTC network includes trial sites across the globe (see Map, Figure 1) in areas with higher TB case rates. This both facilitates faster enrollment into studies and reflects the ways in which TB in the United States is so closely linked to the TB pandemic.

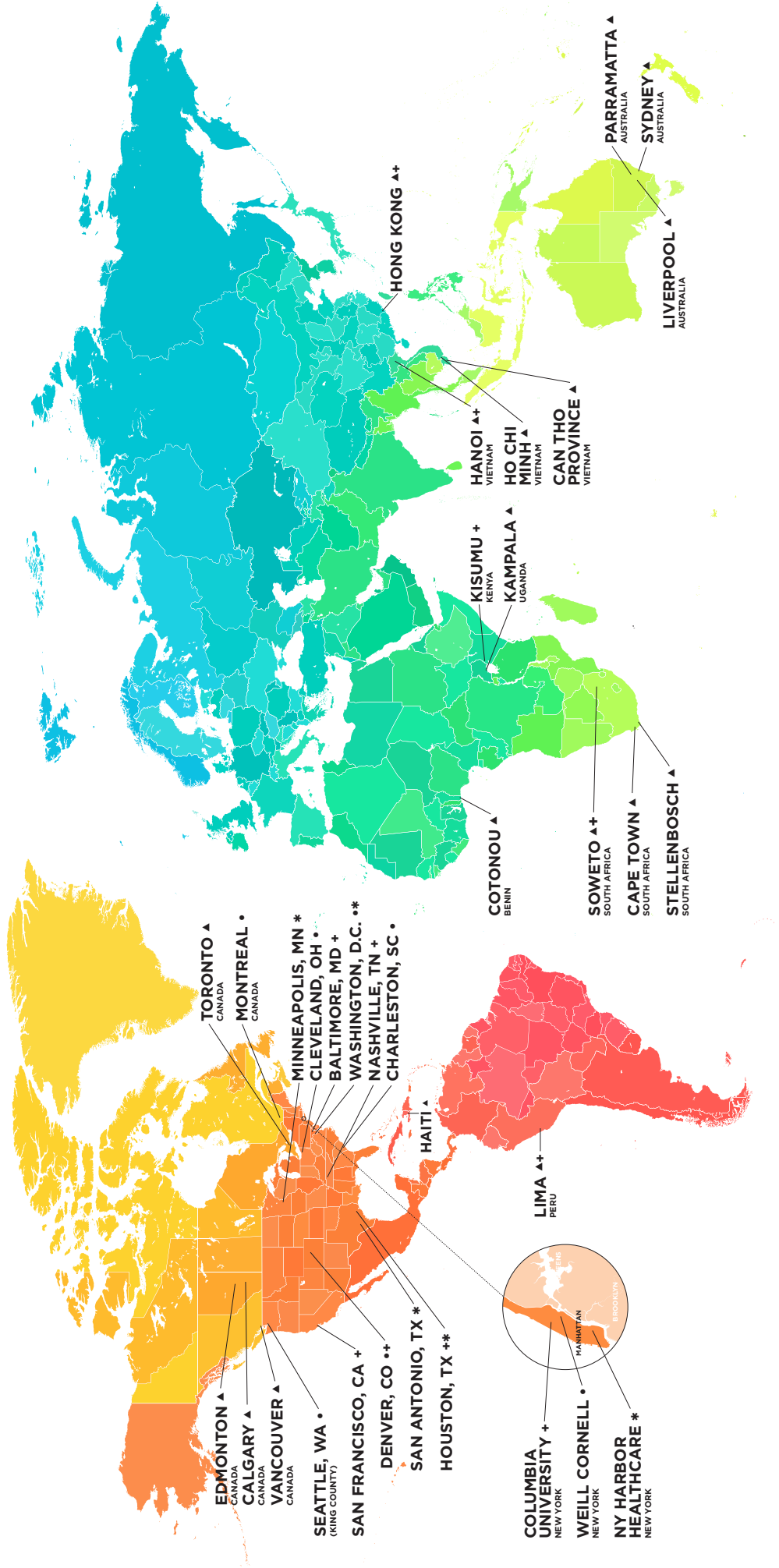
Every 10 years, institutions funded through the TBTC are invited to reapply for the next funding cycle. This competitive application process allows the CDC to review which areas of innovation will be most needed for TB programs going forward, direct funding to these areas, and add new trial sites, thereby bringing on board specific expertise or accessing certain priority patient populations. The 2009 competition process led to an expansion of clinical sites internationally, linking U.S. academic institutions with trial sites in TB- endemic countries. From 2010 to 2020, the TBTC built research partnerships between U.S. academic centers in New York City, Baltimore/ Washington D.C., Cleveland, Nashville, Denver, San Francisco, Dallas, San Antonio, and Houston and global sites in Peru, Brazil, Uganda, Kenya, Hong Kong, Vietnam, South Africa, and Spain.

Since its inception, CDC-funded research has enrolled more than 14,000 research participants in nine major trials and 15 sub-studies, expanded TB programmatic research capacity both domestically and globally, and led to successful innovations in treatment and prevention of TB, all at a modest annual budget of \$9.0 million.

However, stagnant funding for the DTBE and TBTC has prevented the network from building on these successes. In the most recent competition, a process that selected TBTC sites for the 2021-2030 period, limited funding forced harmful cuts that threaten to upend the historical investments, the growth of the network, and the successes by TBTC researchers.

TBTC Research Network

Figure 1: Map of TBTC Sites Across the United States and the World*



LEGEND • DIRECTLY FUNDED SITES (2021-2030) ▲ GLOBAL PARTNER SITES * VETERANS AFFAIRS (VA) AFFILIATED SITES + STUDY-SITE

Stagnant Investments Threaten the Future of TB Research

Despite the critical role that the CDC’s DTBE has played in both public health infrastructure and R&D, the fiscal year 2021 funding levels allocated by Congress to it are approximately the same as they were in fiscal year 1994 (see Figure 2). Due to inflation and the rising costs of conducting even the most efficient research, this flat funding has effectively amounted to a funding cut for DTBE programs and the TBTC’s research agenda. As a result, the number of TBTC priority studies now significantly outstrips the available DTBE funding to conduct the research required to end TB.

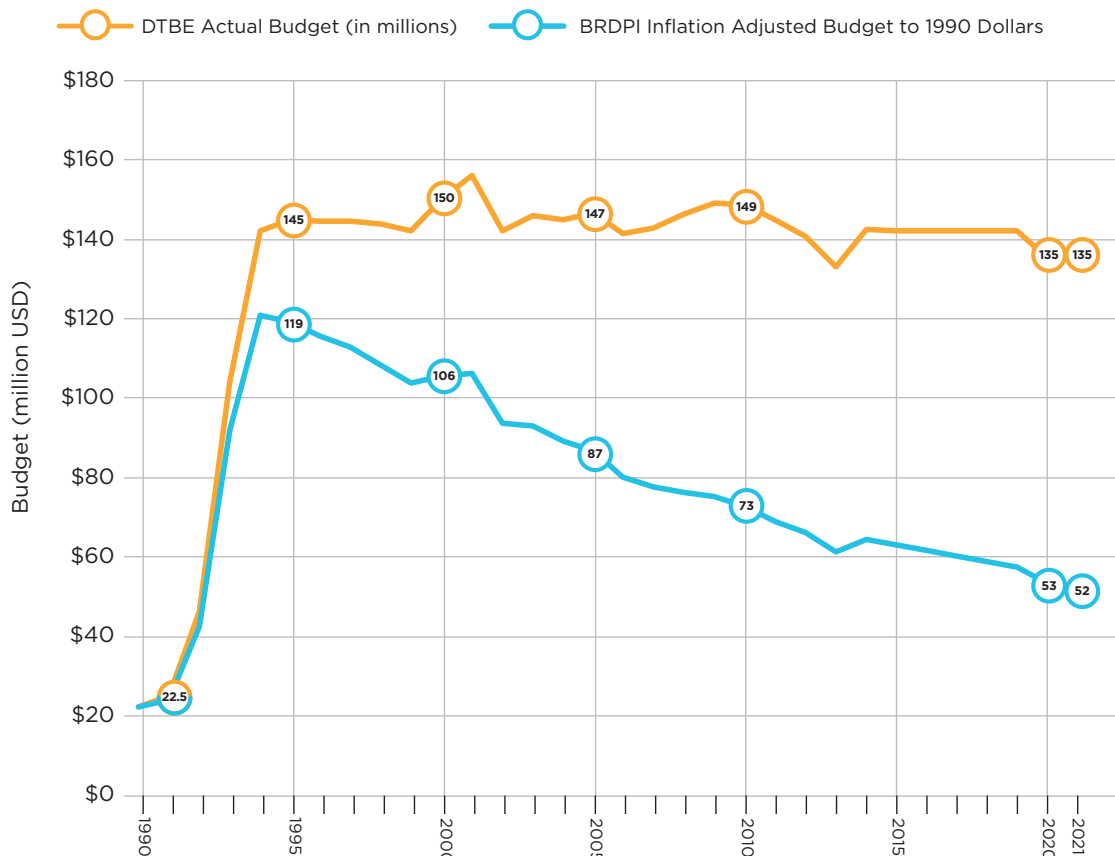
The implications of budget stagnation are profound. In early 2021, four academic centers and their linked international study sites, which had been leading some of the highest-priority research for the TBTC, were informed that their funding had not been renewed for the next 10-year cycle (2021–2030). This outcome fails

to acknowledge the groundbreaking contributions these four sites made to the field of TB research. In particular, these sites house the scientific leadership and statistical expertise of almost every TBTC study conducted in the past 10 years, in addition to resources such as specialized laboratories for animal modeling. If funding is not secured through alternative sources, decades of institutional knowledge and expertise and those sites’ relationships with U.S. health departments and research partners outside of the United States will be lost.

Both TB programs and researchers need funding to support their shared work and to understand what patients need to prevent and treat TB. Sustained resources are also what enable the critical analysis and policy translation of research findings. For example, the groundbreaking results of TBTC Study 31 (see textbox) can only be disseminated and implemented—and subsequently made to benefit TB programs and patients—if the institutions that conducted such research are funded to do so.

Impact of Inflation on Flat DTBE Funding

Figure 2: CDC DTBE Overall Budget (FY 1990 - FY 2021)



TBTC Study 31: Shorter TB Treatment Breakthrough

THE PROBLEM: For almost 40 years, researchers' attempts to shorten TB treatment failed, leaving programs treating drug-sensitive TB reliant on the same regimen of four drugs taken for 6–9 months since 1984. Without any changes to this standard of care, patients with TB had no other option than to undergo lengthy periods of isolation, side effects, and treatment monitoring. TBTC Study 31/A5349 researchers finally cracked the code, discovering and validating a regimen that could cure TB in just four months.

THE STUDY: Study 31 was a phase III clinical trial that compared two different four-month regimens to the existing six-month standard of care. This was the largest TB treatment trial in decades, one that included populations often left out of research on TB and other diseases. The TBTC conducted this study in partnership with a U.S. National Institutes of Health (NIH)-funded research network called the AIDS Clinical Trials Group at 34 sites in 13 countries, including the United States. Together, the two networks enrolled over 2,500 people, including adolescents, people living with HIV, and people with serious forms of TB disease. After evaluating the safety and efficacy of each regimen, one of the experimental regimens was shown to be as effective at treating and curing drug-sensitive TB as the existing standard of care but did so in one-third less time.

THE IMPACT: These study results will significantly improve the quality of life of TB patients by making it easier and faster to complete treatment. Shorter treatment translates directly to faster recovery times, reduced disruptions to housing and familial relationships, greater income stability and continued employment, decreased side effects and comorbidities, and improved overall health. Study 31 will also bring tremendous benefits to TB programs, requiring less staff time on treatment monitoring and freeing public health resources to reach even more people in need of TB treatment and prevention services.

Recommendations to Safeguard TB Innovation

RECOMMENDATION 1:

Increase CDC DTBE funding level to \$225 million

Increased investments in the DTBE and TBTC are needed to make up for decades of budget erosion and to avert further damaging cutbacks to TBTC research. As shown in Figure 2, the rate of inflation has decreased the purchasing power of stagnant congressional appropriations to DTBE over time. As a result, the DTBE has been subjected to functionally decreased funding for decades. In order to strengthen the DTBE and grow TB research at the TBTC, legislators should appropriate \$225 million to the DTBE, an increase of \$90 million over fiscal year 2021 levels. Furthermore, an increase in funding to the DTBE/TBTC will:

- **Grow the TB research field and retain scientific leadership.**
- **Ensure the completion of studies and translation of results into policy and guidance.**
- **Help the United States meet its global TB R&D fair-share funding target of \$444.5 million.**
- **Mitigate the impact that the COVID-19 pandemic has had on TB R&D efforts at the TBTC.**

RECOMMENDATION 2:

Facilitate TB research resource-sharing among U.S. governmental agencies

Federal agencies should be brought together to facilitate resource-sharing for improved efficiency and effectiveness of TB research efforts. Some of the other agencies that could collaborate with the TBTC in an even greater capacity include the NIH and the US Agency for International Development (USAID). As illustrated by Figure 3, each agency's unique contributions feed TB research priorities overall and maximize the capacity of U.S. investments.

Contributions of Key Government Agencies to TB Research

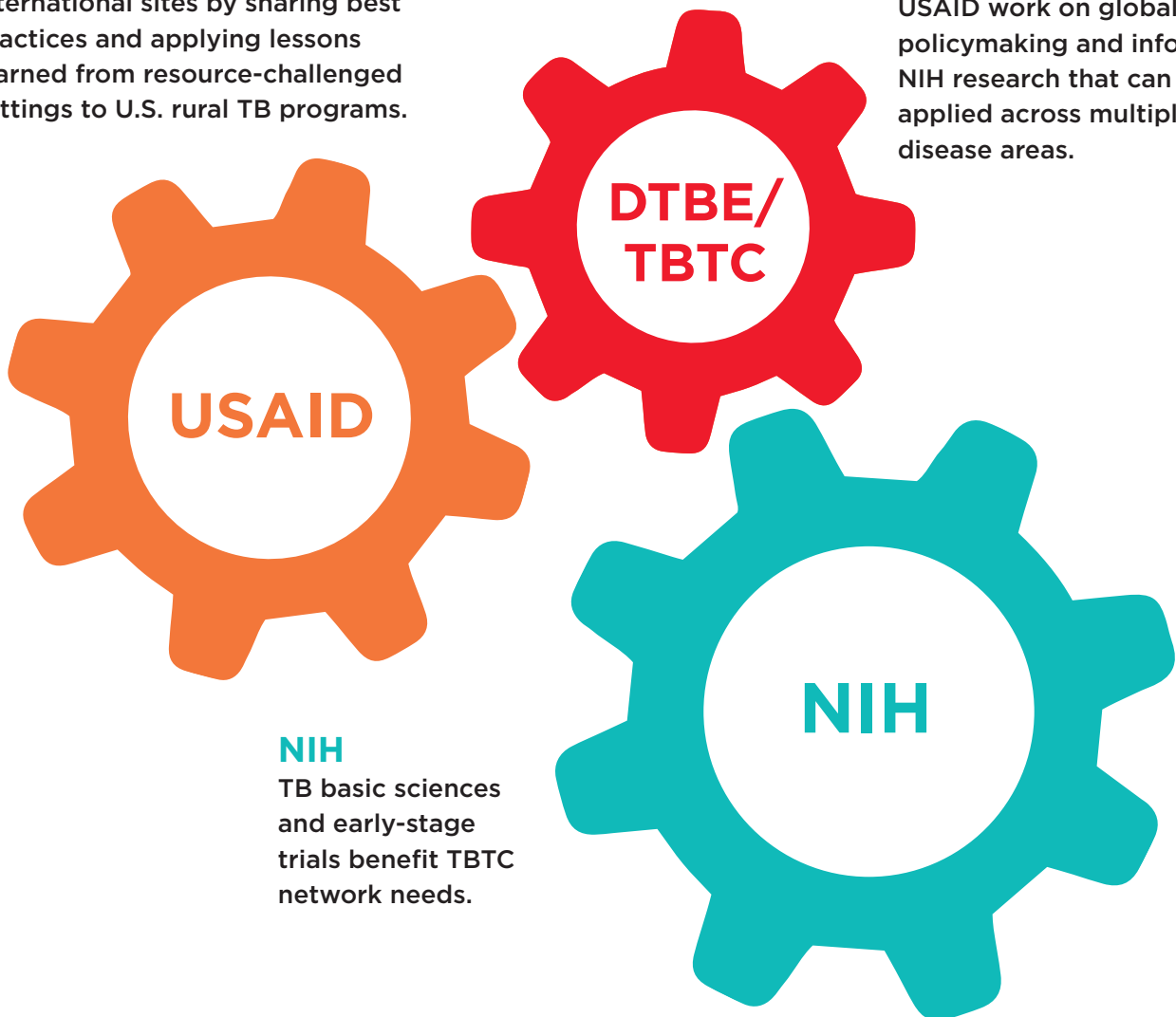
Figure 3: DTBE/TBTC: An Essential Cog in the U.S. Government's TB Research Machine

USAID

TB program implementation in high-burden settings benefits TBTC international sites by sharing best practices and applying lessons learned from resource-challenged settings to U.S. rural TB programs.

TBTC

TB research benefits USAID work on global policymaking and informs NIH research that can be applied across multiple disease areas.



NIH

TB basic sciences and early-stage trials benefit TBTC network needs.

Conclusion

In conclusion, the TBTC offers a unique and valuable model of TB R&D that highlights the remarkable contributions of U.S. researchers, public health programs, and global partnerships. In order to extend the benefits of this research into the next decade, legislators must increase funding for the

DTBE and build upon the momentum of this highly efficient and successful research driver within the federal government. Investing in the cutting-edge scientific leadership of the TBTC today will have lasting benefits for future generations.

For a full list of references by section, please visit:

www.treatmentactiongroup.org/publication/the-tb-research-engine-that-could/