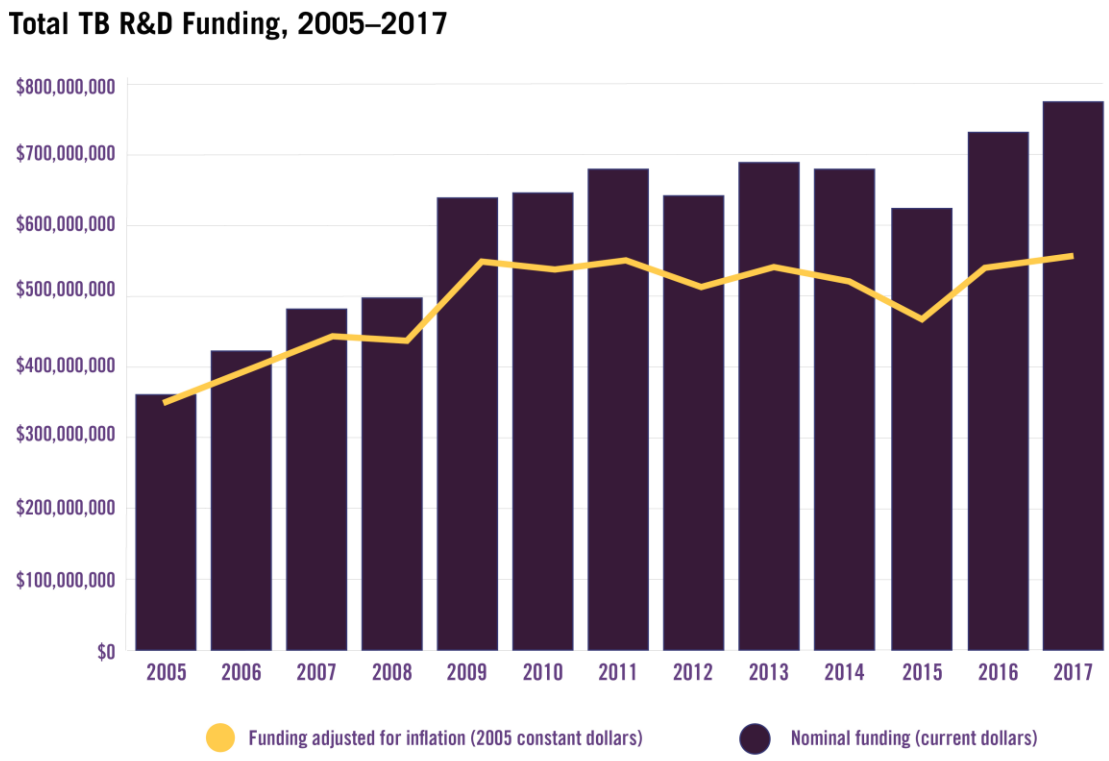
Building an Evidence Base to Advocate for TB Research

In December 2018, Treatment Action Group (TAG) published its 13th annual *Report on Tuberculosis Research Funding Trends*. The report tracks global expenditures on tuberculosis (TB) research and development (R&D) by funders from the public, philanthropic, private, and multilateral sectors in six areas of TB research: basic science, diagnostics, drugs, vaccines, operational research, and infrastructure/unspecified projects. For the second year in a row, the report had some good news to share: funding for TB R&D reached an all-time high of $772 million in 2017, surpassing the previous high of $726 million in 2016. This marked the second consecutive year of increased spending (**Figure**).

These findings come from an annual online survey TAG sends to over 180 confirmed and possible funders of TB research in more than 30 countries. The survey is the longest running and most comprehensive record of global funding for TB R&D, and has provided the evidence base for advocacy to increase support—financial, political, and institutional—for TB innovation.



Why track funding for TB research?

Funding peaks in 2016 and 2017 point to progress, but higher funding levels in the past two years have been hard won and remain far below the investment required to bring forth the transformative science required to eliminate TB by 2030—a goal set by United Nations member states in the Sustainable Development Goals (SDGs). In pursuit of this

goal, the Stop TB Partnership has called for $2 billion in funding for TB research annually. Careful efforts to track funding for research over the last 13 years have turned this $2 billion figure from an aspirational slogan into a concrete, measurable target.

The first TAG survey of TB research funders in 2005 grew out of a need to understand why scientific progress against TB was progressing so slowly. At that time, the preventive, diagnostic, and therapeutic tools public health programs relied on were decades old (or over a century old in the case of sputum smear microscopy for TB diagnosis). Since 2005, TB researchers have made notable strides, including bringing two new drugs to market, introducing shorter regimens to prevent TB, developing new diagnostic tests and screening tools, and completing several large vaccine trials. Fundamental understandings of *Mycobacterium tuberculosis* and its dynamic interplay with the human immune system have also undergone significant shifts.

But scientific advances have not kept pace with the TB epidemic itself. TB has surpassed HIV as the world's leading cause of death from a single infectious agent and remains one of the top 10 leading causes of mortality in the world. The deadly persistence of the global TB epidemic in large part reflects decades of underfunding research, which has left public health systems and people with and at risk of TB reliant on outdated—or nonexistent—technologies to prevent, diagnose, and treat TB. TB advocates knew that accelerating research across its full spectrum—from basic science to the development of new drugs, diagnostics, and vaccines to implementation science and applied health systems research—would have to be a central focus of advocacy to end TB. In order to conduct informed advocacy, TAG first had to build an evidence base.

The importance of publicly available data for resource tracking

In building this evidence base, TAG had to start from scratch—*mostly*. In the early years of the TAG survey, there was little publicly available information on how much specific institutions spent on TB research in any given year. The exception to this was the U.S. National Institutes of Health (NIH), which began publicly posting its spending by research area via the Research Portfolio Online Reporting Tools (RePORT). Beginning in 2008, the NIH published detailed information on support given to various research, condition, and disease categories (RCDC), encompassing grants, contracts, and other funding mechanisms. Access to this level of information proved essential to understanding TB research funding over time, since the NIH is far and away the largest funder of TB research globally. In 2017, funding for TB R&D across NIH institutes and centers comprised 32% of the global total, or nearly $250 million.

RePORT has expanded to include information on science funding provided by other U.S. federal agencies through the Federal RePORTER system. For TAG, the Federal RePORTER platform has been particularly useful for gaining visibility into work undertaken by agencies that are not typically seen as research funders, but support critical translational and clinical TB research activities (e.g., the U.S. Department of Veterans Affairs).

More recently, the NIH partnered with some of the world's largest biomedical research funders to create World RePORT, which maps both direct awards and research collaborations across the globe. Users can now visualize all research organizations participating in a funded activity irrespective of which institution receives the award. The World RePORT platform includes public R&D agencies such as the Canadian Institutes of Health Research and the U.K. Medical Research Council, philanthropic donors like the Bill & Melinda Gates Foundation (Gates Foundation) and Wellcome Trust, and development agencies such as the Swedish International Development Cooperation Agency. Although TAG still relies on direct surveys sent to TB R&D funders for its annual report, the World Report database provides a way to validate information reported to TAG (or to capture information not reported in the event of unreturned surveys).

The World RePORT mapping tool also provides a powerful interface for visualizing where TB research takes place. TAG used the map tool to help produce the first-ever visualization of TB research funding flows, or how funding for TB R&D moves from funders to funding recipients (**Image**). This analysis was included in a policy paper released by the World Health Organization (WHO) in preparation for a Ministerial Conference on TB hosted by the Russian Federation in Moscow in 2017. The resulting analysis explored how funding moved from 25 public and philanthropic funders to recipient organizations between 2011 and 2015. From this, we identified the 15 largest principal recipients of TB R&D funding over the period (only two of which turned out to be organizations located in high-TB-burden countries). We quickly discovered that funders from some countries primarily give to domestic institutions, while others support recipients around the world. Mapping efforts that encompass more groups than the 25 funders included in this initial analysis would provide a more nuanced picture of how funding for TB R&D is distributed, with important implications for understanding how agencies allocate funding; where TB research is most heavily concentrated; the balance between funding received by institutions in TB low- versus high-incidence settings; and overlap in the support given by different funders to similar projects or to the same institutions.

From evidence to action

Nearly 15 years of tracking global funding for TB research has demonstrated the power of understanding how expenditures in a particular area of research change over time, sometimes evolving in response to the science itself and sometimes due to shifts in the donor landscape. Thanks to these resource-tracking efforts—and to the information made available by research funders, particularly the NIH—TB advocates have identified and responded to several trends, including:

- **The pullback of pharmaceutical industry spending on TB R&D**. Between 2011 and 2017, pharmaceutical industry investment in TB R&D fell by 40% as major companies closed or scaled back TB R&D programs (often as part of a larger industry-wide shift away from anti-infectives research). The $85 million that private industry invested in TB research in 2017 was less than 0.1% of the $97.2

billion EvaluatePharma has estimated the pharmaceutical industry spent on R&D that same year.

- **The longstanding reliance on public money to support TB R&D**. In nearly every year of the TAG survey, public-sector funders contributed 60% of total global expenditures on TB research. This demonstrates the irreplaceable role government plays in supporting innovation—particularly for neglected diseases such as TB—and highlights the importance of governments taking purposive, proactive steps to finance TB research.
- **The emergence of non-traditional donors as major funders of TB research**. For example, in 2017 the global health financing mechanism Unitaid was the fifth largest funder of TB research with an investment of $29 million (up from $15 million in 2016). Unitaid is not traditionally identified as a research funder, describing its work as supporting projects that take new innovations to scale. That Unitaid now counts among the largest funders of TB research says as much about the absence of traditional R&D funders from the TB field as it does about Unitaid's laudable commitment to filling a gap in TB innovation.
- **The reliance on a handful of institutions for the bulk of TB research funding**. In any given year, 90% of TB R&D expenditures come from just 30 institutions, most based in high-income countries. An analysis of TAG data from 2005–2015 published in the WHO policy paper mentioned above found that the NIH and the Gates Foundation—the two largest TB R&D funders— together contributed 37% of all money spent over this period.

In response to these trends, TB research advocates began to ask what a country ought to spend on TB R&D—in relation to its resources, scientific infrastructure, TB burden, and other factors. Based on the Stop TB Partnership's TB R&D funding target of $2 billion, and historical data from TAG showing actual funding has never surpassed one-third of this desired level, TB advocates calculated that the resulting $1.3 billion funding gap could be closed if each country devoted just 0.1% of what it spends on all forms of R&D to TB research. (Spending on all forms of R&D is a statistic called *gross domestic expenditure on research and development* [GERD] and is reported by national statistics offices to UNESCO.) This resulted in a series of country-specific TB R&D funding targets that advocates named the 'fair share' targets and took forward in negotiations for the first-ever UN High-Level Meeting on TB. Advocates celebrated a small victory when the political declaration resulting from the UN High-Level Meeting contained an oblique reference to these targets:

> "*Commit to mobilize sufficient and sustainable financing, with the aim of increasing overall global investments to 2 billion dollars, in order to close the estimated 1.3 billion gap in funding annually for tuberculosis research,* ***ensuring that all countries contribute appropriately*** *to research and development*."

Advocates are now taking these 'fair share' targets forward at the country-level to secure greater financial investments in TB research in line with the commitment expressed in the UN High-Level Meeting political declaration that all countries "contribute appropriately" and approach TB R&D as a "shared responsibility."

Strengthening the evidence base for more effective advocacy

The resource tracking undertaken by TAG takes considerable effort—not only by TAG, but also on the part of research funders who compile information for the TAG survey each year. Platforms such as World RePORT represent a way to institutionalize reporting on research expenditures across disease areas and to standardize the way in which information on R&D funding is shared. In the long run, this may be the most sustainable way to maintain the type of data compiled by TAG. World RePORT might also be well positioned to enable analyses not yet possible with available platforms, particularly if it were expanded to include the following elements:

- **Broader geographic scope**: Expanding World RePORT to include the participation of more funding bodies, particularly those in the Global South or emerging economies, would provide insight into funding that originates outside of North America, Europe, Japan, and Australia. For example, TAG has had difficulty obtaining reliable data from funders in China, Russia, Brazil, Nigeria, Indonesia, and Vietnam. We know these countries are supporting TB research with domestic resources—and quite a bit, in the case of China and Russia—but have not been able to obtain regular information through our survey-based method. A common platform for sharing funding information with broad geographic reach would represent a significant advancement.

- **Linking funding to the pipeline**: Tracking funding is one thing. Understanding how funding levels correlate with research output is another. Up until now, TAG has tracked funding for TB research in one report and reviewed progress in the clinical pipelines for new TB prevention, diagnostic, and therapeutic technologies in a separate report called *The Pipeline Report*. Connecting these two efforts is an area where World RePORT could play a pivotal role if it developed interoperability with other platforms. For example, if World RePORT entries were linked to corresponding projects in ClinicalTrials.gov.

- **Understanding funding flows**: Mapping how money for research moves from funding institutions to recipient organizations is a powerful way to understand the ecosystem supporting TB research. However, this type of mapping only provides part of the picture. There is still little insight into how and where the principal recipients of grants, contracts, and awards spend money. For example, the bulk of NIH money for TB research is awarded to R1 universities in the United States, but many of the supported projects are actually carried out in TB high-burden countries. Understanding where research is conducted will require a much more granular picture of funding flows. This would be an enormous undertaking, and the type of project that could only be supported if built on top of the existing knowledge infrastructure made possible by a platform like World RePORT.

After 13 years, it is clear to TAG that tracking funding for TB research did much more than produce a picture of TB R&D expenditures over time. It allowed TB advocates to

get organized; make arguments based on evidence; translate these arguments into political commitments at the highest levels of government attention; respond to emerging trends in the donor and scientific landscapes; and keep our arguments in support of TB research fresh and relevant to evolving scientific, public health, and patient priorities.

The flow of public and philanthropic funding for TB R&D between countries, 2011–2015 (Source: World Health Organization)