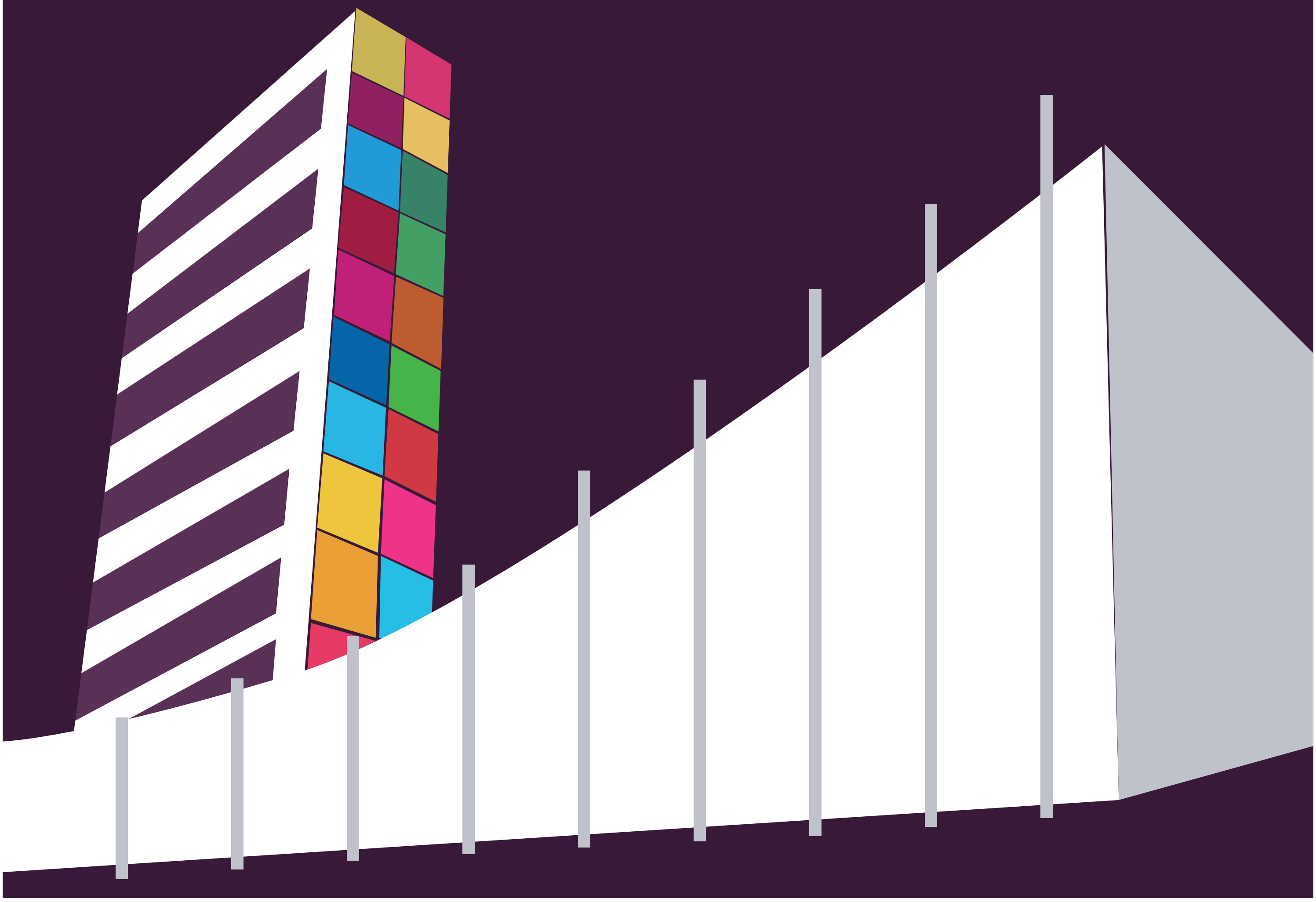
Treatment Action Group

Stop TB Partnership

Tuberculosis Research Funding Trends
2005-2017



ACKNOWLEDGMENTS

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ABOUT TAG

Treatment Action Group (TAG) is an independent, activist, and community-based research and policy think tank fighting for better treatment and prevention, a vaccine, and a cure for HIV, tuberculosis (TB), and hepatitis C virus (HCV).

TAG works to ensure that all people with HIV, TB, or HCV receive lifesaving treatment, care, and information. We are science-based treatment activists working to expand and accelerate vital research and effective community engagement with research and policy institutions. TAG catalyzes open collective action by all affected communities, scientists, and policy makers to end HIV, TB, and HCV.

TB PROJECT

TAG's TB project works to create a policy, funding, and advocacy environment that is conducive to TB research, the uptake of evidence-based interventions, and the promotion of human rights of people affected by TB.

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Tuberculosis Research Funding Trends, 2005–2017

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TREATMENT ACTION GROUP

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DEDICATION

We dedicate this report to a policymaker, a physician-researcher, and a patient advocate.

The policymaker: We dedicate this publication to **Dr. Aaron Motsoaledi**, South Africa's minister of health and chair of the Stop TB Partnership. Motsoaledi has been a driving force behind the renewed political will we've seen in the TB response in recent years. He has also made South Africa a world leader in introducing new technologies such as the TB drug bedaquiline and the GeneXpert TB diagnostic test. Through the introduction of new technologies, and by overseeing the large-scale rollout of antiretroviral therapy to people in South Africa living with HIV, he has probably helped save hundreds of thousands of lives that would not have been saved with less-courageous leadership. In South Africa he has also taken a brave stance against corruption, something that impacts healthcare services as much as all other spheres of society. At a time when calls for political will in the TB response outnumber actual political actions and solutions, Motsoaledi embodies the decisive leadership the world needs to end TB.

The physician-researcher: We dedicate this report in memory of **Dr. Fred Gordin**, chief of the infectious diseases section at the Veterans Administration Medical Center in Washington, D.C. Fred was a visionary HIV and TB clinician and researcher and was instrumental in establishing the Community Programs for Clinical Research on AIDS (CPCRA), a clinical trials network that conducted research on HIV treatment and the prevention and treatment of its comorbidities, including TB, and was notable for carrying out research within local communities. The CPCRA provided a model for several of the clinical trial networks that play a leading role in TB research today, including the U.S. Centers for Disease Control and Prevention (CDC) Tuberculosis Trials Consortium, which Fred helped to found. We will remember him as a steadfast friend of the activist community and as a scientist who championed the meaningful involvement of people affected by HIV and TB in all aspects of clinical research.

The patient advocate: We dedicate this report in memory of **Shreya Tripathi**, the brave young woman with extensively drug-resistant TB (XDR-TB) who successfully sued a public Indian hospital for access to new drugs to treat her disease. Last year, we dedicated this report to Shreya under the pseudonym Siya Trivedi. At that time, Shreya had recently won a case before the Delhi High Court, which ruled in January 2017 that the government could not deny her access to bedaquiline based on her legal domicile being located outside one of the six sites at which the drug was initially available through the government-run clinical access program. After winning her case before the court, Shreya sought care at Mumbai's esteemed Hinduja Hospital, where she received bedaquiline as well as a second new drug, delamanid, under compassionate use. Shreya passed away in early October 2018. Although her XDR-TB was cured, the delays in accessing bedaquiline and delamanid left her with overwhelming damage to her lungs that cost Shreya her life. We will remember Shreya for her courage, for the hope her legal battle gave to a great many people, and for the undeniable truth at the core of her determination to overcome TB: access to medicines is a human right.

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Executive Summary

Treatment Action Group (TAG) has been tracking global investment in tuberculosis (TB) research and development (R&D) since 2005. In this report, we present data on TB research funding trends from 2005 to 2017.

In 2017, global investment in TB research reached a new high of USD $772 million. This represents a $46 million (6%) increase on the previous high of $726 million set in 2016.

After a nominal increase of 29% from 2008 to 2009, funding was relatively stable from 2010 to 2015, increasing again substantially in 2016 and 2017. However, after adjusting for inflation, the 2017 figure is worth only $552 million in 2005 constant dollars, only marginally above the 2009 figure of $544 million. In real terms, there has been no substantial increase in funding for TB research in the last decade.

Total global investment in TB research over the 13 years from 2005 to 2017 adds up to $7.8 billion. In order to meet the Stop TB Partnership's *Global Plan to End TB* (*Global Plan*) target of investing $9 billion from 2016 to 2020, the world will now have to invest almost as much ($7.5 billion) in the three years from 2018 to 2020, since investments in 2016 and 2017 only amounted to $1.5 billion combined. Strictly speaking, meeting the *Global Plan* target now requires investment of $2.5 billion per year, rather than the widely quoted $2 billion.

Sixty-six percent ($510 million) of global TB funding in 2017 came from public sources, 19% ($145 million) from philanthropies, 11% ($85 million) from private industry, and 4% ($32 million) from multilateral entities. Public funding showed the greatest growth over 2016 levels, with an increase of $27 million.

The U.S. government remains by far the largest funder of TB research, having invested $312 million in 2017 through eight different agencies. This accounts for 40% of global TB R&D funding and 62% of all public funding—more than all other governments added together. The European Union invested $37 million, the United Kingdom $36 million, Germany and Canada $19 million each, India $17 million, and South Korea $15 million. No other countries reported spending more than $10 million in 2017.

Spending on TB research relative to the capacity of states to invest in R&D is also low. Only three countries reported investing more than 0.1% of gross domestic expenditure on research and development (GERD) on TB research in 2017. South Africa topped the list on this metric, exceeding its target by 83%. The Philippines surpassed its target by 61% and New Zealand by 14%. Among countries that did not meet the 0.1% target, the United Kingdom came closest, investing 89% of its target, followed by Canada with 73% and the United States with 70%. The 0.1% of GERD target has gained traction over the last year as a means to calculate a country's fair share of global TB R&D funding.

The Bill and Melinda Gates Foundation (Gates Foundation) was the second largest funder of TB research in 2017, with an investment of $128 million. This is multiple times more than the contribution from any government except for the United States, is more than all private sector investments combined, and makes up 17% of total TB research funding. Together, the U.S. government and the Gates Foundation contributed 57% of TB R&D funding in 2017. Philanthropic funding for TB research has, however, been relatively flat in recent years and has never climbed far beyond the $154 million reported in 2008.

The next largest funder after the U.S. government and the Gates Foundation was Unitaid, with an investment of $29 million. With U.S. government funding split across various funding entities, Unitaid ranks fifth on the list of top funders. Unitaid funding in 2017 nearly doubled from $15 million in 2016. That Unitaid, an organization whose core mission is to take innovations to scale by supporting implementation, now counts among the largest funders of research says just as much about the absence of traditional R&D funders from the TB field as it does about Unitaid's commendable commitment.

With an investment of $23 million in 2017, the pharmaceutical company Otsuka ranks sixth overall and was the top private-sector investor in TB R&D. It is one of four pharmaceutical companies in the top 20 funders. Together, these four companies contributed $66 million of the total $85 million reported by private-sector groups in 2017.

"I think 2018 has been an extraordinary year for TB research. In the last year, we've had these extraordinary announcements. We had the NIX-TB trial, and it's looking like we're making real progress in MDR-TB treatment. We had, from the diagnostic perspective, the results of the STAMP trial and TB urine LAM looking like it's making a real difference for hospitalized HIV patients and mortality. And then we had BCG revaccination looking really exciting and now a subunit vaccine looking exciting. I almost feel like I've just stepped into some kind of parallel TB research universe. A year ago, it was a really difficult place, and suddenly there's just lots of potential and excitement."

Helen Fletcher, Professor of Immunology, TB Centre at the London School of Hygiene and Tropical Medicine

Total private-sector investment in TB research was above $100 million from 2010 to 2013 and has been under this threshold ever since. Although a few companies, most notably Otsuka, Johnson & Johnson (Janssen), and GlaxoSmithKline (GSK) remain active in this area, a number of major pharmaceutical companies are not investing in TB R&D. These include Pfizer, AstraZeneca, Gilead, Bristol Myers Squibb, Merck, and Abbott, among others. EvaluatePharma has estimated that total pharmaceutical industry investment in R&D in 2017 was $97.2 billion; the $85 million that industry invested in TB research in 2017 is less than 0.1% of this figure. Attempts to incentivize greater private-sector participation in TB research through prize funds (e.g., the Life Prize) have so far been unsuccessful—mainly because governments have not yet funded any such prizes.

In 2017, 41% of total global TB R&D funding went to TB drug research, 19% to TB basic science, 13% to TB vaccine research, 12% to operational research, 10% to TB diagnostics research, and 5% to infrastructure/unspecified projects.

All areas except for basic science and infrastructure/unspecified showed increases over 2016 levels. The largest year-on-year increase was in drug research, where spending rose by $58 million from $257 million to $315 million. Over a third of this increase can be attributed to the Gates Foundation, whose funding for drug research rose from $40 million in 2016 to $63 million in 2017. The year 2017 marked the third consecutive year in which funding for operational research increased. In contrast to recent increases in operational and drug research, investment in basic science has been relatively flat from 2014 to 2017.

Funding for pediatric TB research nearly doubled between 2016 and 2017, jumping from $29 million to $56 million. The European and Developing Countries Clinical Trials Partnership (EDCTP) was the largest funder in this area with $10.6 million, followed by the U.S. Agency for International Development (USAID) with $9.5 million.

In all years from 2005 to 2017, TB drug R&D has been the research area with the highest level of annual investment. In all years except for 2008, basic research ranked second. Vaccines ranked third in all years except for 2008, when it ranked second.

Of the total $7.8 billion invested in TB R&D from 2005 to 2017, 37% was invested in drug research, 21% in basic science research, 15% in vaccine research, 10% in operational research, and 9% in diagnostic research.

Introduction

"It's now or never! If we cannot really move things after a Ministerial Conference and having TB for the first time on the agenda of the United Nations General Assembly, why would we be able to move it ahead next year or in three years?"

Kitty van Weezenbeek, Executive Director, KNCV Tuberculosis Foundation

In September 2018, the global TB movement had arguably the most important political moment in its history, when over 15 heads of state addressed the first-ever United Nations High-Level Meeting (HLM) on TB in New York.[1] The meeting was a critical moment for TB more broadly, but also for TB research in particular—with the need for greater investment in TB R&D standing out as one of the most prominent themes at the meeting.

"Investing in research and development is critical if we are to develop new diagnostics, vaccines and medicines—and find innovative ways to deal with the social determinants of tuberculosis and its transmission," South African president Cyril Ramaphosa told the meeting. "It is only with new tools that we can achieve the dramatic reduction in the incidence of TB needed to ensure total elimination of this disease by 2030 or earlier."[2]

Although governments made relatively few concrete and specific commitments in the political declaration endorsed at the HLM, the declaration nevertheless reflected wide agreement about the need for much greater investment in TB R&D.[3] UN member states committed "to mobilize sufficient and sustainable financing, with the aim of increasing overall global investments to US$2 billion, in order to close the estimated US$1.3 billion gap in funding annually for tuberculosis research." The broad intent is thus present, but unfortunately the $2 billion per year is an "aim" rather than a concrete commitment.

If the declaration had made a concrete commitment of $2 billion per year for TB research, the question would have arisen as to what amount each country would be responsible for contributing. To the extent that this problem is implicit in the text, UN member states committed to "ensuring all countries contribute appropriately to research and development." In this report, we provide some data that can be useful in determining which countries are contributing "appropriately" and which ones are not.

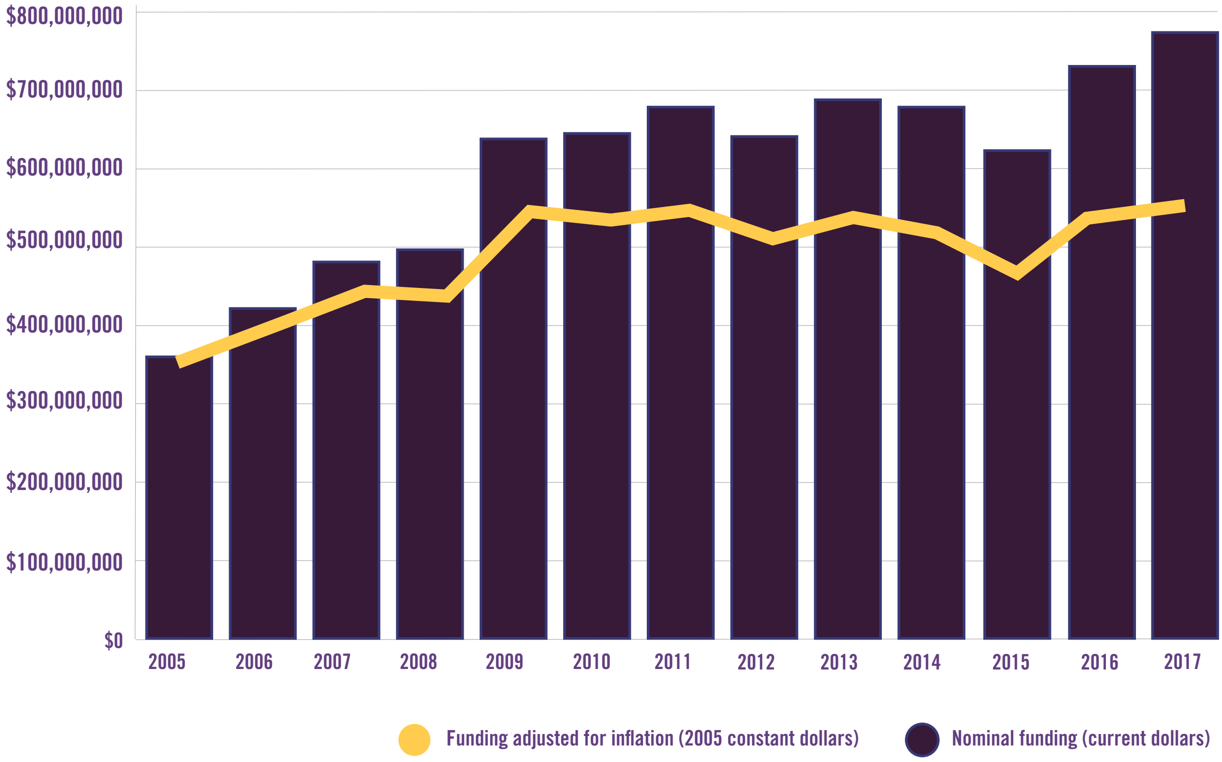
A few months after the TB cause's big moment in New York, several important questions remain unanswered. Where will we find the $2 billion per year that is needed for TB research? How will we get countries to contribute their fair share? How will governments be held accountable for closing the funding gap? Where will we find the political will and money to trial new delinkage-based innovation models for TB drug and diagnostic development?

Of course, the HLM was never going to provide the answers to all of these questions. Rather than an end in itself, the meeting is best understood as just another stop on the long walk toward eliminating TB—be it in 15 or in 50 years. What the HLM has provided, however, is unprecedented political visibility. This political attention may or may not be leveraged into real momentum toward finding the money we need for TB research. Part of the function of this report, as well as future reports, is to track how well this political momentum is being converted into concrete increases in TB research funding.

In this report, we present data on TB research funding trends for the 13 years from 2005 to 2017. Although there have been spurts of notable growth, particularly in 2009 and again in 2016 and 2017, funding for TB research has lagged far behind internationally agreed-upon targets and has remained dependent on a few large funders. This extreme reliance on a handful of major funders makes the progress we have seen over the last decade precarious. In addition, when adjusted for inflation, funding for TB research has not increased from where it was a decade ago.

FIGURE 1

Total TB R&D Funding, 2005–2017



Year	Nominal funding (current dollars)
2005	$358,119,753
2006	$418,928,300
2007	$478,343,421
2008	$494,168,892
2009	$636,979,349
2010	$643,360,390
2011	$675,328,887

Year	Nominal funding (current dollars)
2012	$638,783,272
2013	$686,303,295
2014	$674,036,492
2015	$620,600,596
2016	$726,080,643
2017	$772,001,759

TAG collected the investment data presented here through a global survey of TB research funders (see Appendix 1 for a detailed description of the methodology). Not all funders of TB research reported to us, but the vast majority did. Our survey also does not fully capture indirect funding through salaries, overhead, or infrastructure that is not TB specific. In addition to documenting TB research expenditures, we spoke to scientists, activists, TB program managers, policy makers, and other experts in the field to gather their opinions on TB research and funding for it in the context of the HLM. Interviewees had each seen a preliminary summary of this year's data, which TAG published the week of the HLM.[4] Overall, interviewees spoke of gaps—gaps in funding, in implementation, in access to information and new technologies, in political will, and in human rights and accountability. We quote from these rich interviews throughout the report to put the numbers and financial analyses into their bigger context.

In absolute terms, global funding for TB research reached a new high of $772 million in 2017. This amount is more than $1.2 billion behind the $2 billion target mentioned in the HLM Political Declaration. Although that $2 billion target was set based on a target in the *Global Plan*,[5] it did not take into account what we now know

> "We should never confuse these [high-level] meetings with success. They are really just catalysts, and the proof is in what we do coming out of those meetings. I hope people don't get too stuck on the declaration but rather get stuck [on]: What are the targets for the next three years? How are we going to measure it? How are we going to hold people accountable, and how are we going to ensure that actions happen?"
>
> **Mitchell Warren, Executive Director, AVAC**

has been two years of dramatic underspending against the *Global Plan* target. The *Global Plan* estimates that a total of $9 billion should be invested in TB R&D from 2016 to 2020. This amounts to $1.8 billion per year. Given that the 2016 and 2017 figures are well below this target, annual investment for the period 2018 to 2020 must average $2.5 billion to reach the target. This is more than triple the current funding and would require spending in three years an amount that is almost equal to the total $7.8 billion invested in TB research in the 13 years from 2005 to 2017.

Whether or not these funding targets are met may have serious implications for the future of the global TB epidemic. As succinctly stated in the 2018 World Health Organization (WHO) *Global TB Report:* "The SDG [Sustainable Development Goal] and End TB Strategy targets set for 2030 cannot be met without intensified research and development."[6] This assertion is based on epidemiological modeling that suggests current tests and treatments will not bring TB rates down quickly enough and that, accordingly, the world must develop breakthrough new tests, treatments, and vaccines by 2025. Triangulating from the End TB Strategy, the latest *Global TB Report*, and the figures we report here, it seems clear that a major scale-up in funding over current levels is required if we are to have any chance of ending TB in the next decade. As yet, we cannot report any such major scale-ups. At best, we can describe recent data as incremental growth. As stated in the 2018 *Global TB Report*, "the development pipelines are progressing, but slowly."

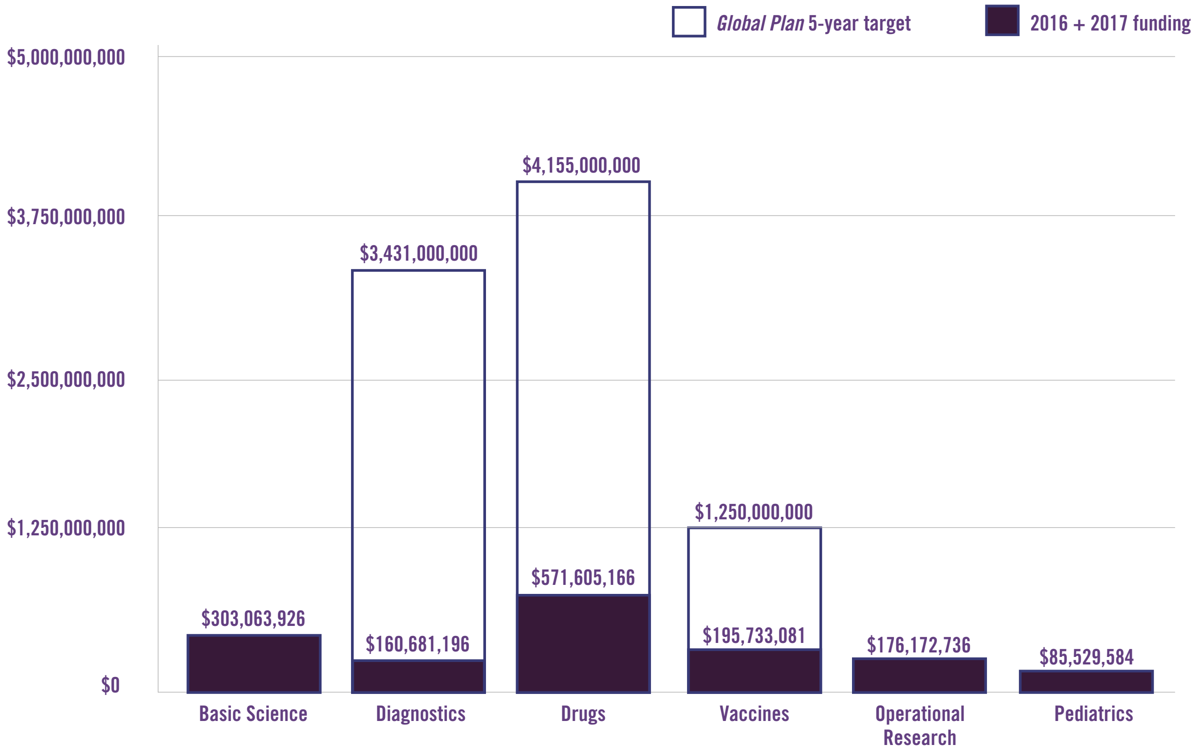
There are, however, a number of reasons for optimism.

First, with the unprecedented political momentum created by the HLM and the substantial focus on TB research in its resulting political declaration, the potential is now there for substantial funding increases in 2018 and 2019. New investments announced by the governments of the United States and the United Kingdom during the HLM are the first concrete sign of this increased commitment. From the U.K. side, the U.K. Department for International Development (DFID) announced a new award of £7.5 million to the TB Alliance, a product development partnership (PDP), to develop shorter, simpler TB treatments.[7] DFID was the seventh largest funder of TB research in 2017,with contributions totaling $20.6 million. The U.S. commitment followed the release of a new strategic plan for TB research by the National Institute of Allergy and Infectious Diseases (NIAID) at the U.S. National Institutes of Health (NIH), the largest funder of TB research globally.[8] At a side event to the HLM, an official from the NIH shared the agency's intention to increase annual funding for TB research to $440 million per year, in line with the TAG-derived target for the U.S. government's "fair share" of the global TB R&D funding need (for more on country-specific targets, keep reading).

Second, as we saw with the large increase in TB research funding in 2009, it is possible to increase funding substantially and then maintain it at those higher levels. In 2009, funding for TB research increased by 29% from 2008's $494 million to $637 million. As illustrated in figure 1, those gains have been maintained in the years since. Most of this increase came from the U.S. government as part of an $800 billion stimulus package released in response to the 2008 economic crisis. That funding for TB research did not drop back down to pre-stimulus levels after the economic spending package ended is largely owed to the strong bipartisan support for the NIH, which has enjoyed several years of increasing appropriations. (Other U.S. government agencies active in TB research have seen some budget increases since 2009, but not at the level or with the consistency seen at the NIH.)

FIGURE 2

Progress toward *Global Plan* 5-Year TB Research Funding Targets



The Global Plan to End TB did not set funding targets for TB basic science, operational research, or pediatric TB R&D.

Third, the establishment of the BRICS TB Research Network, in addition to various national TB research networks in countries from Thailand to Ethiopia, signals that more high-burden countries are prioritizing TB research. (BRICS stands for Brazil, Russia, India, China, and South Africa, a group of emergent economic powers that together account for nearly half of the world's new TB cases each year.[9]) In addition, new evidence published this year shows that the BRICS countries have substantially increased their TB research outputs over the decade from 2007 to 2016 (measured as number of publications),[10] something that indicates both increased research activity and greater capacity. Many of these countries have relatively large economies and as such have the ability to invest much more given sufficient political will. As pointed out by Afrânio Kritski, a founding member of the Brazilian TB Research Network: "To achieve the End TB Strategy, we need to have BRICS on board. If we cannot combat TB properly in BRICS, we will never achieve the targets set by End TB or the Sustainable Development Goals."

Ultimately, the amount of money governments are willing to invest in TB research provides one of the most concrete and objective measures of their commitment to the fight against TB. As this report shows, all countries, even leading donor nations like the United States and the United Kingdom, can do a lot better.

Results

"I would like to see a year-on-year increase in TB R&D funding, rather than targets being set for five or 10 years' time without any interim analysis of how we are on course to achieve those targets."

Grania Brigden, Deputy Director, TB and HIV Department, International Union Against TB and Lung Disease (The Union)

The big picture

In 2017 annual global investment in TB research reached a new high, totaling $772 million. This represents a $46 million (6%) increase from the previous high of $726 million set in 2016. This upward movement was primarily driven by a $27 million increase in public funding and a $12 million increase in multilateral funding. In terms of research areas, this increase is mostly accounted for by the $58 million year-on-year increase in funding for TB drug R&D.

After an increase in global investment in TB R&D of 29% from 2008 to 2009, funding was relatively stable from 2010 to 2015, increasing again substantially in 2016 and 2017. However, after adjusting for inflation, the 2017 figure of $552 million (in 2005 constant dollars) is only marginally above the 2009 figure of $544 million. In real terms, there has thus been no substantial increase in funding for TB research in the last decade.

Total global expenditures on TB research over the 13 years from 2005 to 2017 add up to $7.8 billion. In order to meet the End TB target of investing $9 billion from 2016 to 2020, the world will now have to invest almost as much ($7.5 billion) in the three years from 2018 to 2020—with only $1.5 billion having been invested in 2016 and 2017 combined. Strictly speaking, meeting the End TB target now requires investing $2.5 billion per year, rather than the widely quoted $2 billion.

In 2017, investment in TB research continued to be dominated by the U.S. government and the Gates Foundation. This long-running dependence on two large funders represents a critical vulnerability of the global TB research infrastructure.

Trends in public-sector funding

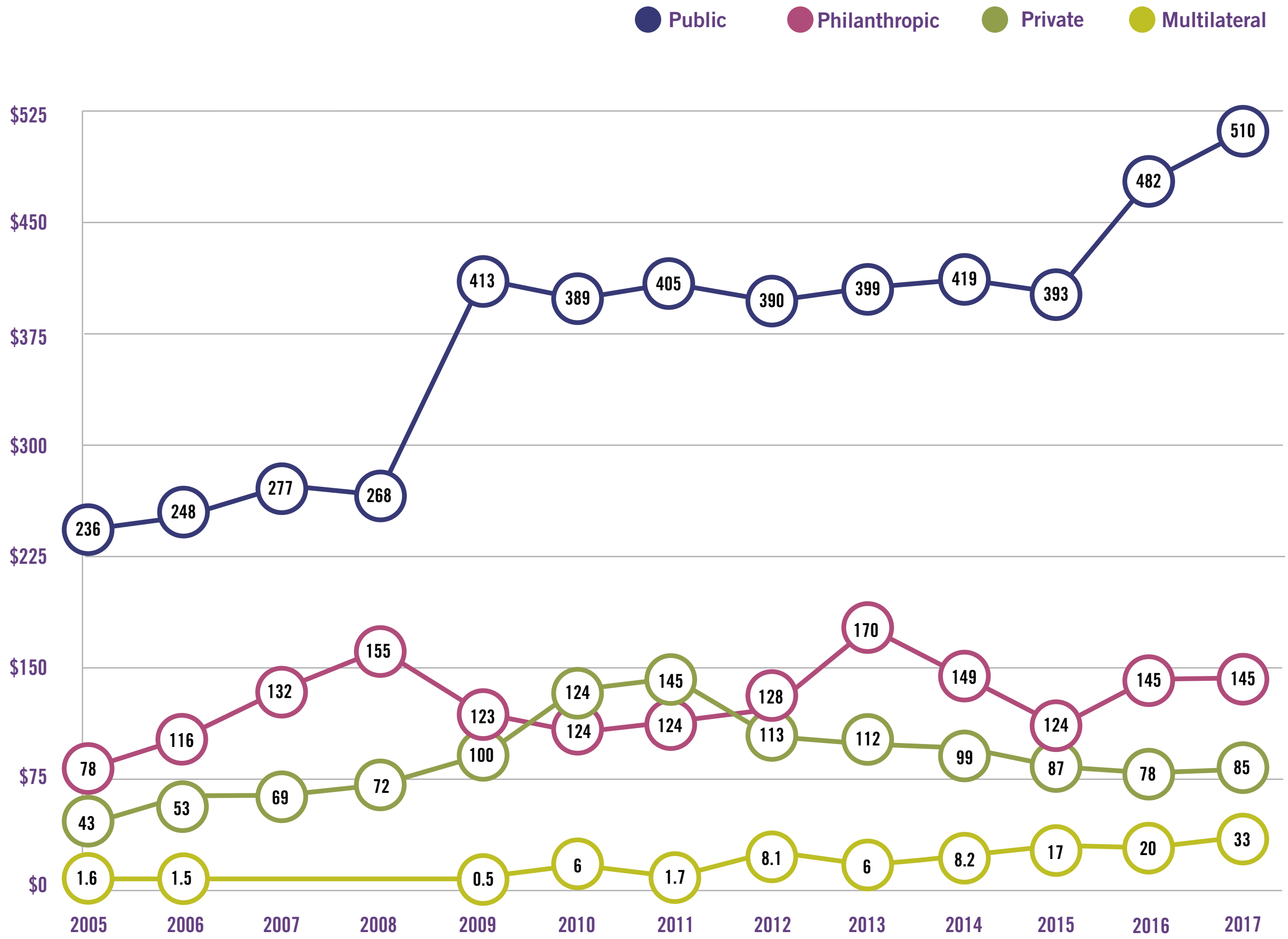
In 2017, the U.S. government remained by far the largest funder of TB research, investing $312 million through eight different agencies. This accounts for 40% of global TB research funding and 62% of all public funding and thus exceeds spending by all other governments combined. This investment is slightly down from 2016's $316 million but is nevertheless part of a positive trend given that from 2009 to 2015 annual U.S. government spending remained relatively stable in the band between $247 million and $268 million.

The European Union invested $37 million in TB research in 2017, the United Kingdom $36 million, Germany and Canada $19 million each, India $17 million, and South Korea $15 million. No other countries reported spending more than $10 million in 2017. India, a country with 27% of the global TB burden, invested only $85 million in TB R&D over the entire period from 2009 to 2017—just over a quarter of what the United States invested just in 2017.

Total public funding for TB research increased from $482 million in 2016 to a new high of $510 million in 2017. This $28 million increase was primarily driven by year-on-year increases in the European Union ($13.5 million), United Kingdom ($8.5 million), and Germany ($4 million). Although the increase is relatively modest, it is notable that funding did not drop back down to the relatively narrow $389–$419 million band where it was every year between 2009 and 2015. However, it is clear that there has not been a large spike from 2016 to 2017, as some may have expected ahead of the HLM.

FIGURE 3

Total TB R&D Funding by Funder Category, 2005–2017 (in Millions)



Out of 17 countries for which TAG has sufficient data and which have invested more than $10 million over the last nine years, only seven reached new annual investment highs in 2017. It is encouraging that these seven countries include three of the BRICS: Brazil, India and South Africa. (Neither China nor Russia provided data in time for this report.) Of the wealthier countries, Canada, Germany, and HLM co-facilitator Japan also achieved new highs in 2017. U.S. investment dropped only very slightly, and as yet there are no major cuts to report as some feared would be the case under the Trump administration.

> "We can't always rely on the Gates Foundation. We need many other foundations to contribute to TB and TB research and development."
>
> Albert Makone, Global Health Advocate

Trends in philanthropic funding

Total philanthropic spending on TB research in 2017 was $145 million—about a million less than in 2016. This constituted 19% of total investment in TB research and was 69% more than total private-sector investment over the same period. The 2017 figure was lower than the $170 million reported in 2013, the highest number reported by philanthropic organizations since TAG started tracking in 2005. There has thus been no real growth in philanthropic funding in recent years.

Much as public funding for TB research is dominated by the United States, philanthropic funding is dominated by the Gates Foundation, whose $128 million investment in 2017 constituted 89% of total philanthropic funding in that year. The Gates Foundation was also the second largest funder of TB research overall. Its spending is multiple times more than any government's except for the United States, exceeds all private-sector investments combined, and makes up 17% of total TB research funding. Together, the U.S. government and the Gates Foundation contributed 57% of TB R&D funding in 2017.

Trends in private-sector funding

With an investment of $23 million in 2017, the pharmaceutical company Otsuka was the sixth largest funder overall and the top private-sector investor in TB research in 2017. Four pharmaceutical companies rank among the top 20 funders. Together, these four companies contributed $66 million of the $85 million spent by private industry in 2017.

The $85 million invested by the private sector in 2017 is a $7 million increase on the $78 million reported in 2016. Although private-sector spending was above $100 million from 2010 to 2013, it has been below the $100 million mark in all other years since 2005.

While a few companies, most notably Otsuka Pharmaceuticals, Johnson & Johnson (Janssen), and GSK remain active in this area, a number of major pharmaceutical companies are not investing anything in TB research. These include Pfizer, AstraZeneca, Gilead, Bristol Myers Squibb, Merck, and Abbott, among others. EvaluatePharma has estimated that total pharmaceutical industry investment in research and development in 2017 was $97.2 billion; the $85 million industry investment in TB research in 2017 is less than 0.1% of this figure. Attempts to attract greater private-sector participation in TB research through prize funds (e.g., the Life Prize) have so far been unsuccessful—mainly because governments have not yet funded any such prizes.

"We can't just keep repeating the problems of the past in terms of sweetening the deal for the private sector to get involved without any recognition of the need to have affordability and access provisions built in [to public funding agreements]."

Sharonann Lynch, HIV and TB Policy Advisor, Médecins Sans Frontières Access Campaign

"In addition to Big Pharma, we also have biotech industries. [The problem] there is: how are we going to ensure that they get the capital to be able to take their compounds forward? We need to think about, in addition to incentivizing big pharmaceutical companies, how do we ensure that biotech companies, [which] may not have the same financial structure, are able to have adequate investment to advance their TB compounds?"

Grania Brigden, Deputy Director, TB and HIV Department, The Union

Trends in multilateral funding

With $32 million in multilateral funding for TB research, this sector achieved new relevance in 2017. After resting below the $10 million mark from 2005 to 2014, multilateral funding has now broken above this level in each of the last three years.

The significant increase in multilateral funding can primarily be attributed to increased investment from Unitaid. In 2017, Unitaid's investment of $29 million (up from $15 million in 2016) made it the fifth largest funder of TB research overall. Beyond research-specific spending, Unitaid's overall funding for TB projects jumped from $127 million in 2016 to $215 million in 2018 and is on track to hit $300 million in 2020.[11] Not traditionally thought of as an R&D funder, Unitaid has become an increasingly large player in a field short on resources. Unitaid describes its work as supporting projects that "harness innovation to improve preventive treatment, diagnostics and better, faster-acting treatments, setting them up for wide-scale introduction by funding partners."[12]

FIGURE 4

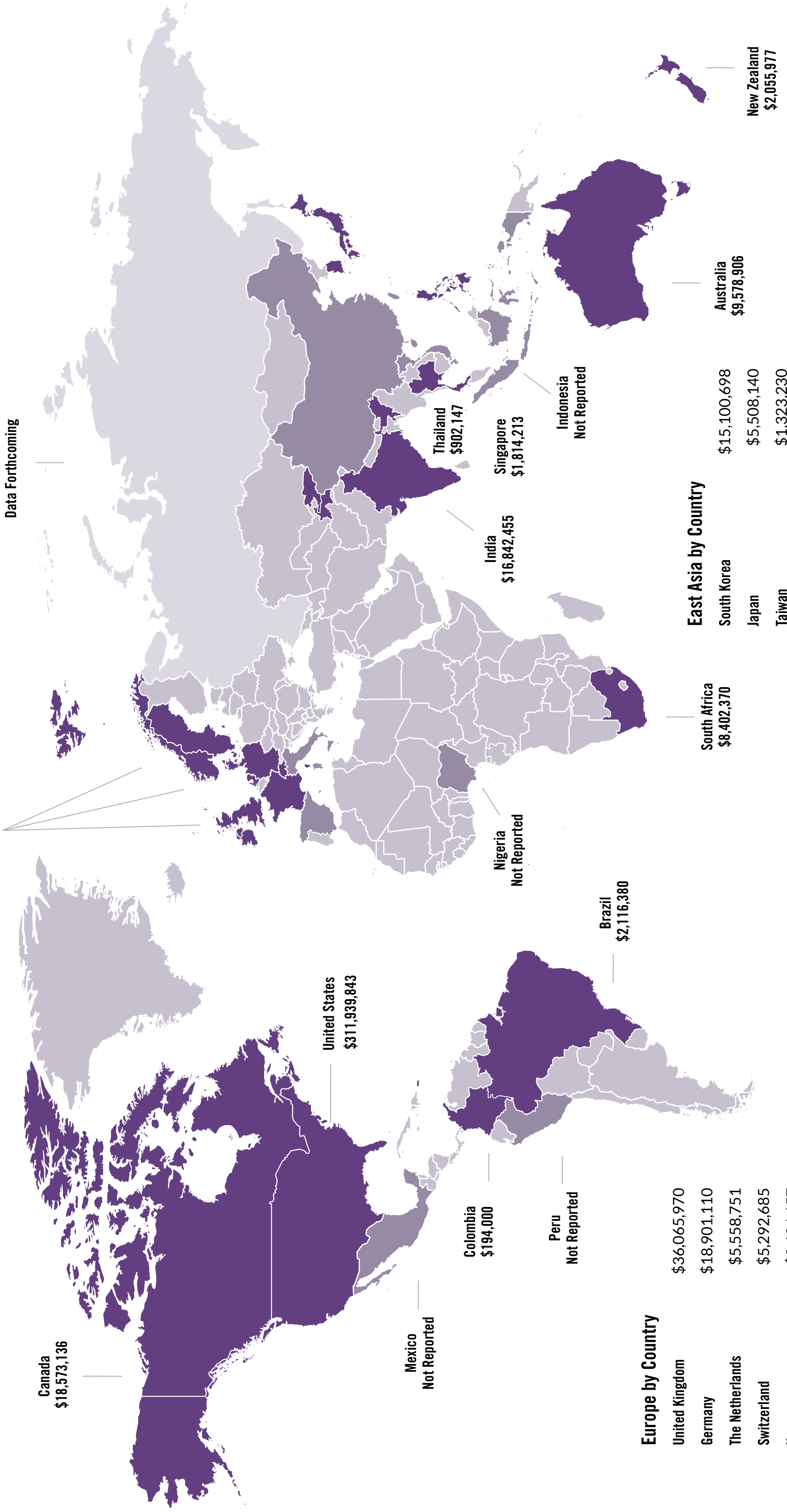
Total TB R&D Funding by Funder Category, 2017
Total: $772,001,759

The second largest multilateral funder is the Japan-based Global Health Innovative Technology Fund (GHIT), a partnership between the Japanese government, 16 Japanese pharmaceutical companies, the United Nations Development Program (UNDP), and two charitable organizations (the Wellcome Trust and the Gates Foundation). The Global Fund to Fight AIDS, TB and Malaria (Global Fund) may, in actuality, be the largest multilateral funder of TB research. The Global Fund reports spending $166.7 million on TB operational research since its creation in 2002; however, it cannot disaggregate this total figure by year, making it difficult to evaluate its funding for TB research over time.[13]

> "As wealth and resources to support research are increasingly concentrated in middle- and high-income countries, and TB burden is highest in low- and middle-income countries, the commitments have to come from the former."
>
> **Paul Farmer, Co-Founder, Partners in Health**

FIGURE 5

Country Contributions to TB R&D, 2017



Europe by Country

United Kingdom	$36,065,970
Germany	$18,901,110
The Netherlands	$5,558,751
Switzerland	$5,292,685
Norway	$3,424,657
Sweden	$2,644,386
Ireland	$2,098,544
France	$958,927
Denmark	$176,652
Spain	Not Reported
Italy	Not Reported

East Asia by Country

South Korea	$15,100,698
Japan	$5,508,140
Taiwan	$1,323,230
Hong Kong	$127,300
Philippines	$1,128,864
China	Not Reported
Vietnam	Not Reported

What Is a Country's Fair Share of TB R&D Funding?

"The lack of middle-income countries as top public funders [is surprising] because there's all this research showing the huge return on investment to TB control."

Kathryn Snow, doctoral candidate, University of Melbourne

In the HLM political declaration, governments committed to "mobilize sufficient and sustainable financing, with the aim of increasing overall global investments to US$2 billion, in order to close the estimated US$1.3 billion gap in funding annually for tuberculosis research." Governments also committed to ensure that "all countries contribute appropriately to research and development," although without defining what was meant by "contribut[ing] appropriately."

Apart from absolute investment in TB research (shown in figure 5), we provide two additional measures that may be of use in calculating a country's appropriate share of global TB R&D investment. The first is TB research funding as a percentage of what a country spends on all forms and types of R&D (GERD); we call these the 0.1% fair-share targets. The second is a new measure we call the burden-investment index (BII).

TB research investment as a percentage of GERD

"Even though it was not included explicitly in the final political declaration of the HLM, the 0.1% fair-share target has gained traction over the last year as a means to calculate a country's fair share of global TB funding. GERD is a measure of how much a country spends on all forms of R&D (including but not limited to health). The world could reach the $2 billion annual target if all high-TB-burden countries and a list of wealthy countries devoted 0.1% of their overall R&D spending to TB research. The 0.1% fair-share target asks countries to reprioritize within existing funding envelopes and as such is theoretically achievable in most countries given sufficient political will. It also has a solidarity element built in because it does not distinguish according to TB burden and it asks proportionally more of wealthier countries. The HLM political declaration affirmed the importance of solidarity and committed member states to advancing research and innovation through global collaboration.

Only three countries met their 0.1% fair-share targets in 2017. South Africa topped the list on this metric, exceeding its target by 83%. The Philippines surpassed its target by 61% and New Zealand by 14%. Of countries that did not meet the 0.1% target, the United Kingdom came closest, satisfying 89% of its target, followed by Canada with 73% and the United States with 70%. Some wealthy countries, such as Japan and South Korea, have substantial R&D capacity but dedicate relatively little of this capacity to TB research. Japan, co-facilitator of the UN HLM, met only 4% of its $154.9 million fair-share target.

TABLE 1

Majority of Countries Have Not Met TB R&D Fair Share Funding Targets

RANK	COUNTRY	2017 FUNDING	ANNUAL FAIR SHARE TARGET	PERCENT OF TARGET MET IN 2017
1	United States	$311,939,843	$444,500,000	70%
2	European Union	$36,983,994	$202,400,000	18%
3	United Kingdom	$36,065,970	$40,400,000	89%
4	Germany	$18,901,110	$99,700,000	19%
5	Canada	$18,573,136	$25,300,000	73%
6	India	$16,842,455	$46,500,000	36%
7	South Korea	$15,100,698	$64,000,000	24%
8	Australia	$9,578,906	$21,200,000	45%
9	South Africa	$8,402,370	$4,600,000	183%
10	The Netherlands	$5,558,751	$15,100,000	37%
11	Japan	$5,508,140	$154,900,000	4%
12	Switzerland	$5,292,685	$13,400,000	39%
13	Norway	$3,424,657	$5,300,000	65%
14	Sweden	$2,644,386	$13,700,000	19%
15	Brazil	$2,116,380	$35,000,000	6%
16	Ireland	$2,098,544	$3,300,000	64%
17	New Zealand	$2,055,977	$1,800,000	114%
18	Singapore	$1,814,213	$8,400,000	22%
19	Taiwan	$1,323,230	$4,369,762	30%
20	The Philippines	$1,128,864	$700,000	161%
21	France	$958,927	$55,400,000	2%
22	Thailand	$902,147	$4,900,000	18%
23	Colombia	$194,000	$1,748,730	11%
24	Denmark	$176,652	$7,500,000	2%
25	Hong Kong	$127,300	$9,900,000	1%
26	Russian Federation	Data forthcoming	$36,500,000	---
27	China	Not reported	$305,600,000	---
28	Italy	Not reported	$27,500,000	---
29	Mexico	Not reported	$10,300,000	---
30	Nigeria	Not reported	$7,000,000	---
31	Indonesia	Not reported	$2,100,000	---
32	Vietnam	Not reported	$1,300,000	---

Table includes countries that reported more than $100,000 in TB R&D funding to TAG and select other high-income or high-TB-burden countries.

Countries that met the target of spending 0.1% of overall R&D expenditures on TB research are shaded.

"To achieve the End TB Strategy, we need to have BRICS on board. If we cannot combat TB properly in BRICS, we will never achieve the targets set by End TB or the SDGs."

Afrânio Kritski, Founding President, Brazilian TB Research Network

"Even though the burden is mostly in middle-income countries, it is a handful of high-income countries that are predominantly funding TB. And that needs to be addressed."

Tenu Avafia, Team Leader, Human Rights, Law, and Treatment Access, HIV, Health and Development Group, UNDP

Burden-investment index

The BII is a measure of a country's investment in TB research relative to its TB burden. It is calculated by subtracting a country's share of the global TB burden (expressed as a percentage) from the country's share of the total investment in TB research of all countries (also expressed as a percentage). Positive BII scores indicate that a country's share of global TB research investment is greater than its TB burden. Negative scores indicate that a country's share of investment is lower than its TB burden. BII scores do not account for wealth and therefore do not reflect the expectation that wealthier countries should contribute more than poorer countries. Even so, the BII is a useful metric since it helps identify outliers and provides some indication as to whether high-burden countries are contributing sufficiently.

The United States, home to around 0.1% of the world's TB burden but the source of 62% of public investment in TB research, has the best BII score by far (0.62). By comparison to the United States, investments from elsewhere in the developed world, particularly Europe and Japan, are woefully low.

At the other end of the scale, India has 27% of the global TB burden but contributes only 3% of public funding for TB research, giving it a BII score of –0.24. The BRICS countries together have 41% of the global TB burden but contribute only around 6% of public funding for TB research. Given that the BRICS countries all have relatively large economies, it should be possible to close this ratio if governments prioritize TB research.

As pointed out by TB researcher Madhukar Pai in an editorial for the journal *PLoS Medicine*: "The world cannot depend on a few wealthy countries with very low TB incidence to support all the research that is required to tackle TB. High-burden, middle-income countries with high TB rates must step up. They have the potential to transform the global TB research agenda through increased domestic funding, collaborative networks, and transnational research partnerships."[14]

TABLE 2

Burden-Investment Index: Country Funding for TB R&D in Relation to Disease Burden

Burden-Investment Index (BII) is a measure of a country's investment in TB research relative to its TB burden. BII is calculated by subtracting a country's share of the global TB burden (expressed as a percentage) from its share of total public investments in TB R&D (also expressed as a percentage).

BII > 0: A country's share of global TB R&D funding is greater than its TB burden; BII < 0: A country's share of global TB R&D funding is less than its TB burden

RANK	COUNTRY	SHARE OF GLOBAL TB BURDEN	SHARE OF GLOBAL PUBLIC INVESTMENTS IN TB R&D	BII SCORE
1	United States	0.10%	61.72%	0.6162
2	European Union	0.57%	7.32%	0.0675
3	United Kingdom	0.06%	7.14%	0.0708
4	Germany	0.06%	3.74%	0.0368
5	Canada	0.02%	3.67%	0.0365
6	South Korea	0.36%	2.99%	0.0263
7	Australia	0.02%	1.90%	0.0188
8	The Netherlands	0.01%	1.10%	0.0109
9	Switzerland	0.01%	1.05%	0.0104
10	Japan	0.19%	1.09%	0.0090
11	Norway	0.00%	0.68%	0.0067
12	Sweden	0.01%	0.52%	0.0052
13	Ireland	0.00%	0.42%	0.0041
14	New Zealand	0.00%	0.41%	0.0040
15	Singapore	0.03%	0.36%	0.0033
16	Taiwan	0.10%	0.26%	0.0016
17	France	0.05%	0.19%	0.0014
18	Denmark	0.00%	0.03%	0.0003
19	Hong Kong	0.05%	0.03%	-0.0002
20	Colombia	0.16%	0.04%	-0.0012
21	Brazil	0.91%	0.42%	-0.0049
22	Thailand	1.08%	0.18%	-0.0090
23	South Africa	3.21%	1.66%	-0.0154
24	The Philippines	5.78%	0.22%	-0.0556
25	India	27.28%	3.33%	-0.2395
26	China	8.85%	Unknown	Unknown
27	Indonesia	8.38%	Unknown	Unknown
28	Italy	0.04%	Unknown	Unknown
29	Mexico	0.28%	Unknown	Unknown
30	Nigeria	4.16%	Unknown	Unknown
31	Russian Federation	0.86%	Unknown	Unknown
32	Vietnam	1.23%	Unknown	Unknown

Table includes countries that reported more than $100,000 in TB R&D funding to TAG and select other high-income or high-TB-burden countries.

Funding By Research Area

FIGURE 6

Total TB R&D Funding by Research Area, 2005–2017 (in Millions)

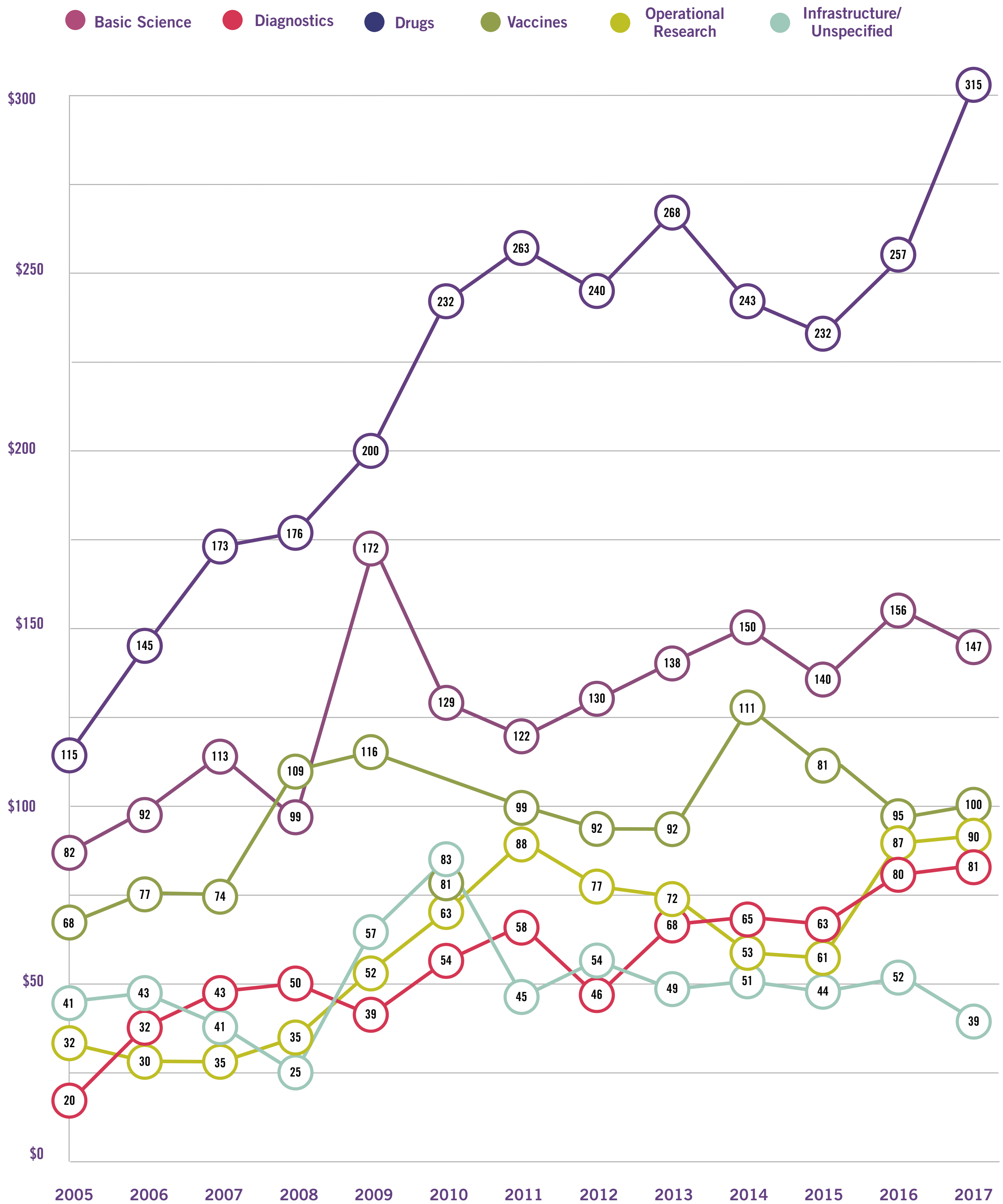
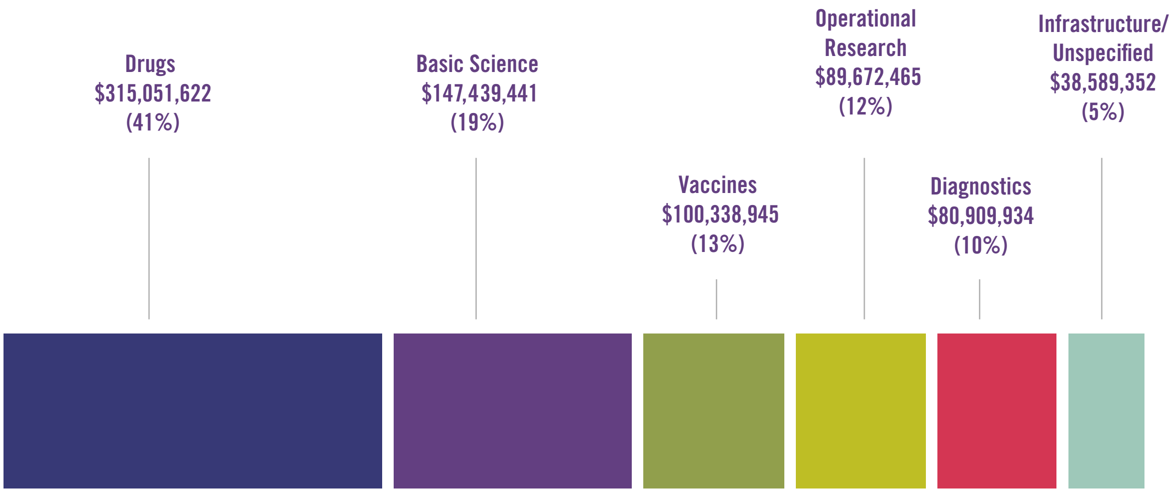


FIGURE 7

Total TB R&D Funding by Research Area, 2017
Total: $772,001,759



In 2017, 41% of total global funding for TB research was invested in TB drug research, 19% in basic science, 13% in TB vaccine research, 12% in operational research, 10% in TB diagnostics research, and 5% in infrastructure/unspecified projects.

All areas except for basic science and infrastructure/unspecified showed increases over 2016 levels in 2017. The largest year-on-year increase was in drug research, where funding jumped by $58 million from $257 million to $315 million. The year 2017 marks the third consecutive year in which funding for operational research increased. By contrast, funding for basic science has been relatively flat from 2014 to 2017.

In all years from 2005 to 2017, drug research has been the research area with the highest level of annual investment. Basic science ranked second in all years except for 2008. TB vaccine R&D ranked third in all years except for 2008, when it ranked second.

Of the total $7.8 billion invested in TB research from 2005 to 2017, 37% has been invested in drug research, 21% in basic science, 15% in vaccine research, 10% in operational research, 9% in diagnostic research, and 8% in infrastructure/unspecified projects.

According to the 2018 WHO *Global TB Report*, TB research priorities include "a vaccine to lower the risk of infection, a vaccine or new drug treatment to cut the risk of TB disease in the 1.7 billion people already latently infected, rapid diagnostics for use at the point of care, and simpler, shorter drug regimens for treating TB disease." The comparatively low level of investment in TB diagnostics seems at odds with the WHO's emphasis on the importance of this research area. Other trends in funding by research area are discussed in the sections that follow.

"At the end of the day, product development doesn't have a lot of certainty, but there is one certainty, and that is if we don't fund it at all, we will not get better drugs, we will not get better vaccines, we will not get better diagnostics."

Mitchell Warren, Executive Director, AVAC

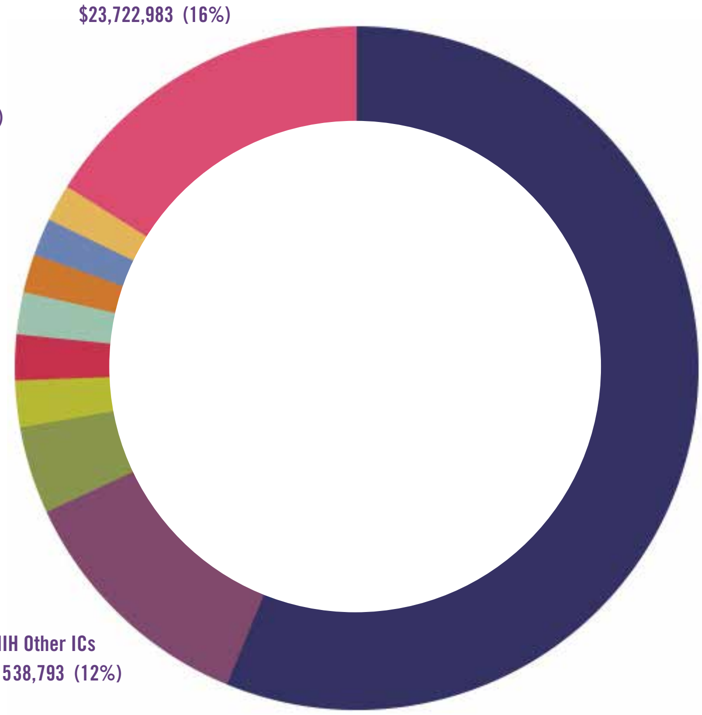
"In addition to more funding, one of the things that we need if we want to keep talented people in TB is to provide them with job security—and that [means] creating longer-term funding that creates a clear career path. Longer-term funding and funding with more flexibility to support people through research is really important."

Kathryn Snow, doctoral candidate, University of Melbourne

Basic Science

FIGURE 8

Basic Science: $147,439,441



Funders with investments under 2%

Marsden Fund	$2,055,977
Institut Pasteur	$2,036,863
Swedish Research Council	$1,924,179
Canadian Institutes of Health Research	$1,790,029
South African Medical Research Council (SAMRC)	$1,475,643
South African Department of Science and Technology (DST)	$1,440,709
Max Planck Institute for Infection Biology	$1,211,000
Japan Agency for Medical Research and Development (AMED)	$1,141,760
Swiss Federal Institute of Technology in Lausanne (EPFL)	$1,044,240
Taiwan Centers for Disease Control	$1,037,594
Bill & Melinda Gates Foundation	$1,018,473
Korean Ministry of Science, ICT and Future Planning	$805,840
National Research Foundation of South Africa	$760,417
Norwegian Agency for Development Cooperation (NORAD)	$692,053
Indian Ministry of Science and Technology	$525,364
U.S. Department of Veterans Affairs	$500,000
Norwegian Ministry of Education and Research	$451,781
Korean Ministry of Health and Welfare	$426,666
Natural Sciences and Engineering Research Council of Canada	$388,956
Thailand National Science and Technology Development Agency	$344,833
Korean Ministry of Education	$254,487
Singapore Agency for Science, Technology and Research (A*STAR)	$217,788
University of the Philippines Manila—National Institutes of Health	$207,399
Norwegian Ministry of Health and Care Services	$204,787
Australian Research Council	$194,068
Indian Council of Medical Research (ICMR)	$179,677
BioFabri	$170,292
Else Kröner Fresenius Foundation	$156,000
Thailand Ministry of Public Health	$151,645
Japan BCG Laboratory	$125,871
Howard Hughes Medical Institute	$100,000
Singapore National University Health System	$92,994
CRDF Global	$76,963
Hong Kong Health and Medical Research Fund	$75,637
Public Health England	$67,349
Taiwan Ministry of Science and Technology	$60,000
Other funders with investments less than $50,000	$315,648

* All acronyms and abbreviations of organization names are defined in Appendix 2.

"In the basic science space . . . we've seen a lot of progress over the last five years, through big cohort studies [advancing] basic understandings of the immune mechanisms and pathways associated with risk of TB disease. More recently, there's been some indication of correlates of protection or parameters which might be associated with lower risk. We've also, as a field, been spending a lot of time looking at the animal models we use for TB."

Helen Fletcher, Professor of Immunology, TB Centre at the London School of Hygiene and Tropical Medicine

Of the $147 million spent on TB basic science research in 2017, $100 million (68%) came from the NIH ($83 million from NIAID and $17 million from other NIH institutes and centers). If investments from the U.S. National Science Foundation and U.S. Department of Veterans Affairs are added, U.S. government contributions make up more than 70% of total global expenditure on TB basic science.

Though paling in comparison to the United States, Germany ($4.4 million), Switzerland ($4.3 million), South Africa ($3.7 million), Australia ($2.8 million), the United Kingdom ($2.7 million), and New Zealand ($2.1 million) all invested more than $2 million in TB basic science. Apart from South Africa, no other high-TB-burden country invested more than $1 million in TB basic science in 2017. The $3.7 million investment made up 44% of South Africa's total $8.4 million investment in TB R&D in 2017—more than the country spent in any other research area. The $2.1 million New Zealand gave to TB basic science made up the entirety of this country's investment in TB research.

With spending of $6 million in 2017, the Wellcome Trust (a charity) is the third largest funder in this area and invests more in TB basic science than any government apart from the United States.

Annual funding for TB basic science has been relatively flat in the last five years, staying within the band between $137 and $156 million and decreasing by $8 million from 2016 to 2017. This band is well below the high of $172 million set in 2009 when the NIH received a one-time 34% budget increase of $10.4 billion in stimulus money released by the U.S. government in response to the 2008 economic crisis.[15] With 19% of total TB research funding in 2017, TB basic science ranks second among the research areas tracked by TAG.

Helen Fletcher, professor of immunology at the TB Centre at the London School of Hygiene and Tropical Medicine, sees a connection between limited funding for TB R&D generally and the reticence of some funders to invest in basic science, an area of research that inherently contains more uncertainties. "The reason why funders have had to be so brutal in their decisions about funding one research area over another is because, if there hasn't been enough money invested in research, then they can't take the high-risk approaches. Basic science is high risk. TB vaccines—they're high risk. It's a lot of money. It's going to take maybe five to ten years before you know whether that investment paid off or not."

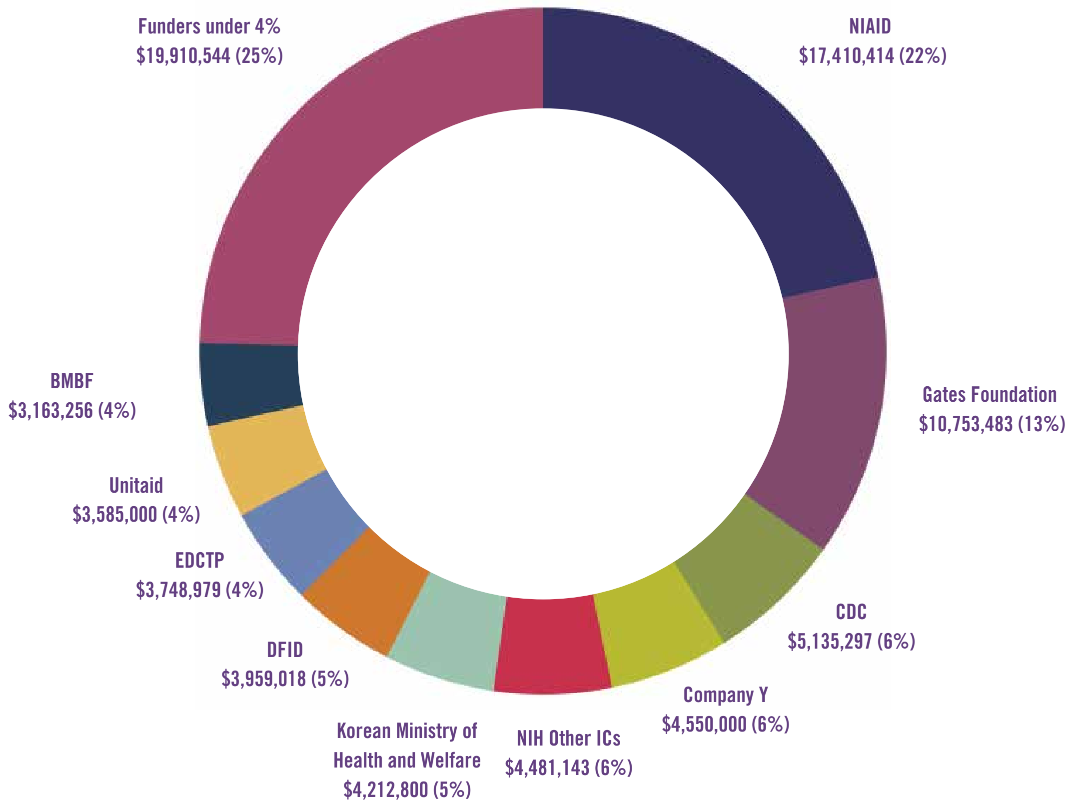
The risk-taking and timelines required to support basic discovery call for a different definition of success than product development. Mitchell Warren, executive director of AVAC, a nongovernmental organization that advocates for HIV prevention, pointed out that although the five-to-ten year arc of product development may be long, it is no longer than other public goods that governments invest in, such as development assistance aimed at improving education, health systems, or the material conditions of life. "Funding research is different than funding development, and funding product development is even different than funding some areas of what is basic research. This is hard stuff. It's about a different mindset, it's about a different set of deliverables, a different set of success metrics, and we have to orient people that way."

In Warren's view, sustained, predictable funding may be just as important as increased funding when it comes to supporting basic science, which in some respects is the engine of product development: "The only thing worse than having declines [in funding] is having fluctuations that are unpredictable."

Diagnostics

FIGURE 9

Diagnostics: $80,909,934



Funders with investments under 4%

Australian Department of Foreign Affairs and Trade (DFAT)	$2,561,833
U.K. Medical Research Council (U.K. MRC)	$1,954,934
Molbio Diagnostics	$1,851,600
European Commission	$1,805,289
Indian Council of Medical Research (ICMR)	$1,620,653
Korean Ministry of Science, ICT and Future Planning	$1,200,333
Australian National Health and Medical Research Council (NHMRC)	$1,167,233
Korean Ministry of SMEs and Startups	$1,015,500
U.S. National Science Foundation	$778,555
U.S. Department of Defense Medical Research and Development Program (DMRDP)	$606,368
University of the Philippines Manila—National Institutes of Health	$577,710
Japan International Cooperation Agency (JICA)	$503,819
South African Technology Innovation Agency	$458,647
Genedrive	$457,660
Norwegian Agency for Development Cooperation (NORAD)	$346,006
South African Medical Research Council (SAMRC)	$309,448
South African Department of Science and Technology (DST)	$276,434
Carlos III Health Institute	$275,287
Japan Agency for Medical Research and Development (AMED)	$251,544
Taiwan Centers for Disease Control	$195,636
Canadian Institutes of Health Research	$190,458
Swedish Research Council	$183,334
Wellcome Trust	$179,903
Thrasher Research Fund	$150,868
CRDF Global	$120,994
Korean Ministry of Trade, Industry and Energy	$110,000
Thailand Ministry of Public Health	$103,082
Damien Foundation Belgium	$91,181
French National Agency for AIDS Research (ANRS)	$83,478
Hong Kong Health and Medical Research Fund	$51,663
Korean Ministry of Education	$51,035
Other funders with investments less than $50,000	$380,059

> "It's one thing to develop a new innovation, but if they're not being used where they should be, then it's a waste of resources. For example, if we look at GeneXpert—it should be a point-of-care test, but it really isn't, the way we are utilizing it."
>
> **Welile Sikhondze, Technical Advisor and Research Coordinator, eSwatini National TB Control Program**

As in most areas, the U.S. government is the largest investor in TB diagnostics research by some distance. Of the $81 million invested globally in TB diagnostics R&D in 2017, $21.9 million (27%) came from the NIH ($17.4 million from NIAID and $4.5 million other NIH institutes and centers). With an additional $5.1 million from the CDC plus smaller contributions from the U.S. National Science Foundation and the U.S. Department of Defense, total U.S. government investment in TB diagnostics R&D adds up to $28 million, or 35% of the global total.

With an investment of $10.8 million in 2017, the Gates Foundation ranks second among all funders of diagnostics research. An unnamed pharmaceutical company (Company Y) ranks fourth with $4.6 million. The Gates Foundation invested more in TB diagnostics R&D in 2017 than any country apart from the United States.

Aside from the United States, governments that invested more than $2 million in TB diagnostics research in 2017 include South Korea, the United Kingdom, Germany, and Australia. Of the high-TB-burden countries, India stands out with 2017 spending of $1.7 million. South Africa is the only other high-burden country to have invested over $1 million in TB diagnostics R&D in 2017.

After hovering around $60 million between 2013 and 2015, annual funding for TB diagnostics research jumped to $80 million in 2016, where it remained virtually unchanged in 2017.Given the widespread consensus on the need for new and improved TB diagnostics, it is puzzling that investment in this area remains so low in comparison to other areas—2017 investment in diagnostics R&D was only 26% of that invested in TB drug research and only 10% of total TB R&D funding.

Global health advocate Albert Makone summarized the situation this way: "Progress has been moving at a slow pace. If you look at diagnostics R&D, the funding increase between 2016 and 2017 is less than $2 million. Yet we are missing a lot of [TB] cases each year. So for me, both the donors and the countries, especially high-burden countries, haven't been coming to the table to do their parts."

In some ways, the fitful, slow pace of progress in diagnostics development mirrors the uneven scale-up of new technologies that have emerged from the pipeline in recent years. Makone pointed to the pitiful scale-up of TB LAM, a simple, inexpensive, urine-based dipstick test for detecting TB in people with advanced HIV who are at highest risk of death. In 2018, the STAMP trial—funded by the U.K. Medical Research Council, DFID, and the Wellcome Trust—published results showing that using TB LAM to systematically screen hospitalized people with HIV increased TB diagnosis and treatment initiation and reduced mortality in three most-at-risk patient populations (people with low CD4 count, severe anemia, or clinically suspected TB), even in the presence of high HIV treatment coverage.[16] Uptake of the test has been dismal, despite positive findings from the STAMP trial and other evidence indicating that TB LAM testing reduces TB mortality. By March 2018, Abbott, the manufacturer of TB LAM, reported it only receives 100,000 orders of TB LAM tests from countries per quarter, when the estimated number of people in need of LAM testing per WHO guidance is 725,000 per quarter.[17]

Despite disappointing uptake, research on urine LAM testing continues to show promise. Shortly before the HLM, the diagnostics PDP FIND announced what it called a "technological breakthrough in point-of-care testing using urine samples."[18] The test in question, Fujifilm SILVAMP TB LAM, may offer improvements in sensitivity over the currently available LAM test. The FIND press release announcing promising preliminary data from evaluations of Fujifilm SILVAMP TB LAM is a testament to the collaboration required to advance

> "GeneXpert has been brought out to many countries, but still another question comes: the issue of utilization. Yes, many countries have managed to buy GeneXpert, but we are failing to utilize it to the optimal level. . . . Or the TB LAM test—how can a country like Zimbabwe, being a TB/HIV high-burden country, only order 20 LAM test kits within a year?"
>
> **Albert Makone, global health advocate**

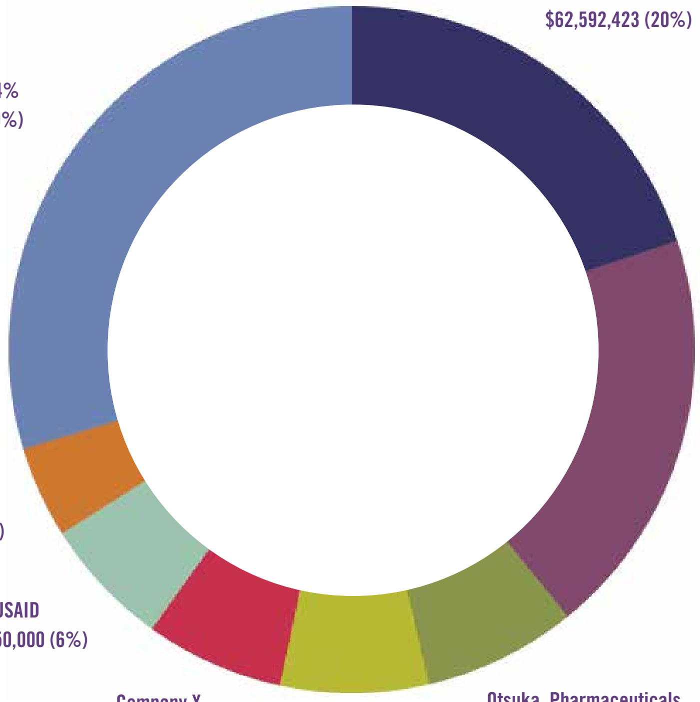
TB diagnostics R&D. The release notes that early work on this test was supported by the governments of the Netherlands, Australia, and the United Kingdom and by the Gates Foundation. Clinical trials to generate further evidence are being funded by GHIT and Germany's Federal Ministry of Education and Research.[19]

Collaboration among funders must extend beyond cost-sharing and co-financing to include the coordination of research itself. Taking GeneXpert as an example, Kitty van Weezenbeek, KNCV Tuberculosis Foundation executive director, commented: "What we really need is simultaneous R&D. We knew that Xpert would be coming in 2007. And we didn't have the MDR-TB regimens, the tools to take advantage of the test. . . . What happened was predicted by many—we diagnosed many more people, but the R&D in drugs was not at the same level." In van Weezenbeek's view, research priority setting should aim to construct a "comprehensive package of R&D." That is, development efforts in one area should anticipate and respond to progress in another. This may be especially important for TB diagnostics research. Diagnostic technologies touch every part of TB care—from treatment initiation to drug-resistance testing to side-effect monitoring to adherence support. Just as "treatment is blind without good diagnostics," efforts to prevent TB will also depend on developing better diagnostics.[20] For example, new TB vaccines may require accompanying new TB diagnostics to identify people who are priority candidates for vaccination, which, depending on the vaccine, could include those individuals most likely to progress from infection with *Mycobacterium tuberculosis* (MTB) to active TB disease or those not yet infected with MTB.

Drugs

FIGURE 10

Drugs: $315,051,622



Funders with investments under 4%

U.K. Department for International Development (DFID)	$10,401,360
European and Developing Countries Clinical Trials Partnership (EDCTP)	$9,934,061
U.S. Centers for Disease Control and Prevention (CDC)	$7,399,574
German Federal Ministry of Education and Research (BMBF)	$5,933,768
U.K. Medical Research Council (U.K. MRC)	$5,303,483
U.S. National Institutes of Health, Other Institutes and Centers (NIH Other ICs)	$4,930,426
Dutch Ministry of Foreign Affairs (formerly listed as DGIS)	$3,495,346
U.S. Department of Defense Medical Research and Development Program (DMRDP)	$3,320,851
European Commission	$3,298,128
LegoChem Biosciences	$3,000,000
Australian Department of Foreign Affairs and Trade (DFAT)	$2,561,834
Novartis Pharma AG	$2,400,000
Dutch National Postcode Lottery	$2,273,117
Qurient	$2,175,000
Wellcome Trust	$2,055,519
Global Health Innovative Technology Fund (GHIT)	$1,978,314
Korean Ministry of Science, ICT and Future Planning	$1,952,764
South African Medical Research Council (SAMRC)	$1,702,863
Company N	$1,500,000
Indonesian philanthropic donors to TB Alliance	$1,500,000
Korean Ministry of Health and Welfare	$1,437,069
Indian Council of Scientific and Industrial Research (CSIR)	$1,387,157
Sequella	$1,356,000
Irish Aid	$1,142,270
Singapore Ministry of Health, National Medical Research Council	$1,049,705
U.S. Food and Drug Administration (FDA)	$1,017,990
French National Agency for AIDS Research (ANRS)	$875,448
Swiss Federal Institute of Technology in Lausanne (EPFL)	$710,083
U.S. Department of Veterans Affairs	$679,524
Japan Agency for Medical Research and Development (AMED)	$624,400
Molbio Diagnostics	$617,200
Canadian Institutes of Health Research	$600,036
Public Health England	$588,197
Company R	$472,041
Swedish Research Council	$454,077
Singapore Agency for Science, Technology and Research (A*STAR)	$453,725
Norwegian Ministry of Education and Research	$423,418
U.S. President's Emergency Plan for AIDS Relief (PEPFAR)	$381,205
University of the Philippines Manila—National Institutes of Health	$334,966
Swiss National Science Foundation (SNSF)	$283,498
Ireland Health Research Board	$271,157
Indian Council of Medical Research (ICMR)	$267,500
South African Department of Science and Technology (DST)	$209,414
Corporate donors to TB Alliance	$200,646
Korean Ministry of Agriculture, Food and Rural Affairs	$187,000
Other funders with investments less than $100,000	$376,469

"What I don't want to happen is for good drugs or good regimens not to go to trials because of cost rather than science. We can't let cost be a factor on what goes forward. We should be making sure the best science goes forward."

Grania Brigden, Deputy Director, TB and HIV Department, The Union

The Gates Foundation was the single largest investor in TB drug research in 2017 with $63 million, or 20% of the $315 million global total. This was only slightly more than the $61 million given by NIAID. However, at $98 million, total U.S. government investment (including funding from eight different agencies) is greater than that of any other government, foundation, or pharmaceutical company, and it comprised 31% of total funding for TB drug research in 2017.

Otsuka was the third largest investor in TB drug R&D in 2017 with $23 million. Two unnamed pharmaceutical companies—Company X and Company V—reported investments of $21 million and $14 million, respectively. Three of the top 10 and five of the top 20 funders of TB drug research in 2017 were pharmaceutical companies. Eleven pharmaceutical companies reported spending a combined $68 million on TB drug R&D in 2017. This is 80% of the $85 million contribution that private industry made to TB research overall and 22% of total expenditures on TB drug research. This concentration of pharmaceutical industry investment is an important factor contributing to TB drug research receiving more investment than any other area of TB R&D.

After the United States, the United Kingdom stands out from other country governments, with an investment of $16 million in TB drug research in 2017. Other countries above $3 million include Germany ($5.9 million), the Netherlands ($3.5 million), and South Korea ($3.6 million). The European Union invested $13 million.

In addition to attracting greater investment than other areas of TB research, drug R&D also has the most diverse funding pool, with governments, philanthropies, and private industry all contributing meaningfully. This stands in stark contrast to TB basic science, which is almost entirely dependent on government funding.

The total $315 million invested in TB drug research in 2017 represents a $58 million increase over the $257 million spent in 2016 and amounts to 41% of total funding for TB research in 2017. While this year-on-year improvement is impressive, it is less so when one considers that annual investments had already reached $263 million by 2011. There was no great increase over the 2011 level until 2017.

The last 12 months have been unusually active for TB drug development. Among the major events, Otsuka released results from its phase III trial of delamanid—the first phase III trial of a new anti-TB compound from a novel class in decades. (This achievement was clouded by the trial's lack of a clinical primary endpoint and difficult-to-interpret findings that have muddied normative guidance on how to best incorporate the drug into drug-resistant TB [DR-TB] treatment.) Preliminary data from the TB Alliance's Nix-TB trial continued to offer hope that a three-drug regimen of bedaquiline, pretomanid, and linezolid (BPaL) can cure people with the most drug-resistant forms of TB in six to nine months.[21] Based on Nix-TB results to date, the TB Alliance launched the ZeNix study, looking at whether the BPaL regimen can be efficacious when linezolid is given at lower doses and/or for shorter durations designed to reduce the serious toxicities associated with that drug.[22] In addition, the TB Alliance announced the launch of the SimpliciTB trial, which will test a four-month regimen of bedaquiline, pretomanid, moxifloxacin, and pyrazinamide (BPaMZ) in people with drug-sensitive TB (DS-TB; as well as a controversial uncontrolled evaluation of BPaMZ given for six months to people with DR-TB).[23]

The year's biggest news in TB treatment came when the South African Department of Health announced that bedaquiline would become part of the initial treatment regimen for all people with DR-TB.[24] Notably, this bold yet evidence-based move preceded WHO advice on the topic. South African officials felt compelled to act after reviewing the records of 19,617 people treated for DR-TB in South Africa between 2014 and 2016, 1016 of whom received bedaquiline. Those who received bedaquiline had a higher rate of treatment success and were significantly less likely to die during treatment.[25] Shortly after South Africa's decision, the WHO convened a guidelines development group, which after reviewing the evidence issued a rapid communication recommending bedaquiline as a "core agent" for treating DR-TB.[26] The same communication downgraded other drugs commonly used in DR-TB treatment—including five of the seven agents used in the so-called shorter regimen studied in the STREAM trial.[27] This seismic shift in DR-TB treatment is expected to improve treatment outcomes and end the hearing loss induced by previous regimens that incorporated injectable drug agents (including the shorter regimen evaluated in STREAM). That said, the optimal treatment regimens for drug-resistant forms of TB are not yet known, and guidelines are set to keep changing as findings from ongoing trials are reported in the coming years.

In the realm of TB preventive therapy, two phase III trials published results supporting the efficacy and safety of shorter alternatives to isoniazid preventive therapy (IPT). A study by the NIH-funded AIDS Clinical Trials Group showed that a one-month regimen of isoniazid and rifapentine (1HP) is noninferior to six months of daily isoniazid, with fewer safety concerns and better adherence in people with HIV.[28] Supported by the Canadian Institutes of Health Research, investigators at McGill University showed that four months of daily rifampicin is noninferior to and safer than nine months of isoniazid in adults and children.[29] And the International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) completed a phase IV study assessing the safety of IPT in pregnant and postpartum women—finally providing high-quality clinical trial data on IPT use in this population decades after IPT was first used for TB prophylaxis.[30]

These achievements have incontrovertibly moved the field forward, but each came with its own caveats, and some illustrated structural vulnerabilities in the way TB drug development is conducted.[31] Under the status quo, new agents are more likely to be developed singly rather than in combination as part of new regimens; for instance, only after approval were bedaquiline and delamanid combined together and with other drugs in trials seeking new, shorter regimens. Most of these efforts have relied on public funding.[32] Moving forward, there is growing consensus that a different approach to funding innovation will be required to develop wholly novel regimens backed by the high-quality data necessary to produce clinical guidelines with minimal ambiguities, patient exclusions, and evidence gaps.

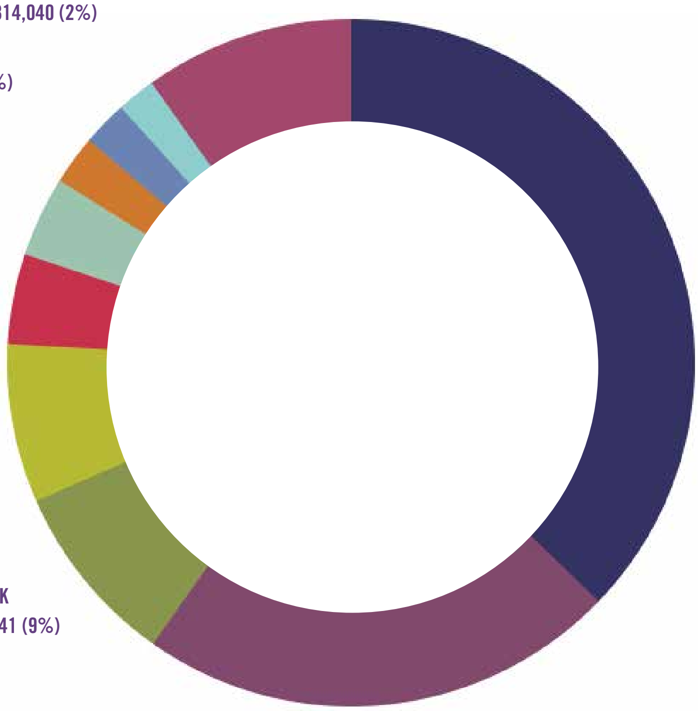
Grania Brigden, deputy director of the TB and HIV Department at the International Union Against TB and Lung Disease (The Union), pointed to open data sharing as one necessary ingredient: “We need data sharing for regimen development. That data sharing may have unexpected benefits that in five to ten years’ time [will] completely change how we do TB regimen trials to make them easier or less expensive or to push forward regimens in a quick way. So I think, from a funder perspective, everyone wins if we can make the whole framework much more transparent.”

The call for data sharing is about several ideas—collaboration, for one, but also transparency and efficiency. Tenu Avafia, human rights, law, and treatment access team leader at UNDP, elaborated: “There are sort of two elements to the calls for things like transparency and efficiency. There’s the element of being more accountable . . . but then there’s another aspect where working with funders to encourage researchers to work [together] may unlock new efficiencies for the way researchers collaborate.” Sharonann Lynch of the MSF Access Campaign offered a more blunt diagnosis: “Simply put, because of the way R&D is performed, the profit-seeking nature is that there is not much incentive for companies to collaborate, to share molecules, to share data. So that competitiveness stymies research, stymies . . . what could otherwise be a more efficient process, and not just for regimen development but across the board.” The challenge will be to swing R&D for TB drugs and other new tools from a market-driven system to one driven by human and public health need.

Vaccines

FIGURE 11

Vaccines: $100,338,945



Funders with investments under 2%

Korean Ministry of Health and Welfare	$1,483,800
Public Health England	$1,115,546
U.K. Department for International Development (DFID)	$1,040,136
Max Planck Institute for Infection Biology	$807,000
Korean Ministry of Science, ICT and Future Planning	$735,591
Canadian Institutes of Health Research	$732,263
Ireland Health Research Board	$685,118
U.K. Medical Research Council (U.K. MRC)	$552,296
Norwegian Agency for Development Cooperation (NORAD)	$494,764
Japan BCG Laboratory	$446,604
U.S. National Institutes of Health, Other Institutes and Centers (NIH Other ICs)	$426,417
Wellcome Trust	$385,885
Brazilian Ministry of Health	$302,340
Industry donors to TBVI	$228,454
Danish Council for Independent Research	$176,652
U.K. Biotechnology and Biological Sciences Research Council	$110,514
Other funders with investments less than $100,000	$174,176

"Data from recent clinical trials are changing the way we think about TB vaccine development. The combination of scientific advances and increased political attention suggests that this is a pivotal moment in the decades-long quest to develop more widely effective TB vaccines. We are no longer asking whether we can develop new TB vaccines, but how we can expedite promising candidates and how we can use new immunologic insights to design even better approaches."

Mark Feinberg, President and CEO, International AIDS Vaccine Initiative (IAVI)

In 2017, the Gates Foundation invested $37 million in TB vaccine research. This is more than any other philanthropy, government, or pharmaceutical company, and 37% of the global total of just over $100 million. NIAID ranks second with $23 million, and total U.S. government investment in TB vaccine R&D in 2017 stands well ahead of other governments at $25 million. Vaccine R&D is the only TB research area where the U.S. government is not the top funder, trailing the Gates Foundation by $12 million.

At $8.7 million, GSK is the third largest funder of TB vaccine research. During the HLM, GSK and its collaborator, Aeras, published promising phase IIb findings showing that two doses of GSK's TB vaccine candidate M72/AS01E conferred 54% protection against developing active TB in HIV-negative people with MTB infection.[33] At the time of this writing, it was not known whether the company would move the vaccine into a phase III trial and how public and philanthropic funding would figure into such an endeavor. GSK is the only major pharmaceutical company that reported major investments in this area. Earlier in the year, Sanofi Pasteur ended its support for TB vaccine candidate H4:IC31 when a phase IIa trial showed that the vaccine did not offer significant protection against MTB infection in South African adolescents (although a second arm of that trial, evaluating revaccination with BCG, looked more promising).[34,35]

The European Union with $11 million, as well as the governments of Germany, Japan, South Korea, and the United Kingdom, all invested more than $2 million in TB vaccine research in 2017. High-TB-burden countries such as India and South Africa, which made substantial investments in other research areas, invested only very small amounts in TB vaccine R&D (although South Africa hosts a significant share of the world's TB vaccine clinical trials). The government of India's support for TB vaccine R&D is expected to increase in coming years as the Indian Council of Medical Research prepares to launch a massive efficacy trial of two vaccine candidates (VPM1002 and MIP) with an anticipated enrollment of 19,000 participants.[36,37]

Even though investment in TB vaccine R&D has increased in each of the last two years, not much can be read into these increases given the lack of a discernible upward trend over the last decade. The $100 million invested in TB vaccine research in 2017 is only the fourth highest annual investment since TAG started tracking in 2005, with higher annual totals reported in 2008, 2009, and 2014. With 13% of total investment in TB research in 2017, vaccines rank third among research areas.

One explanation for the relatively low levels of government funding for vaccine research is that TB vaccine development may be perceived as comparatively high risk. However, with higher risk comes the potential for greater public health reward. The rapid reductions in TB incidence envisioned by the WHO End TB Strategy 2030 targets will only be possible with the advent and rapid introduction of new TB vaccines. Of course, the potential public health impact of any new vaccine will depend on many factors—vaccine efficacy, whether the vaccine prevents MTB infection or blocks reactivation of established infection, and the age group it targets, to name a few. But nearly all of the epidemiological models agree that one (or more) new TB vaccines will be required to end the TB epidemic.

"When funders put in money, they want to be able to see impact for investment, and research doesn't always show an immediate impact—especially when we are talking about developing a vaccine, it takes a long time."

Welile Sikhondze, Technical Advisor and Research Coordinator, eSwatini National TB Control Program

"The reward in public funding is even greater—eliminating a disease, ending an epidemic, having people live longer and higher-quality lives. Those are remarkable returns on investment, hard to quantify, and I think the hardest thing is that they are hard to see in the short term. So when I look at the last 15 years of funding [for vaccine R&D], no one expected a quick win . . . I don't think people thought 'Oh, this is a slam dunk.' But I don't know that anyone thought 15 years later we wouldn't have a next-generation vaccine for TB or an HIV vaccine. . . . We've not seen as many great advances as we'd like. That's just the reality."

Mitchell Warren, Executive Director, AVAC

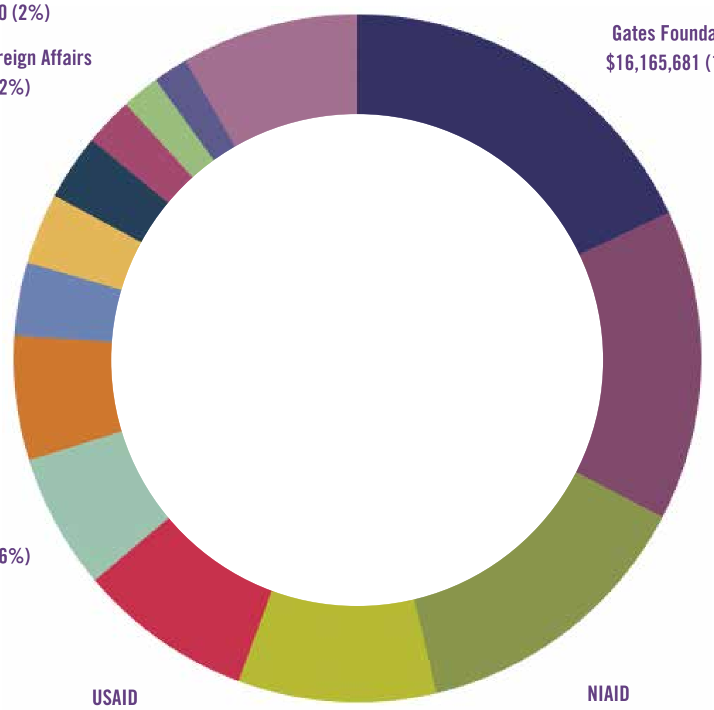
Although the long-term importance of TB vaccines is clear, in the short term, where funding decisions are made in three- and five-year cycles, investments in vaccination and other prevention tools may appear less urgent than the need for new drugs or diagnostics. As eSwatini National TB Control Program technical advisor Welile Sikhondze explained: "Over the years, because we're in such an emergency mode, we were focused on improving treatment or improving how we care for those that we know about. So we've done all we can do from the case management [perspective]. Let's also try to find new innovations to help find those we do not yet know about. We also need to look at those who are not in the [risk] pool [for TB] but are at risk of falling into the pool. So we also need to focus on prevention. . . . A lot more focus needs to be put into prevention and vaccinology."

Vaccine R&D will always be laden with risk, but governments should put these uncertainties into their proper context: TB vaccine R&D is in the midst of its most productive and promising period maybe ever, at the very least since the field's revitalization at the turn of the century after decades of inactivity.[38] By one count, at the start of 2018, there were eight clinical trials with efficacy endpoints either soon to start or approaching completion.[39] The biological samples generated from this body of work will provide a trove of data on how different vaccine candidates perform in humans, an invaluable resource for conducting the kind of basic immunology and biomarker discovery needed to improve current candidates and sustain the pipeline with innovative strategies and novel vaccine constructs. The protective effect observed in the M72/AS01E phase IIb trial—although a relatively modest 54% and bookended by wide confidence intervals—should put to rest any lingering doubts about whether developing a vaccine that can improve on the body's adaptive immune response to TB is possible. We now know it is possible, but bringing such a vaccine from discovery through licensure will require much more investment than what funders have given over the past 12 years.

Operational Research

FIGURE 12

Operational Research: $89,672,465



Funders with investments under 2%

U.S. President's Emergency Plan for AIDS Relief (PEPFAR)	$1,213,130
World Health Organization	$997,004
Global Health Innovative Technology Fund (GHIT)	$907,513
Norwegian Agency for Development Cooperation (NORAD)	$594,560
Médecins Sans Frontières	$588,773
German Federal Ministry of Education and Research (BMBF)	$347,344
Korean Ministry of Health and Welfare	$306,790
Japan Agency for Medical Research and Development (AMED)	$285,440
Thailand Health Systems Research Institute	$257,811
Australian Department of Foreign Affairs and Trade (DFAT)	$230,565
European and Developing Countries Clinical Trials Partnership (EDCTP)	$230,317
Indian Council of Medical Research (ICMR)	$204,120
Australian National Health and Medical Research Council (NHMRC)	$193,365
ELMA Foundation	$175,000
Wellcome Trust	$163,275
Colombia Administrative Department of Science, Technology and Innovation	$100,000
Korea Foundation For International Healthcare	$93,786
Thrasher Research Fund	$86,428
Indian Ministry of Science and Technology	$83,091
Swedish Research Council	$82,796
Indian Ministry of Health and Family Welfare (MOHFW)	$56,715
Other funders with investments less than $50,000	$287,417

> "We can rattle the world's attention by introducing the next cool tool. But it is difficult to get as enthusiastic about the cool tools that might emerge from the pipeline as long as we have such a standard of mediocrity in terms of scale-up. We can see this from all of the missed opportunities to provide TB LAM today, in outpatient facilities and especially hospitals where there is high TB-HIV coinfection."

Sharonann Lynch, HIV and TB Policy Advisor, Médecins Sans Frontières Access Campaign

The largest single investor in TB operational research in 2017 was the Gates Foundation, with $16 million, or 18%, of the $90 million total. The highest-ranking U.S. government entity, NIAID, is ranked third highest, and total U.S. government investment in this area adds up to $35 million—nearly $20 million more than the Gates Foundation.

Global Affairs Canada ranks second with $13 million, most of it channeled through the Stop TB Partnership's TB REACH program. This is the lion's share of the Canadian government's total TB R&D investment of $19 million. Other countries with TB operational research expenditures over $1 million are the United Kingdom ($8 million), the Netherlands ($2 million), and South Africa ($1.5 million). The European Union spent $3.3 million through the European Commission and the EDCTP.

The $90 million reported in 2017 marks a new high and the third consecutive year of growth in this area. These three good years follow directly on three consecutive years of falling investment in which funding for operational research dropped from $88 million in 2011 to $53 million in 2014. With 12% of the total TB research investment in 2017,operational research ranks fourth among research areas.

Operational research is where the research conditions of the pipeline meet reality and where new technologies that worked well in the clinic may require additional tailoring to meet the practical demands of patient care. Another way to understand this is to see operational research as the place where the biomedical R&D system meets the health system. As the TB community has learned time and again, scale-up of new technologies and ideas cannot be taken for granted. Health systems must prepare for new tools, access barriers must be overcome, new knowledge about TB must be translated into evidence-based policies and practices, and patients and communities must be given information about new interventions.

In the words of Tenu Avafia of UNDP: "It's one thing to talk about insufficient biomedical R&D. . . . That aside, it's also critical to invest in strengthening health systems so that when you have technologies available they can be efficiently absorbed into the health system, and that includes [things like] new vaccines and diagnostics for TB." Avafia continued by saying that "once R&D is done, the value gap of when you have a product and when it reaches a patient requires strengthening capacity and making specific, deliberate interventions in health systems to address bottlenecks where they occur."

There has been an attempt over the last year to reframe operational research as "applied health research," a term that encompasses operational, implementation, and health systems research as distinct domains without paving over their nuanced but important distinctions.[40] Broadly speaking, advocates of applied health research in TB seek to improve equity in health access and outcomes, translate knowledge into practice, and generate knowledge that lends itself to policy and implementation in the first place.[41] Signs that this broader concept is gaining traction can be found in the HLM political declaration, in which member states committed "to advance a new research and innovation environment" through, *inter alia*, supporting "operational, qualitative and applied research, to advance effective tuberculosis prevention, diagnosis, treatment, and care and actions on the economic and social determinants and impacts of the disease."

What should this aspect of the HLM political declaration look like in practice? Irene Ayakaka, senior research associate at Makerere University Lung Institute, articulated a simple but powerful operational research agenda: "There are many unanswered questions about how to reach every person with TB, and I think that's an important one—to find the individuals with TB that health systems don't see. What quality can we give to all people with TB we find, irrespective of who they are, where they are from? We need to protect everyone from the catastrophic costs of access to care and management. . . . We need to see that communities, healthcare workers—everyone—changes their attitudes about the stigma that comes from being an individual with TB."

To address these questions, TB operational research must adopt a multidisciplinary outlook—something that is still lacking. "There's a huge amount of qualitative research that still needs to be done in TB to identify good models of care. And that's not expensive compared to developing and manufacturing a vaccine, for example," said Kathryn Snow, a University of Melbourne doctoral candidate. "Qualitative research is really cheap, but we don't seem to do very much of it in TB." The qualitative dimensions of operational research also make it relevant for tackling many of the human-rights-related barriers to an effective TB response. In the words of Albert Makone: "One thing that is lacking in terms of TB is the issue of human rights. This applies both to funders and to governments, especially in high-burden countries. They need to focus more on patient-centered care and human-rights-based approaches to TB diagnosis and treatment. For example, in Zimbabwe, yes, the treatment is free. But one challenge people face before diagnosis is that a chest X-ray costs a minimum of $20. That in itself is a barrier . . . [one] that we need a human rights approach to address."

"In operational research, you can see an increase in funding in the last five years and various efforts to optimize the use of new tools that we have or that are emerging in the pipeline. We are seeing a renewed call for patient-centered TB management that is context specific. We are seeing calls for partnerships that enable access to all key populations that we consider when talking about TB . . . but there's still a lot of work to be done."

Irene Ayakaka, Senior Research Associate, Makerere University Lung Institute

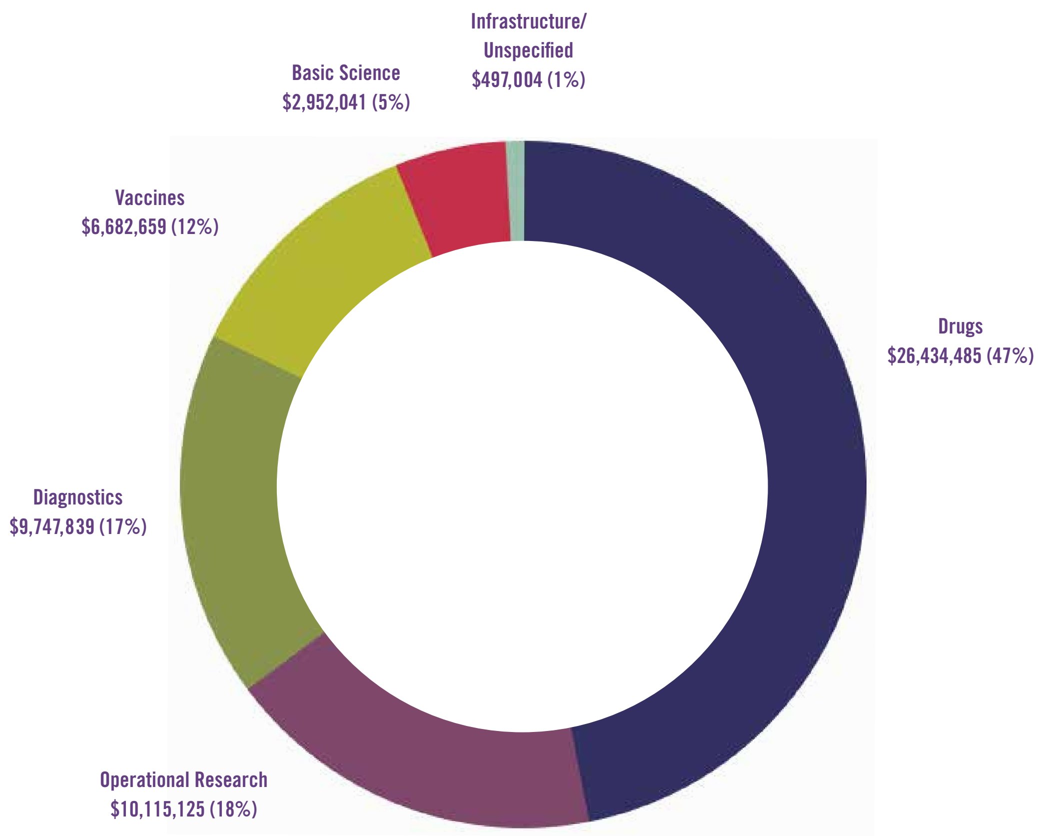
"For all the research to be beneficial, we do need to look at how our health systems function and what countries can already do without spending huge amounts of money to really strengthen and have robust health system infrastructures in place that can make the environment ready to receive a new vaccine, a new test, a new drug, or any other innovative technology that is developed."

Welile Sikhondze, Technical Advisor and Research Coordinator, eSwatini National TB Control Program

Pediatric TB Research

FIGURE 13

Pediatric TB R&D Funding by Research Area, 2017
Total: $56,429,152



The EDCTP is the top single investor in pediatric TB research, having spent $10.6 million in 2017, almost 20% of the total $56 million put into this research area. The EDCTP is funded by the European Union and also made multimillion-dollar investments in diagnostic, drug, and vaccine research in 2017. In 2017, the EDCTP reported supporting pediatric-related research projects ranging from a phase II trial of the TB vaccine candidate MTBVAC in South African neonates to a study of how TB affects respiratory infection risk in South African children to an evaluation of a household-level TB/HIV intervention that is enrolling adolescents.

USAID ranks second in pediatric TB research with $9.5 million. Most USAID funding in this area went to support TB transmission studies that included children and adolescents alongside other age groups. As in most research areas, total U.S. government expenditures are greater than that of any single investor at $22 million and double the EDCTP investment.

The only other countries with investments above $1 million in pediatric TB research in 2017 are the United Kingdom with $4.5 million and South Africa with $1.1 million. Company X reported an investment of $5.7 million and Unitaid invested $6.6 million. Previous investments by Unitaid led to the development of appropriately dosed pediatric fixed-dose formulations of first-line TB drugs by the TB Alliance and generic drug manufacturer Macleods. Current Unitaid funding for pediatric-related research is split between two projects. One, led by the University of Bordeaux, is seeking to reduce childhood TB morbidity and mortality through enhanced diagnosis.[42] The second, led by the Elizabeth Glaser Pediatric AIDS Foundation, is trialing innovative models of TB care for children with the goal of improving the market for new, child-friendly TB medicines.[43]

TABLE 3

Pediatric TB R&D Funders by Rank, 2017

2017 RANK	FUNDING ORGANIZATION	FUNDER TYPE	2017 PEDIATRIC TB R&D FUNDING	PERCENTAGE OF TOTAL PEDIATRIC FUNDING
1	European and Developing Countries Clinical Trials Partnership (EDCTP)	P	$10,604,544	18.8%
2	U.S. Agency for International Development (USAID)	P	$9,500,000	16.8%
3	U.S. National Institutes of Health, National Institute of Allergy and Infectious Diseases (NIAID)	P	$6,886,622	12.2%
4	Unitaid	M	$6,615,400	11.7%
5	Company X	C	$5,700,000	10.1%
6	U.S. National Institutes of Health, Other Institutes and Centers (NIH Other ICs)	P	$5,562,805	9.9%
7	U.K. Medical Research Council (U.K. MRC)	P	$4,535,821	8.0%
8	Brazilian Development Bank	P	$1,814,040	3.2%
9	South African Medical Research Council (SAMRC)	P	$1,083,446	1.9%
10	World Health Organization	M	$600,000	1.1%
11	Norwegian Agency for Development Cooperation (NORAD)	P	$437,361	0.78%
12	Novartis Pharma AG	C	$320,000	0.57%
13	Australian National Health and Medical Research Council	P	$311,383	0.55%
14	Molbio Diagnostics	C	$308,600	0.55%
15	Brazilian Ministry of Health	P	$302,340	0.54%
16	Médecins Sans Frontières	F	$261,742	0.46%
17	Japan Agency for Medical Research and Development (AMED)	P	$251,544	0.45%
18	Thrasher Research Fund	F	$237,296	0.42%
19	German Federal Ministry of Education and Research (BMBF)	P	$231,310	0.41%
20	ELMA Foundation	F	$175,000	0.31%
21	Wellcome Trust	F	$171,040	0.30%
22	Swedish Research Council	P	$141,936	0.25%
23	Company V	C	$114,227	0.20%
24	Canadian Institutes of Health Research	P	$65,823	0.12%
25	Thailand Ministry of Public Health	P	$62,798	0.11%
26	Thailand Health Systems Research Institute	P	$61,993	0.11%
27	Other public funders with investments less than $50,000	P	$72,083	0.13%
	TOTAL		**$56,429,152**	

C = Corporation/Private Sector; F = Foundation/Philanthropy; M = Multilateral; P = Public-Sector R&D Agency

Otsuka Pharmaceuticals, which is close to completing its pharmacokinetic and safety study of delamanid in children, notified TAG that it cannot disaggregate pediatric expenditures from its overall investment and is therefore not listed in the table.

"We're lacking some of the most critical tools necessary to effectively address pediatric TB. From developing appropriate and accurate diagnostics to defining the most efficient ways to deliver care, investment in R&D is required to accomplish the goal of ending childhood TB. Children have been waiting for decades for real advances that can address their unique needs. Significantly increased investment is needed if we are to see game-changing advancements that achieve measurable impacts."

Jennifer Cohn, Senior Director of Innovation, Elizabeth Glaser Pediatric AIDS Foundation

After three years of relatively flat funding, global pediatric TB research expenditures nearly doubled from $29.1 million in 2016 to $56.4 million in 2017, a 93% increase. Much of this can be attributed to Unitaid, which doubled its investment, as well as to the EDCTP, which went from spending nothing on pediatric research in 2016 to being the largest funder in this area in 2017. This latter move indicates the extent to which pediatric TB research funding may depend on grant cycles and the inclusion of children in large, periodic funding calls. TAG only started tracking investments in pediatric TB research in 2010 and, accordingly, does not have the same historic (2005–2017) data series as for the other research areas (see Appendix 1 for a note on the methodology TAG used to collect pediatric TB R&D funding data).

One of the best pieces of news in the pediatric TB research community came when the Division of AIDS at NIAID announced that it would re-fund the IMPAACT network for another seven years. IMPAACT is jointly funded by NIAID and the NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development and is the largest sponsor of clinical trials that include children with and at risk of TB, as well as pregnant and postpartum women. Work by IMPAACT and its associated investigators has been critical to filling pediatric pharmacokinetic (PK) and safety data gaps for TB drugs. IMPAACT reported spending $2.6 million on TB research in 2017, about a third less than what it spent in 2016, but a figure that will likely rise as its new seven-year funding cycle gets underway.

A review of the pediatric TB treatment pipeline by Lindsay McKenna, TAG TB Project co-director, notes: "PK and safety studies in children continue . . . to produce a steady flow of data, yet the translation of R&D gains into policy and access for children with TB remains pitifully slow."[44] Aside from progress in safety/PK work and implementation concerns, several efficacy studies underway or planned will evaluate whether it is possible to shorten DS- or DR-TB treatment in children. TB disease presentation in children is highly variable. Young children with disseminated or less severe forms of disease may achieve good treatment outcomes with shorter, simplified regimens. On the other side of the spectrum, children with more severe disease require safer, optimized regimens, with studies of TB meningitis in children being one of the most pressing—but difficult—areas of work. In the field of diagnostics, McKenna calls for "scale-up of pediatric-specific discovery, validation, and implementation research efforts to develop novel assays that can detect TB . . . in children."[45]

These research priorities and others are described in *Research Priorities for Pediatric Tuberculosis*, a brief released at the HLM in conjunction with a new edition of the *Roadmap towards Ending TB in Children and Adolescents*.[46,47] The first edition of the Roadmap, published in 2013, drew global attention to the near-total neglect of childhood TB in global health priority setting. The new edition includes a clearer focus on adolescents and argues that pediatric populations merit a dedicated, focused research agenda, one that goes beyond the mere adaptation of products first studied in adults for use in kids: "Pediatric TB R&D efforts have largely focused on generating evidence to inform the use of existing technologies and treatments, which are designed for and proven in adults, for children. Yet children affected by TB have specific needs that merit a pediatric-focused research agenda."[48]

Advocacy for such an agenda received a boost in the HLM political declaration, which calls on UN member states to advance "global collaboration to ensure accelerated development of accessible and affordable diagnostic tools, and shorter and more effective oral regimens, including those that meet the unique needs of children." The political declaration also singled out children when it articulated TB research commitments, asking states to "deliver, as soon as possible, new, safe, effective, equitable, affordable, available vaccines, point-of-care and child-friendly diagnostics, drug susceptibility tests and safer and more effective drugs and shorter treatment regimens for adults, adolescents and children for all forms of tuberculosis and infection." The prominent inclusion of children within the HLM political declaration is a sign that advocates have finally broken through the longstanding silence on pediatric TB. Future versions of this report will assess whether this critical attention translates into concrete funding for the research and implementation required to end unnecessary suffering and death due to TB among children and young people.

"Pediatric TB R&D efforts have largely focused on generating evidence to inform the use of existing technologies and treatments, which are designed for and proven in adults, for children. Yet children affected by TB have specific needs that merit a pediatric-focused research agenda."

Research Priorities for Pediatric Tuberculosis[53]

Discussion

"The highest known standard of care should be delivered to all patients suffering from all forms of TB in the world. There shouldn't be distinct rich-world and poor-world standards."

Paul Farmer, Co-Founder, Partners in Health

With around 1.6 million TB deaths and 10 million people falling ill with TB in 2017, it seems clear that TB should be a global research priority. Either through their own investments, or through creating an enabling environment, it should be the role of governments to ensure that sufficient funds are invested and the right incentives and legal and regulatory frameworks are put in place. Even so, the global TB research effort has until now been relatively haphazard—and haphazardly funded.

At least one long-standing problem, however, that we are now well on our way to solving, is determining how much we can reasonably expect governments to invest in TB R&D. Until recently, the TB research community has had no real benchmarks by which to judge whether an extra $10 million from the Indian government, or an extra $100 million from the United States, are major steps forward or simply what these countries should have been spending anyway.

In 2018, UN member states signed the HLM political declaration and collectively agreed to "aim" to increase annual global investment in TB research to $2 billion. Even though a binding commitment to the $2 billion would have been a preferable outcome, this "aim" nevertheless helps solidify a shared global target. The $2 billion is derived from an earlier *Global Plan* target that aimed for $9 billion from 2016 to 2020—a target the world has already fallen far behind. Either way, to have agreement among UN member states on the $2 billion annual target sets an important marker.

But how do we translate a global target into country-specific targets? By design, the 0.1% fair-share targets devised by TAG and partners add up neatly to this $2 billion target. If all high-burden countries and a list of the world's wealthiest countries all contributed 0.1% of their total annual research spending to TB, then the world would hit this $2 billion target. The 0.1% target has gained significant traction this year and has the benefit of tailoring a country's target to its existing levels of research spending.

What all this means is that we now have agreement on a $2 billion annual target and we know the fair-share amount that each country should be contributing (Table 1).

Doing research differently

We are also, albeit more slowly, making progress on the question of how research funds should be invested. That we need large infusions of funding for everything from basic science to clinical trials is not controversial. That increased research collaboration between the BRICS and between other countries are important steps forward is also not controversial. What was controversial, however, in the run-up to the HLM was the role of intellectual property in all this.[49] Negotiations on the political declaration remained open throughout the Northern Hemisphere summer due to disagreements regarding whether and how TRIPS flexibilities* and delinkage would be mentioned in the text.[50]

What the last 13 years of TB research funding data show unequivocally is that the private sector has largely withdrawn from TB research (with industry contributing only 11% of TB research funding in 2017). It thus seems clear that the current patent-based innovation model does not provide companies with sufficient incentives to invest in TB R&D. If it had, we would no doubt see more investment from the private sector.

* The agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) is a legal agreement between members of the World Trade Organization (WTO) that came into effect in 1995. The agreement set certain minimum standards for intellectual property protection in WTO member states while also leaving members with some flexibility in formulating their domestic intellectual property laws. In 2001, the WTO Doha Declaration on TRIPS and Public Health affirmed that these flexibilities may be used to protect public health.

"Success should be measured by the degree to which effective treatment, diagnosis, and prevention reaches the poorest of the poor—those most vulnerable to TB and made more vulnerable by the disease. This last mile of delivery—adequately resourced systems with staff, stuff, and space—is the ultimate metric for success of research. The only way to measure true success is to see a rapid drop in TB mortality. After a rise in incidence, as would be expected with active case-finding and treatment of TB infection in contacts, we should see a very rapid drop in rates of new TB. For the last quarter century, this has largely not been observed. Now is a chance to put programs in place that can achieve these attainable goals."

Paul Farmer, Co-Founder, Partners in Health

It is in the context of this market failure that the discussion around delinkage should be understood. In short, the idea behind delinkage is to replace patent-based incentives for investing in R&D with mechanisms such as prize funds. In other words, rather than rewarding a developer through market exclusivity, states pay the developer a prize, likely in the tens or even hundreds of millions of dollars, but then have generic competition from day one. The economics are not straightforward, but modeling suggests this will not only work but also save money while contributing to better health outcomes.[51,52]

Even though the HLM political declaration explicitly mentions the Life Prize, an example of such a delinkage-based model, and also describes delinkage (without mentioning the concept by name), governments have yet to support prize funds in TB. Thus, even as hands are wrung about the exodus of pharmaceutical companies from TB in the current patent-based system, no governments have yet been willing to put up the money to test alternative innovation models. Whether this will change in the wake of the HLM is a critical measure of how seriously governments take the innovation problem in TB.

As an aside, it seems likely that United States' resistance to delinkage language in the declaration was driven not by what it means for TB—the idea suits TB better than almost any other disease area—but by what it might mean for other disease areas should such prize funds succeed in TB. In this sense, tough negotiations on the declaration were a proxy for a much larger global battle between pharmaceutical companies and patients.

Making medicines accessible

That is the innovation problem; the other side of the intellectual property and delinkage debate concerns access to medicines. Here we are on more familiar ground, with a long-standing, ongoing global debate between strict patent enforcement and flexibilities that allow for the overriding of patents in certain situations (so-called TRIPS flexibilities). Here the pre-HLM disagreements between the United States and South Africa served up strong reminders of the early days of the AIDS epidemic in South Africa, when the high prices of AIDS treatment meant many people could not access life-saving drugs.

Some well-worn debates about people versus patents resurfaced this year, but one aspect that was different was the claim by some that TB is different from HIV and that the same access problems do not arise.

In some ways, at least, the issues are familiar. Until recently, the drug linezolid was so highly priced that doctors in Khayelitsha, South Africa, could not give the drug to all the patients who they felt might benefit from it. Smart use of TRIPS flexibilities in this situation could have allowed for a cheaper generic to be imported from India, which likely would have saved many lives. It is also likely that India's threat to consider a compulsory license for bedaquiline contributed to Janssen Pharmaceuticals cutting the price of that drug. No doubt, if we develop the new drugs, vaccines, and diagnostics we wish to see in the coming decade, patents will again be an issue—although it should be acknowledged that patents are one among a number of issues restricting access to new technologies, with registration delays and lax programmatic rollout being other key concerns.

Hopefully, the pre-HLM debate about intellectual property and delinkage will lead governments to ask more tough questions about the terms on which they provide funding for TB research. If governments help fund the development of a breakthrough new drug, what assurances will we have that those same governments will not be charged exorbitant prices to buy back the drug they helped develop from a pharmaceutical company with control over pricing? As Tenu Avafia told us when we interviewed him for this report: “It’s one thing giving someone involved in R&D money up front, but if one is not being deliberate in thinking about how to ensure that the patient at the end of the road is better off, then the objective is not achieved.”

A commitment to affordability of end products, open access publication of all trial results, collaboration with other researchers or groups of researchers, pooling of intellectual property, and data sharing should all be conditions placed upon public funding for TB research.

Moving beyond rhetoric

Next year we will report on funding trends up to 2018, the year of the HLM, and the year after that we will report on 2019. Over these two years, we will see what we cannot yet tell: whether the HLM will be backed up by new investments and whether countries will step up to contribute their fair share. The numbers will not lie. If funding is to take off, the evidence will be clear for all to see in this report.

Over the coming two years, we will also see whether governments are willing to think creatively and responsibly about how they fund TB research and support innovative projects like the Life Prize, or whether we are in fact still in a world where market failure is tacitly accepted. We will see whether exciting new initiatives like the BRICS TB Research Network are just more business as usual—whether it is “all hat, no cattle,” as Sharonann Lynch of the MSF Access Campaign put it—or the start of something unprecedented, on the scale of an Apollo-style program for TB R&D.

Governments or coalitions of governments have in the past put up the money for large technological and scientific endeavors such as the Panama Canal, the Manhattan Project, the Large Hadron Collider, and the International Space Station. A few months after the HLM, the question remains as to why the same cannot be done for a disease that has devastated human lives for millennia—one that still claims more lives than any other infectious agent.

Ultimately, as Paul Farmer reminds us, the measure of whether research is successful is whether it contributes to saving lives and reducing suffering. Investments in anything from basic science to operational research must be guided and motivated by this ultimate goal. This means making the financial investment and doing everything necessary to ensure that the products of that investment are available to all who need it. Like the HLM, funding for TB research is only a means to an end, and that end is the end of the TB epidemic.

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Appendix 1: Methodology

TAG tracks global funding for TB R&D by surveying public, private, philanthropic, and multilateral organizations with known or potential investments in TB research. The survey asks recipients to report the amount of money spent on TB R&D in a given year and categorize spending into six research areas: basic science, diagnostics, drugs, vaccines, operational research, and infrastructure/unspecified projects. Survey recipients may report spending by individual projects or aggregate expenditures by research area. Within these categories, the survey asks recipients to indicate any funding that supported pediatric TB research. TAG surveyed 180 organizations for this year's report and received 120 surveys in return. From these, we identified 131 institutions funding TB research in 2017. Eleven organizations that returned surveys reported spending no money on TB R&D in 2016, and four groups declined to participate.

The survey asks organizations to report TB research expenditures in local currencies, which TAG converts into U.S. dollars using the July 1, 2017, interbank exchange rates published by the OANDA Corporation. All dollar figures in the report are published as U.S. dollars unless otherwise noted and are rounded to the nearest dollar (all calculations, however, are performed on unrounded data). Dollar figures represent disbursements (i.e., the actual transfer of funds made in 2017) rather than commitments or budgetary allocations for future years. Our survey is designed to capture direct expenditures on TB research and so does not necessarily reflect indirect funding through salaries, overhead, or infrastructure that is not TB specific (although some donors may report these costs to TAG).

TAG carefully reviews each returned survey for completeness, taking careful measures to avoid double-counting awards reported by more than one funder. Double counting can arise under several scenarios, including the fact that many organizations fund some projects while receiving outside money for others. To help minimize the risk of double counting, the survey asks recipients to note whether spending represents one of three categories: funding given to others, funding received from others, or self-funded research. Any awards listed by more than one survey enter our database as reported by the original-source donor. For collaborative projects supported by more than one organization, we ask funders to report only their share of the project, not total costs.

In addition to surveying funding institutions, TAG conducted 13 qualitative interviews with leading TB scientists, policymakers, and activists and asked each to reflect on the current state of TB research in relation to available versus required funding. TAG invited interviewees to express their hopes—or reservations—for the outcomes of the UN High-Level Meeting on TB with respect to TB research. Each interviewee received an embargoed copy of preliminary survey findings in early September 2018 with a list of open-ended questions. We interviewed 11 individuals over the phone, and two submitted answers in writing. Each phone interview was recorded and transcribed verbatim. We pulled quotations from the transcripts and written responses, grouped them into common themes, and selected the excerpts that appear within and alongside the text of this report. In some places, TAG edited quotations for length or clarity. TAG checked quotations drawn from phone interviews with speakers prior to publication.

RESEARCH AREAS TRACKED BY TAG:

1. Basic science: undirected, investigator-initiated research to discover fundamental knowledge about MTB and closely related mycobacterial organisms.
2. Diagnostics: preclinical and clinical trials of diagnostic technologies and algorithms.
3. Drugs: preclinical and clinical research on treatments and treatment strategies for MTB infection and TB disease.
4. Vaccines: preclinical and clinical research on TB vaccines, including both preventive and immunotherapeutic vaccines.
5. Operational research: evaluations of new or existing TB control strategies and tools to guide their implementation in program settings. Operational research may include randomized trials, surveillance, and epidemiological and observational studies.
6. Infrastructure/unspecified projects: TB research that the funder is unable to further classify.

Limitations to the Data

The comprehensiveness of the data in this report depends on the proportion of institutions funding TB research that participate in the survey. This proportion cannot be calculated since the true number of TB research funders worldwide is unknown. TAG makes a considerable effort to ensure a wide survey reach and yield. The survey is available in six languages (English, French, Spanish, Russian, Chinese, and Portuguese). TAG routinely updates the survey frame by adding new organizations, most of which do not have known investments in TB R&D but either support health research generally or have a record of investing in related diseases. Finally, TAG makes a particular effort to encourage the continued participation of the 30 largest funders from the previous year. The high degree of concentration of TB research funding means that the top 30 donors typically comprise over 90 percent of total spending, and the composition of this group has remained remarkably stable over time. This year, 29 of the top 30 funders from 2016 participated in the survey (Eli Lilly did not return a survey despite repeated requests by TAG).

PEDIATRIC TB RESEARCH RESOURCE TRACKING METHODOLOGY

TAG's survey asks all funders to delineate support for pediatric research and assign any relevant spending to one of the six core research areas tracked by the report. TAG further identifies research related to pediatric TB by conducting a keyword search of titles and abstracts contained in returned surveys using the following search terms: pediatric, paediatric, infant, child, kid, adolescent, and pregnant. While this methodology provides a reasonable estimate of pediatric TB research spending, it overlooks research that informs the development of pediatric products without enrolling children or studying MTB infection or TB disease in children directly. Some funders have notified TAG that they cannot disaggregate pediatric research funding from their overall expenditure on TB R&D. Otsuka, for example, did not report how much of the nearly $22.8 million it spent on TB drug development in 2017 went to pediatric studies of delamanid. Funders supporting clinical trials, cohort studies, and epidemiological surveys that include people of all age groups can rarely specify the proportion of funds devoted to younger age groups. TAG encourages all funders to develop ways of disaggregating pediatric TB research spending from within larger funding totals to support more accurate estimation here.

In addition to Eli Lilly, several other funders with known investments in TB research did not return surveys this year, including the Howard Hughes Medical Institute, the French National Institute of Health and Medical Research (INSERM), Expertise France, Merck, QuantuMDx, Qiagen, Hain Lifescience, the New Zealand Health Research Council, and the U.K. National Institute for Health Research. TAG received no information from entities in Russia and China, despite attempts to coordinate reporting with the Ministry of Health of the Russian Federation and the Permanent Mission of the People's Republic of China to the United Nations. Understanding the funding landscape and trends over time is the first step toward securing stronger political commitments to TB research. TAG is hopeful that the governments of China and Russia will report their TB research funding as part of their involvement in the BRICS TB Research Network.

TAG encourages donors not included here to participate in future report rounds. Please contact TAG at tbrdtracking@treatmentactiongroup.org if you have information or corrections to share. Any corrections submitted to TAG will enter print in next year's report.

This report would not be possible without considerable time and effort on the part of the dozens of funding officers and administrative staff who complete the survey each year. TAG is grateful to the 120 organizations across the world that participated in this year's survey. **Appendix 2** acknowledges organizations that have reported to TAG every year since 2005 with a dagger (†) appearing next to their names.

Appendix 2

TB R&D Funders by Rank, 2017

2017 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
1	U.S. National Institutes of Health, National Institute of Allergy and Infectious Diseases (NIAID)†	P	$206,577,963
2	Bill & Melinda Gates Foundation†	F	$127,953,459
3	U.S. National Institutes of Health, Other Institutes and Centers (NIH Other ICs)†	P	$41,475,012
4	U.S. Agency for International Development (USAID)†	P	$33,989,472
5	Unitaid	M	$28,556,016
6	Otsuka Pharmaceuticals†	C	$22,773,887
7	U.K. Department for International Development (DFID)†	P	$20,642,634
8	Company X†	C	$20,550,920
9	European Commission†	P	$19,275,723
10	U.S. Centers for Disease Control and Prevention (CDC)†	P	$18,256,200
11	European and Developing Countries Clinical Trials Partnership (EDCTP)†	P	$17,708,271
12	German Federal Ministry of Education and Research (BMBF)	P	$16,883,110
13	Indian Council of Medical Research (ICMR)	P	$14,487,377
14	Company V	C	$13,604,436
15	U.K. Medical Research Council (U.K. MRC)†	P	$13,483,589
16	Global Affairs Canada	P	$13,093,570
17	Wellcome Trust†	F	$8,876,850
18	GlaxoSmithKline (GSK)	C	$8,675,541
19	Korean Ministry of Health and Welfare	P	$7,996,008
20	U.S. Department of Defense Medical Research and Development Program (DMRDP)	P	$6,062,135
21	Dutch Ministry of Foreign Affairs (formerly listed as DGIS)†	P	$5,558,751
22	Australian Department of Foreign Affairs and Trade (DFAT)	P	$5,354,232
23	Korean Ministry of Science, ICT and Future Planning	P	$5,279,528
24	South African Medical Research Council (SAMRC)	P	$5,053,092
25	Canadian Institutes of Health Research (CIHR)†	P	$4,975,348
26	Japan Agency for Medical Research and Development (AMED)	P	$4,616,992
27	Company Y	C	$4,550,000
28	Australian National Health and Medical Research Council (NHMRC)	P	$4,030,606
29	Swiss National Science Foundation (SNSF)	P	$3,538,362
30	U.S. National Science Foundation (NSF)	P	$3,381,548
31	LegoChem Biosciences*	C	$3,000,000
32	Global Health Innovative Technology Fund (GHIT)	M	$2,885,827
33	Swedish Research Council	P	$2,644,386

C = Corporation/Private Sector; F = Foundation/Philanthropy; M = Multilateral; P = Public-Sector Agency
* New Funder; † Organization has reported to TAG each year since 2005

‡ PEPFAR's total reported here includes funding for operational research sponsored by PEPFAR headquarters and non-routine projects that country programs have designated as surveillance, research, and evaluation, but it does not include operational research done as a part of routine programming and therefore likely significantly underestimates PEPFAR's support for TB research.

BASIC SCIENCE	DIAGNOSTICS	DRUGS	VACCINES	OPERATIONAL RESEARCH	INFRASTRUCTURE/ UNSPECIFIED
$82,846,672	$17,410,414	$60,792,339	$22,644,809	$12,264,084	$10,619,645
$1,018,473	$10,753,483	$62,592,423	$37,326,666	$16,165,681	$96,733
$17,538,793	$4,481,143	$4,930,426	$426,417	$8,356,118	$5,742,115
$0	$0	$19,250,000	$0	$7,363,976	$7,375,496
$0	$3,585,000	$21,971,016	$0	$3,000,000	$0
$0	$0	$22,773,887	$0	$0	$0
$0	$3,959,018	$10,401,360	$1,040,136	$5,242,120	$0
$0	$0	$20,550,920	$0	$0	$0
$2,940,086	$1,805,289	$3,298,128	$7,480,058	$3,079,102	$673,060
$0	$5,135,297	$7,399,574	$0	$5,721,329	$0
$0	$3,748,979	$9,934,061	$3,794,913	$230,317	$0
$3,182,141	$3,163,256	$5,933,768	$4,256,601	$347,344	$0
$179,677	$1,620,653	$267,500	$0	$204,120	$12,215,427
$0	$0	$13,604,436	$0	$0	$0
$2,588,633	$1,954,934	$5,303,483	$552,296	$2,774,478	$309,766
$0	$0	$0	$0	$13,093,570	$0
$6,092,268	$179,903	$2,055,519	$385,885	$163,275	$0
$0	$0	$0	$8,675,541	$0	$0
$426,666	$4,212,800	$1,437,069	$1,483,800	$306,790	$128,883
$0	$606,368	$3,320,851	$2,134,915	$0	$0
$0	$0	$3,495,346	$0	$2,063,405	$0
$0	$2,561,833	$2,561,834	$0	$230,565	$0
$805,840	$1,200,333	$1,952,764	$735,591	$0	$585,000
$1,475,643	$309,448	$1,702,863	$26,796	$1,469,942	$68,401
$1,790,029	$190,458	$600,036	$732,263	$1,593,420	$69,143
$1,141,760	$251,544	$624,400	$2,313,848	$285,440	$0
$0	$4,550,000	$0	$0	$0	$0
$2,670,008	$1,167,233	$0	$0	$193,365	$0
$3,254,864	$0	$283,498	$0	$0	$0
$2,602,993	$778,555	$0	$0	$0	$0
$0	$0	$3,000,000	$0	$0	$0
$0	$0	$1,978,314	$0	$907,513	$0
$1,924,179	$183,334	$454,077	$0	$82,796	$0

The Global Fund to Fights AIDS, Tuberculosis and Malaria (Global Fund) informed TAG that it can only report its cumulative expenditure on TB operational research between 2002 and 2017, which totaled $166.7 million. The Global Fund is exploring ways to estimate its annual spending on TB operational research moving forward.

Organizations that reported no new spending on TB research in 2017: Canada Foundation for Innovation; Danish International Development Agency (DANIDA); Netherlands Organization for Health Research and Development (ZonMw); Nigeria Centre for Disease Control; and the Wellington Medical Research Foundation. The following organizations declined to participate: Tampere Tuberculosis Foundation; Singapore Ministry of Health; Singapore National Medical Research Council; and the U.S. Army Military Infectious Diseases Research Program (MIDRP).

Appendix 2

TB R&D Funders by Rank, 2017 (continued)

2017 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
34	Molbio Diagnostics*	C	$2,468,800
35	Novartis Pharma AG	C	$2,400,000
36	Norwegian Agency for Development Cooperation (NORAD)	P	$2,299,287
37	Dutch National Postcode Lottery	P	$2,273,117
38	Qurient	C	$2,175,000
39	Marsden Fund	P	$2,055,977
40	Institut Pasteur	F	$2,036,863
41	Max Planck Institute for Infection Biology	P	$2,018,000
42	South African Department of Science and Technology	P	$1,926,557
43	Brazilian Development Bank	P	$1,814,040
44	Public Health England	P	$1,771,092
45	Swiss Federal Institute of Technology in Lausanne (EPFL)	P	$1,754,323
46	U.S. President's Emergency Plan for AIDS Relief (PEPFAR)‡	P	$1,594,335
47	Company N*	C	$1,500,000
48	Indonesian philanthropic donors to TB Alliance	F	$1,500,000
49	Indian Council of Scientific and Industrial Research (CSIR)	P	$1,425,732
50	Sequella	C	$1,356,000
51	Taiwan Centers for Disease Control	P	$1,233,230
52	U.S. Department of Veterans Affairs*	P	$1,179,524
53	Irish Aid	P	$1,142,270
54	National Institutes of Health—University of the Philippines Manila*	P	$1,128,864
55	Singapore Ministry of Health, National Medical Research Council	P	$1,049,705
56	U.S. Food and Drug Administration (FDA)†	P	$1,017,990
57	Korean Ministry of SMEs and Startups	P	$1,015,500
58	World Health Organization	M	$997,004
59	French National Agency for AIDS Research (ANRS)	P	$958,927
60	Irish Health Research Board	P	$956,274
61	Norwegian Ministry of Education and Research	P	$875,200
62	National Research Foundation of South Africa	P	$778,791
63	Singapore Agency for Science, Technology and Research (A*STAR)	P	$671,513
64	Médecins Sans Frontières (MSF)	F	$670,631
65	Indian Ministry of Science and Technology	P	$664,565
66	South African Technology Innovation Agency*	P	$617,134

C = Corporation/Private Sector; F = Foundation/Philanthropy; M = Multilateral; P = Public-Sector Agency
* New Funder; † Organization has reported to TAG each year since 2005

BASIC SCIENCE	DIAGNOSTICS	DRUGS	VACCINES	OPERATIONAL RESEARCH	INFRASTRUCTURE/ UNSPECIFIED
$0	$1,851,600	$617,200	$0	$0	$0
$0	$0	$2,400,000	$0	$0	$0
$692,053	$346,006	$0	$494,764	$594,560	$171,904
$0	$0	$2,273,117	$0	$0	$0
$0	$0	$2,175,000	$0	$0	$0
$2,055,977	$0	$0	$0	$0	$0
$2,036,863	$0	$0	$0	$0	$0
$1,211,000	$0	$0	$807,000	$0	$0
$1,440,709	$276,434	$209,414	$0	$0	$0
$0	$0	$0	$1,814,040	$0	$0
$67,349	$0	$588,197	$1,115,546	$0	$0
$1,044,240	$0	$710,083	$0	$0	$0
$0	$0	$381,205	$0	$1,213,130	$0
$0	$0	$1,500,000	$0	$0	$0
$0	$0	$1,500,000	$0	$0	$0
$38,575	$0	$1,387,157	$0	$0	$0
$0	$0	$1,356,000	$0	$0	$0
$1,037,594	$195,636	$0	$0	$0	$0
$500,000	$0	$679,524	$0	$0	$0
$0	$0	$1,142,270	$0	$0	$0
$207,399	$577,710	$334,966	$0	$8,789	$0
$0	$0	$1,049,705	$0	$0	$0
$0	$0	$1,017,990	$0	$0	$0
$0	$1,015,500	$0	$0	$0	$0
$0	$0	$0	$0	$997,004	$0
$0	$83,478	$875,448	$0	$0	$0
$0	$0	$271,157	$685,118	$0	$0
$451,781	$0	$423,418	$0	$0	$0
$760,417	$0	$0	$0	$0	$18,374
$217,788	$0	$453,725	$0	$0	$0
$0	$24,745	$57,114	$0	$588,773	$0
$525,364	$15,121	$25,559	$15,430	$83,091	$0
$0	$458,647	$0	$0	$0	$158,487

Appendix 2

TB R&D Funders by Rank, 2017 (continued)

2017 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
67	Japan BCG Laboratory	C	$572,475
68	Japan International Cooperation Agency (JICA)	P	$503,819
69	Company R	C	$472,041
70	Natural Sciences and Engineering Research Council of Canada*	P	$466,362
71	Korean Ministry of Education	P	$464,812
72	Genedrive	C	$457,660
73	Thailand National Science and Technology Development Agency	P	$389,609
74	Brazilian Ministry of Health	P	$302,340
75	Carlos III Health Institute	P	$275,287
76	Thailand Health Systems Research Institute	P	$257,811
77	Thailand Ministry of Public Health	P	$254,727
78	Thrasher Research Fund	F	$237,296
79	Industry donors to TBVI	C	$228,454
80	Japanese Ministry of Health, Labour and Welfare	P	$219,639
81	CRDF Global	F	$212,314
82	Norwegian Ministry of Health and Care Services	P	$204,787
83	Corporate donors to TB Alliance	C	$200,646
84	Australian Research Council	P	$194,068
85	Korean Ministry of Agriculture, Food and Rural Affairs	P	$187,000
86	Danish Council for Independent Research	P	$176,652
87	ELMA Foundation	F	$175,000
88	Indian Ministry of Health and Family Welfare (MOHFW)	P	$173,204
89	Biofabri	C	$170,292
90	Else Kröner Fresenius Foundation	F	$156,000
91	Colombia Administrative Department of Science, Technology and Innovation	P	$133,000
92	Hong Kong Health and Medical Research Fund	P	$127,300
93	U.K. Biotechnology and Biological Sciences Research Council	P	$110,514
94	Korean Ministry of Trade, Industry and Energy	P	$110,000
95	Howard Hughes Medical Institute	F	$100,000
96	Research Institute of Tuberculosis/Japan Anti-Tuberculosis Association	P	$99,862
97	Korea Foundation For International Healthcare	F	$93,786
98	Singapore National University Health System	P	$92,994
99	Damien Foundation Belgium	F	$91,181

C = Corporation/Private Sector; F = Foundation/Philanthropy; M = Multilateral; P = Public-Sector Agency
* New Funder; † Organization has reported to TAG each year since 2005

BASIC SCIENCE	DIAGNOSTICS	DRUGS	VACCINES	OPERATIONAL RESEARCH	INFRASTRUCTURE/ UNSPECIFIED
$125,871	$0	$0	$446,604	$0	$0
$0	$503,819	$0	$0	$0	$0
$0	$0	$472,041	$0	$0	$0
$388,956	$37,740	$25,032	$0	$14,634	$0
$254,487	$51,035	$79,022	$80,268	$0	$0
$0	$457,660	$0	$0	$0	$0
$344,833	$44,776	$0	$0	$0	$0
$0	$0	$0	$302,340	$0	$0
$0	$275,287	$0	$0	$0	$0
$0	$0	$0	$0	$257,811	$0
$151,645	$103,082	$0	$0	$0	$0
$0	$150,868	$0	$0	$86,428	$0
$0	$0	$0	$228,454	$0	$0
$2,676	$0	$0	$0	$31,514	$185,449
$76,963	$120,994	$0	$0	$14,356	$0
$204,787	$0	$0	$0	$0	$0
$0	$0	$200,646	$0	$0	$0
$194,068	$0	$0	$0	$0	$0
$0	$0	$187,000	$0	$0	$0
$0	$0	$0	$176,652	$0	$0
$0	$0	$0	$0	$175,000	$0
$0	$0	$63,980	$0	$56,715	$52,509
$170,292	$0	$0	$0	$0	$0
$156,000	$0	$0	$0	$0	$0
$33,000	$0	$0	$0	$100,000	$0
$75,637	$51,663	$0	$0	$0	$0
$0	$0	$0	$110,514	$0	$0
$0	$110,000	$0	$0	$0	$0
$100,000	$0	$0	$0	$0	$0
$0	$0	$0	$0	$0	$99,862
$0	$0	$0	$0	$93,786	$0
$92,994	$0	$0	$0	$0	$0
$0	$91,181	$0	$0	$0	$0

Appendix 2

TB R&D Funders by Rank, 2017 (continued)

2017 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
100	Foundation Jacqueline Beytout	F	$86,672
101	Japan Society for the Promotion of Science	P	$67,828
102	Colombia National Institute of Health	P	$61,000
103	Taiwan Ministry of Science and Technology	P	$60,000
104	U.K. Department for Environment, Food and Rural Affairs	P	$51,682
105	Korean Institute of Tuberculosis	P	$47,850
106	LHL International	P	$45,383
107	Brazilian Ministry of Science, Technology, Innovation and Communication	P	$45,351
108	Korea Materials & Analysis Corporation	C	$43,500
109	World Bank	M	$43,275
110	Boditech Med Co.	C	$39,150
111	Indian Biotechnology Industry Research Assistance Council	P	$38,575
112	Grand Challenges Canada	P	$37,856
113	LG Life Sciences	C	$34,800
114	Indian Science and Engineering Research Board	P	$34,486
115	Taiwan Ministry of Health and Welfare	P	$30,000
116	Sidaction	F	$28,253
117	South African National Health Laboratory Service Research Trust	P	$26,796
118	German Leprosy and Tuberculosis Relief Association (DAHW)*	F	$22,642
119	Cepheid	C	$20,000
120	Translational Health Science and Technology Institute	P	$18,516
121	Individuals donors to TB Alliance	F	$18,113
122	AFI Corporation	C	$17,840
123	Huons Medicare Co.	C	$13,050
124	Argentina National Administration of Laboratories and Health Institutes (ANLIS)*	P	$10,885
125	Stop TB Partnership (UNOPS)	M	$7,000
126	Nesta (U.K. National Endowment for Science, Technology and the Arts)*	P	$6,459
127	FUJIFILM Wako Pure Chemical Corporation	C	$4,817
128	Medical & Biological Laboratories Co.	C	$4,460
129	Nigerian Institute of Medical Research*	P	$3,612
130	Faber Daeufer	C	$3,000
131	Astellas Pharma	C	$892
	Total		$772,001,759

C = Corporation/Private Sector; F = Foundation/Philanthropy; M = Multilateral; P = Public-Sector Agency
* New Funder; † Organization has reported to TAG each year since 2005

BASIC SCIENCE	DIAGNOSTICS	DRUGS	VACCINES	OPERATIONAL RESEARCH	INFRASTRUCTURE/ UNSPECIFIED
$0	$0	$86,672	$0	$0	$0
$25,163	$0	$0	$0	$42,664	$0
$31,000	$0	$7,000	$0	$23,000	$0
$60,000	$0	$0	$0	$0	$0
$0	$0	$0	$51,682	$0	$0
$47,850	$0	$0	$0	$0	$0
$0	$0	$0	$0	$26,282	$19,100
$0	$0	$0	$0	$45,351	$0
$0	$43,500	$0	$0	$0	$0
$0	$0	$0	$0	$43,275	$0
$0	$39,150	$0	$0	$0	$0
$0	$38,575	$0	$0	$0	$0
$0	$37,856	$0	$0	$0	$0
$0	$34,800	$0	$0	$0	$0
$34,486	$0	$0	$0	$0	$0
$30,000	$0	$0	$0	$0	$0
$28,253	$0	$0	$0	$0	$0
$26,796	$0	$0	$0	$0	$0
$0	$0	$0	$0	$22,642	$0
$0	$20,000	$0	$0	$0	$0
$15,430	$0	$3,086	$0	$0	$0
$0	$0	$18,113	$0	$0	$0
$0	$17,840	$0	$0	$0	$0
$0	$13,050	$0	$0	$0	$0
$2,419	$3,628	$0	$0	$4,838	$0
$0	$0	$7,000	$0	$0	$0
$0	$0	$0	$0	$6,459	$0
$0	$4,817	$0	$0	$0	$0
$0	$4,460	$0	$0	$0	$0
$0	$0	$0	$0	$3,612	$0
$0	$0	$3,000	$0	$0	$0
$0	$0	$892	$0	$0	$0
$147,439,441	$80,909,934	$315,051,622	$100,338,945	$89,672,465	$38,589,352

Appendix 3

TB Experts Interviewed by TAG

1	Tenu Avafia	Team leader, Human Rights, Law, and Treatment Access, HIV, Health, and Development Group, UNDP
2	Irene Ayakaka	Senior research associate, Makerere University Lung Institute
3	Grania Brigden	Deputy director, TB and HIV Department, The International Union Against TB and Lung Disease
4	Jennifer Cohn	Senior director of innovation, Elizabeth Glaser Pediatric AIDS Foundation
5	Paul Farmer	Co-founder, Partners in Health
6	Mark Feinberg	President and CEO, International AIDS Vaccine Initiative
7	Helen Fletcher	Professor of immunology, TB Centre at the London School of Hygiene and Tropical Medicine
8	Afrânio Kritski	Founding president, Brazilian TB Research Network
9	Sharonann Lynch	HIV and TB policy advisor, Médecins Sans Frontières Access Campaign
10	Albert Makone	Global health advocate
11	Welile Sikhondze	Technical advisor and research coordinator, eSwatini National TB Control Program
12	Kathryn Snow	Doctoral candidate, University of Melbourne
13	Kitty van Weezenbeek	Executive director, KNCV Tuberculosis Foundation
14	Mitchell Warren	Executive director, AVAC

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