TAG
Treatment Action Group

Stop TB Partnership

Tuberculosis Research Funding Trends 2005-2018

ACKNOWLEDGEMENTS

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ABOUT TAG

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.

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Cover image is adapted from a photo of TB activists marching in Cape Town, South Africa taken by David Harrison for the Treatment Action Campaign in 2015.

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Tuberculosis Research Funding Trends, 2005–2018

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TREATMENT ACTION GROUP

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DEDICATION

We dedicate this report in memory of Vela Mhlola, a leading voice for community engagement in tuberculosis research.

Vela passed away from TB on September 27, 2019. Beginning in 2013, he served as the community engagement officer at the esteemed TB clinical trial site TASK Applied Sciences in Cape Town, South Africa. At TASK, Vela played an instrumental role in connecting local communities to scientists working on some of the most important TB treatment and vaccine trials in recent history. His work with communities took him from the soccer pitch and youth theater groups in the township of Delft to conferences and scientific meetings across the globe. Vela was a bridge builder; he represented the needs, priorities, and aspirations of TB-affected communities to scientists. He helped bring together the community advisory boards of different clinical research sites in the Cape Town region, and he contributed greatly to the work of several global TB community engagement initiatives. The local Delft Star newspaper called him a "community hero." Wherever he went, Vela stood out for his humility, height, and huge smile, which could light an entire room.

In a video shot for the Delft Youth Theater Project, Vela said: "I've made a decision that I have to go dig, dig, dig deep in myself and ask myself what do I really want to do in life? And then I said, 'the better way for me is to start at home.' So if I start at home, obviously that's going to go to my society, to my community—that's where I can find myself."

Clinical research is more ethical, equitable, efficient, and relevant when it engages with communities as partners on equal footing. Vela's work is a testament to this truth.

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Executive Summary

Tuberculosis (TB) is both preventable and curable, yet it remains a global health crisis. Nearly 1.5 million people lost their lives to TB in 2018, and 10 million fell sick with the disease. It is possible to eliminate TB, but doing so will require continued scientific innovation and equitable access to the benefits and applications of that innovation—both of which require substantial increases in funding.

TAG has tracked TB research and development (R&D) funding since 2005 as one way to evaluate progress on eliminating TB. In every year since then, annual investments have fallen far short of the widely accepted US$2 billion minimum funding target. At the United Nations High-Level Meeting on TB (HLM) in the fall of 2018, delegates endorsed a political declaration that contained a commitment to increase annual global TB research funding to US$2 billion. The data presented in this year's report represent expenditures on TB research in fiscal year 2018 and provide the baseline against which we will measure states' performance towards this US$2 billion annual target in the years to come.

That baseline now also represents a high-water mark: in 2018, global TB R&D expenditures increased to US$906 million—the highest amount ever reported by TAG. Understanding the composition of TB research funding—where the money comes from and what types of R&D activities it supports—is a critical part of advocacy to hold states accountable for meeting the commitments in the HLM political declaration. Key findings from this year's report include:

- Global TB R&D expenditures increased to US$906 million in 2018—a US$134 million jump up from 2017.
- The public sector contributed more than two-thirds of total TB research spending in 2018 (US$617 million) and is the only sector with a substantial increase in funding over 2017.
- The U.S. National Institutes of Health accounted for 37% of the total US$134 million funding increase between 2017 and 2018.
- Sixty percent of public sector expenditures came from the United States government. The U.S. government invests over US$125 million more into TB R&D than every other government combined. The United Kingdom is the second largest public sector funder, providing US$63 million.
- India leads funding among the BRICS nations and other high-TB-burden countries with US$30.8 million in funding. The Indian Council of Medical Research is among the 10 largest funders of TB R&D globally.
- Only three countries met their fair share targets by spending at least 0.1% of what they spend on all forms of R&D on TB R&D: the Philippines, the United Kingdom, and South Africa. (If general investments in non-TB-specific clinical trials infrastructure are counted, the United States also met its fair share target.) If every country redistributed its research spending such that 0.1% of its overall spending on R&D went to TB R&D, we would achieve the goal of US$2 billion per year.
- The private sector provided 9% of total TB R&D funding in 2018 (US$85 million). Private sector spending on TB R&D has remained static since 2015.
- TB R&D funding remains highly concentrated among a few donors. The two largest investors—the U.S. government and the Bill & Melinda Gates Foundation—accounted for 56% of all funding in 2018. The 30 largest funders comprised over 90% of the total.
- Approximately one-third of TB research funding went to drug research, followed by 20% to basic science, 13% to operational research, 12% to vaccines, and 9% each to diagnostics and infrastructure/unspecified research.
- Spending on pediatric TB research surpassed US$60 million in 2018—a notable increase, but one that remains insufficient to achieve global targets in pediatric TB.

In addition to presenting the funding data summarized above, this year's report draws on interviews with 10 leading TB activists. Each was asked to analyze the current state of TB research in relation to available versus required funding. These activists represent a wide diversity of civil society actors, community-based organizations, and TB-affected communities. Their words remind us that TB research is about more than counting dollars, rupees, rand, and pounds—it is an urgent matter of human rights and global solidarity. There is a sense among many activists that as funding for TB research has inched upward, and as new tools for TB prevention, diagnosis, and treatment have started to materialize, the distribution TB research and its benefits has become increasingly inequitable. For this reason, most interviewees see increasing access as a critical—if not *the* critical—issue related to TB research.

To correct this trend toward inequity before it becomes entrenched, many of the activists TAG spoke with called for funders, scientists, and product developers to increase attention to access at every stage of research. At earlier research phases, this should include sharing the means, methods, and materials of scientific discovery—whether data, compounds, techniques, or other forms of intellectual property. At later stages, access will hinge on ensuring the availability, affordability, acceptability, and quality of TB interventions for all people everywhere—a standard established by international human rights law. In addition to access concerns, several other themes emerge from the funding data and activist interviews. First, the need to conduct rigorous research in order to generate quality data to inform implementation. Second, the importance of increasing investments in community engagement in the R&D agenda. And finally, the necessity of improving collaboration and coordination across the entire TB research landscape.

Together, these components of access, quality data, community engagement, and collaboration will be critical to ensuring that TB research remains responsive and accountable to the needs of the people and communities affected by TB.

The following report pairs optimism with pragmatism in equal measure. Funding for TB R&D is higher than ever before. Yet even with the sizeable spending increase reported this year, we remain halfway short of the goal of US$2 billion in annual R&D spending. The resource engine driving scientific progress against TB is either half full or half empty depending on one's outlook. One thing on which everyone can agree: a failure to meet targets for TB R&D threatens the attainment of larger TB elimination goals. The first milestones of the World Health Organization *End TB Strategy* hit in 2020 and include a 35% reduction in the number of TB deaths as compared with 2015, a 20% reduction in TB incidence, and zero families facing catastrophic costs due to TB. The 1.6–2.0% reduction in TB incidence and 11% reduction in TB mortality from 2015 to 2018 indicate that we are falling far behind our benchmarks for success.

Without massive step ups in spending over the next two years—ones that far exceed the increase observed in 2018—the world will miss its TB elimination targets by a considerable distance. The time for making political promises is over; the difficult work of accountability now begins.

Introduction

"Is TB funding increasing? Yes. But is it increasing at the level that we need to end the TB epidemic? No!"

—**Fifa Rahman, board member for NGOs, Unitaid executive board**

Political momentum continues to build around tuberculosis (TB). A little more than a year has passed since the first United Nations High-Level Meeting on TB (HLM) in September 2018 put TB elimination at the forefront of global political attention. The HLM produced a political declaration that included a commitment by governments to increase annual global funding for TB research to US$2 billion. Although this endorsement came with no clear enforcement or accountability mechanisms, and a number of critical questions related to implementation remained, energy was high after the HLM. Many working in TB shared a cautious optimism that political momentum would translate into increased funding.

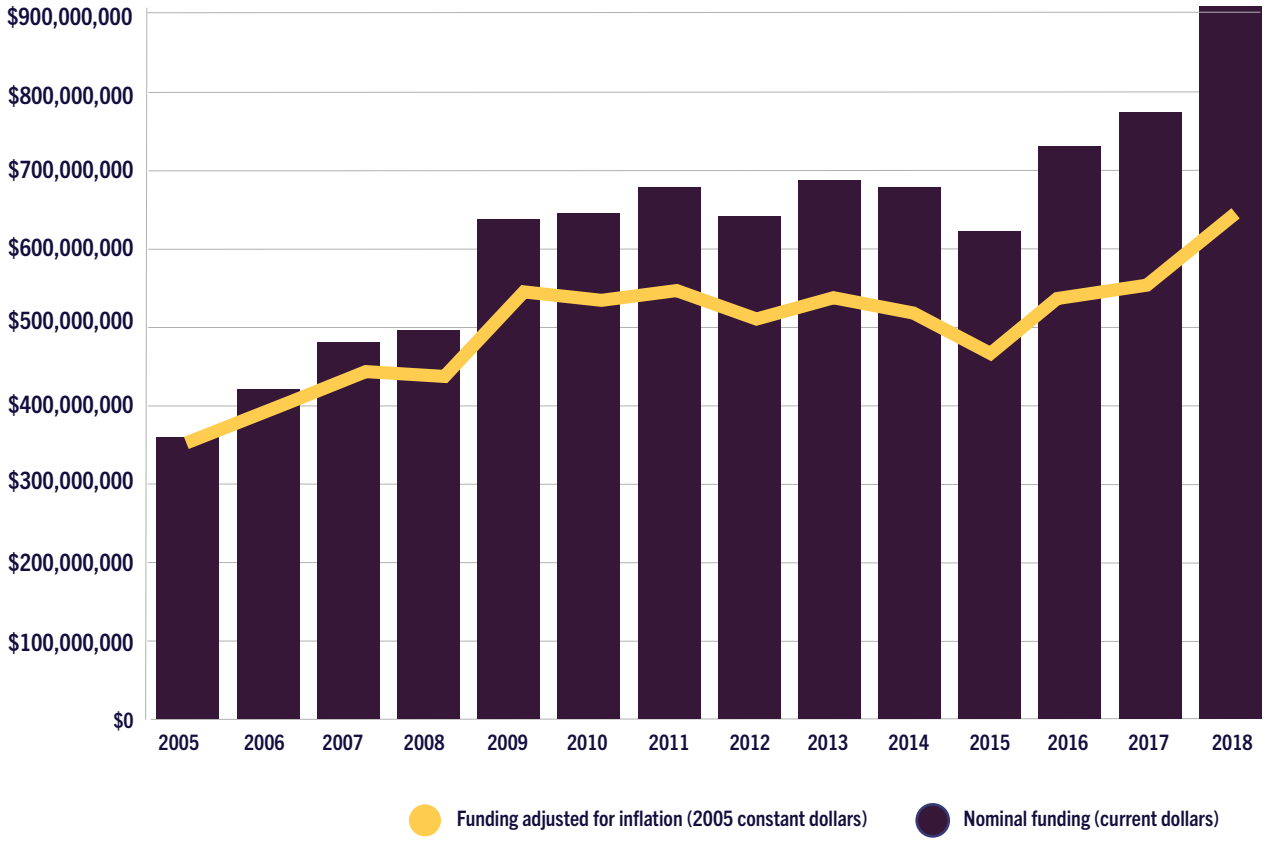
Now, a year removed from the HLM, calls for measurable, concrete, and immediate action have taken center stage—at least from the perspective of the activists interviewed in this report. In addition to presenting quantitative data on TB research expenditures, this year's report quotes from interviews with leading activists from TB-affected communities and civil society organizations. These voices animate the funding data with a sense of urgency by conveying the lives, values, and human rights obligations at stake in meeting the HLM commitments on TB research. A key takeaway is the sobering reminder that increased research and development (R&D) funding, while necessary to eliminate TB, is only one piece of the puzzle. Meeting global TB targets will require not only an influx of money but also substantially increased investments in the community engagement work that underpins advocacy and accountability. Janika Hauser, parliamentary advocacy officer at RESULTS UK, describes how "conversations about TB research, research financing, and policy are often really inaccessible to TB-affected communities." Deliberate efforts to engage communities in the research agenda are needed to ensure that R&D aligns with—and is accessible to—the communities affected by TB.

Eliminating TB will require increased use of existing diagnostics and treatments and the development of new technologies for prevention, diagnosis, and treatment. In other words, ending the TB epidemic requires both innovation and access. The effort will also necessitate continued engagement of TB activists, health care providers, and other stakeholders from affected communities in research and delivery. Kajal Bhardwaj, an independent lawyer working on health and rights in India, reminds us that "advocacy for better funding and newer treatments and diagnostics for TB has seen some critical successes in recent years, and we should take a moment to reflect on and appreciate this as a global community." Diverse stakeholders continue to advocate for increased funding for TB R&D, recognizing that eliminating TB will be impossible without increased investments and robust community engagement in the research agenda.

TAG has reported on global TB research funding levels since 2005 as one way to evaluate public, private, philanthropic, and multilateral commitments to ending TB. In the first 13 years that TAG tracked global TB research funding, total annual investments never approached even half of the US$2 billion that will be needed to eliminate TB. The 2017 global investment of US$772 million—while marking a new high for R&D funding at the time—was still less than 40% of the US$2 billion that is widely agreed upon as a minimum annual R&D target. As Rosa Herrera, a TB doctor and Global TB Community Advisory Board (Global TB CAB) member based in Mexico, explained, "TB research is going to be hard with the money, but it's going to be harder without enough money. Lack of funding is affecting [our ability] to reach the goals we established."

FIGURE 1

Total TB R&D Funding, 2005–2018



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
2018	$906,125,319

> "TB research is going to be hard with the money, but it's going to be harder without enough money. Lack of funding is affecting [our ability] to reach the goals we established."
>
> —**Rosa Herrera, TB physician and Global TB CAB member**

In this report, we present trends in funding for TB R&D for the 14 years from 2005 to 2018. We are heartened to report that global TB R&D expenditures increased to US$906 million in 2018—a US$134 million jump up from 2017. This is the highest level of expenditure ever reported by TAG and the second-largest year-on-year increase in funding (surpassed only by the increase from 2008 to 2009, which came almost entirely from economic stimulus money released under the American Recovery and Reinvestment Act).[1] After weathering seven years of relatively flat funding between 2009 and 2015, TB research has now enjoyed three years of significant funding increases from 2016 to 2018.

Even with this year's historic increases, TB funding targets remain frustratingly out of reach. The Stop TB Partnership's *Global Plan to End TB (Global Plan)* calls for a global investment in TB R&D of US$9 billion from 2016 to 2020. Annualized, this would be a yearly target of US$2 billion per year—the same benchmark set by UN member states in the HLM political declaration. Despite total funding surpassing US$900 million for the first time ever in 2018, we remain halfway short of the goal of US$2 billion in annual R&D spending.

Funding increases in many areas of TB research reflect both continued advocacy as well as heightened political momentum around TB; however, none of these figures approach the five-year TB research funding targets in the *Global Plan*. The *Global Plan* specifies targets of US$4.15 billion for drug research, US$3.43 billion for diagnostic research, and US$1.25 billion for vaccine research. Without a massive increase in funding, these targets will be extraordinarily difficult to achieve. In year three of the five-year plan, vaccine research has only reached 24% of its goal, drug research is at 21%, and diagnostic research is at only 7% of its target. These numbers illuminate the gap between on-the-ground needs—for cheaper and faster diagnostics, improved treatments, and a new vaccine—and the anemic realities of global investment in TB research.

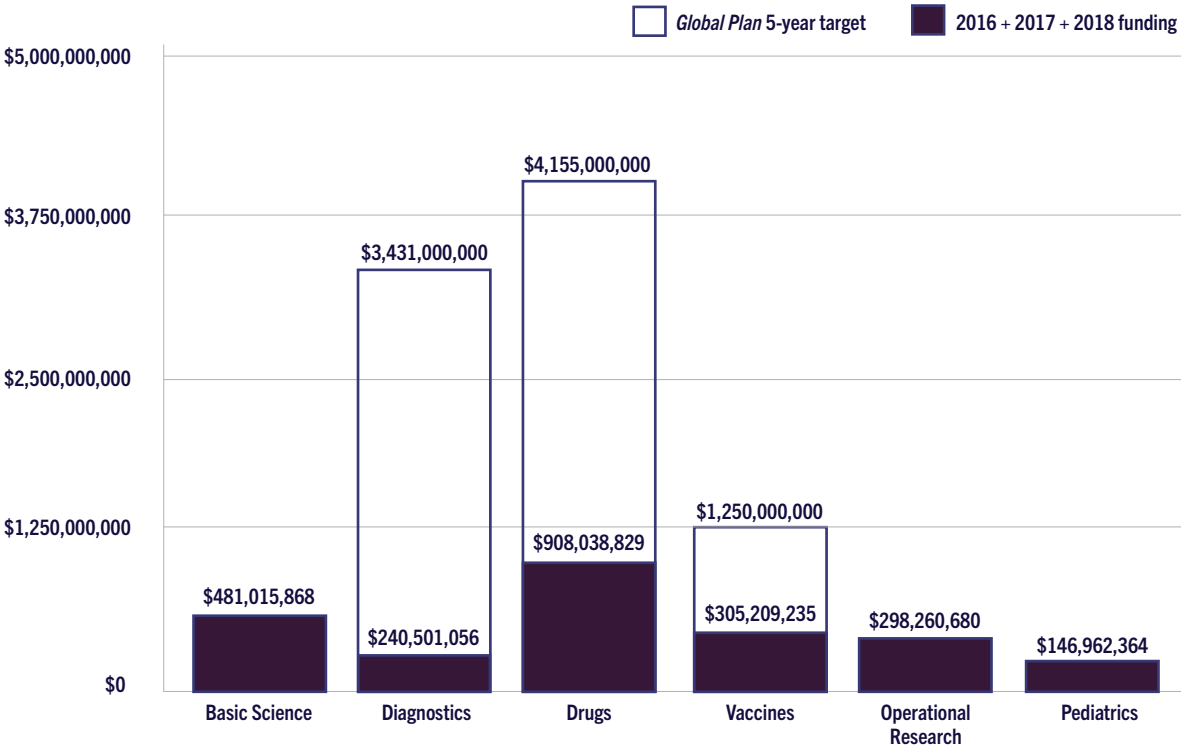
Insufficient research funding not only slows the pace and limits the scope of scientific progress against TB—it also threatens the advancement of larger TB elimination targets. Progress in combatting TB is too slow to meet the milestones laid out in the World Health Organization (WHO) *End TB Strategy*. The *End TB Strategy* includes interim milestones for 2020, 2025, and 2030. The first milestones are looming next year: interim milestones for 2020 include a 35% reduction in the number of TB deaths as compared with 2015, a 20% reduction in TB incidence as compared with 2015, and zero families facing catastrophic costs due to TB.[2] With only a 1.6–2.0% reduction in TB incidence and an 11% reduction in TB mortality from 2015 to 2018, we are quickly falling behind.[3]

TAG collected the expenditure data presented here through a global survey of TB research funders (see Appendix 1 for a detailed description of the methodology). This year TAG surveyed over 200 organizations and received responses from 124—more than ever before. The comprehensiveness of the data TAG collects depends on the number of responses as well as 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 not known. Encouragingly, all 30 of the 30 largest funders of TB research in 2017 participated in 2018. The top 30 donors typically comprise over 90% of total TB research funding in any given year, and the 100% response rate from this segment suggests that the survey captured the majority of global investments.

Historically, TAG's report on TB R&D funding has included interviews with key stakeholders across the sectors involved in TB research. This year, TAG decided to focus on activists' perspectives and interviewed 10 activists working in the field of TB R&D. Interviewees received a summary of this year's data and generously offered their perspectives on the state of TB research funding. The activists TAG spoke to raised concerns about managing the coordination of research priorities, the low level of community engagement

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.

"For me, more than the figures, it's more about 'the what.' The figures don't give a qualitative assessment of what is going on . . . When you think about quantifying R&D efforts, are the most important research questions being addressed? What I think we should be looking at more is how does the research we do contribute to actually improving health outcomes?"

—**Els Torreele, executive director of Médecins Sans Frontières Access Campaign**

with research, and the absence of community oversight and input into R&D. Interviewees recounted their excitement and frustration about the research pipeline and almost unilaterally issued calls for greater accountability in TB R&D. Four themes emerged from the interviews: 1) the need to conduct rigorous research capable of generating quality data to inform implementation; 2) the imperative to increase access at every stage of research, and not just during implementation; 3) the importance of increasing investment in community engagement and developing mechanisms for training community advocates; and 4) the necessity of improving collaboration and coordination across the TB research landscape. For most interviewees, increasing access is a critical—if not *the* critical—issue related to TB research.

Every country in the world continues to diagnose and report TB, and TB remains the leading cause of death from an infectious disease globally.[4] As long as TB research is underfunded, TB will continue to exact a heavy toll on human health. The more than 10 million people who fell ill with TB in 2018 represent 10 million reasons why the global community must rally with a sense of purpose and urgency to accelerate the science needed to end this epidemic.

Results

> "There's an increased sense of excitement among people working in TB research about the innovations that are coming down the track and the progress that has been made, but I don't think there's any sense of relaxation or satisfaction at the rate of that progress. When you look at the kind of donors that are in the space . . . those donors that invest can see how their investment leads to breakthroughs that transform the lives of patients . . . But we're not seeing enough donors come to the table, and we're not seeing that diversity [of funders] that really drives innovation, and those leaps and bounds in research that we're waiting for."
>
> —**Janika Hauser, parliamentary advocacy officer at RESULTS UK**

The Big Picture

In absolute numbers, 2018 TB research funding totaled US$906 million, an increase of 17% over the 2017 total. After a funding plateau from 2009 to 2015, the last three years have seen sizeable—and sustained—increases in funding. When compared with 2005, annual TB research funding has seen a 2.5-fold increase (US$358 million in 2005 to US$906 million in 2018).

Global TB research funding from 2016 to 2018 totaled just over US$2.4 billion. To meet the Global Plan's US$9 billion target, 2019 and 2020 funding will need to total nearly US$6.6 billion. Meeting that goal would require investing just shy of US$3.3 billion each year for the next two years—a staggering annual investment that is nearly four times the total TB research spending in 2018 and 1.5 times the US$2 billion funding target that is widely circulated.

This is the first year that, in real numbers (i.e., inflation-adjusted terms), global TB research investments have seen any significant growth. When adjusted for inflation, 2018 funding works out to US$631 million in 2005 constant dollars. (The US$2 billion annual target equates to US$1.4 million in 2005 constant dollars.) Inflation-adjusted TB R&D expenditures stayed steady in the mid-US$500 million range from 2009 to 2017. So, while US$631 million is nowhere near the amount that will be required to address the public health emergency that is TB, this is the first year in nearly a decade that inflation-adjusted TB research spending has increased significantly: to 1.76 times that of 2005 spending.

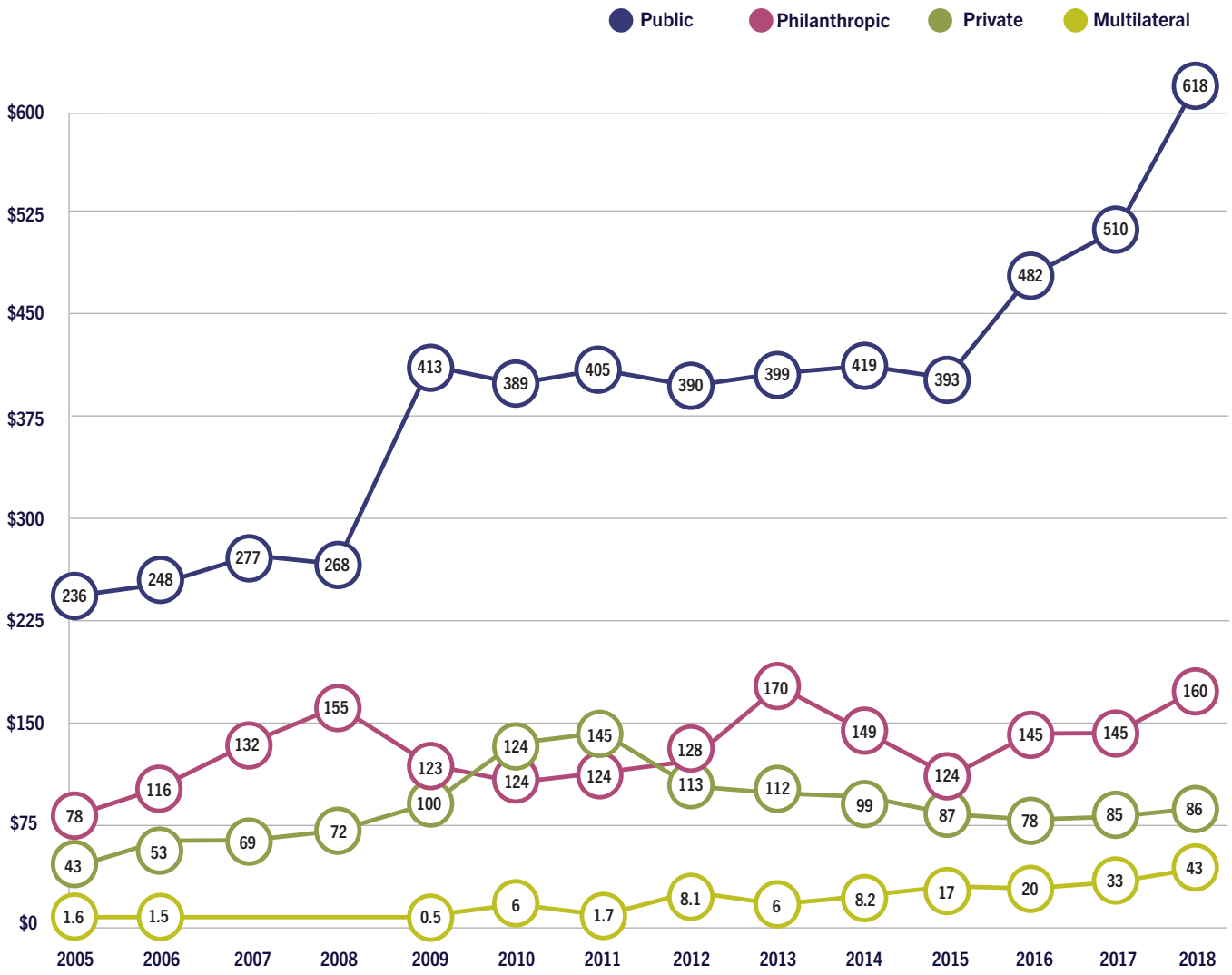
As in previous years, the majority of funding for TB research continues to come from the public sector, led by the U.S. government. A US$108 million increase in public sector funding drove the overall US$134 increase in total TB R&D funding observed between 2017 and 2018 (philanthropic and multilateral funding increased by US$15 million and US$10 million, respectively, and private sector funding remained virtually unchanged). Philanthropic organizations—almost entirely *one* organization, the Bill & Melinda Gates Foundation (Gates Foundation)—accounted for 18% of total R&D funding in 2018. The U.S. government and the Gates Foundation together contributed over US$512 million, or 56% of all funding in 2018. The private sector invested 9% of total research spending, and multilateral agencies contributed 5%.

Trends in Public Sector Funding

In 2018, the public sector accounted for more than two-thirds of total research spending (US$617 million; 68%). Jumping to over 120% of its 2017 amount, the public sector is the only sector that saw a substantial increase over the past year. Broken down by research area, the public sector contributes 49% of total drug research funding, 69% of funding for operational research, 72% of vaccine funding, 73% of diagnostic funding, 85% of funding for basic science, and 95% of infrastructure/unspecified funding. (Public sector contributions by country are presented in later sections of this report.)

FIGURE 3

Total TB R&D Funding by Funder Category, 2005–2018 (in Millions)



"I feel that the government is not doing enough. When it comes to research and access to medication, I think government has their priorities a bit miscast. But despite that difference, our goals are the same."

—**Marie Theunissen, Community Research Advisors Group member and Desmond Tutu TB Centre community advisory board coordinator**

As in previous years, the U.S. government is the largest overall funder of TB research, providing approximately 41% of total global funding. The U.S. government invests over US$125 million more into TB R&D than every other government combined. In 2018, the United States provided US$371 million in funding, up from 2017's US$312 million. U.S. investments accounted for 60% of all public sector expenditures. The United States invests in all areas of research, although basic science and drugs receive the lion's share (US$113 and US$107 million, respectively). U.S.-funded TB research is spread across nine agencies and programs. With a 2018 investment of US$253 million, the National Institute of Allergy and Infectious Diseases (NIAID) at the U.S. National Institutes of Health (NIH) is far and away the largest single TB research funder. Two of the top five funders in 2018 are U.S. federal agencies: the NIH—including NIAID as well as the NIH's other institutes and centers—and the United States Agency for International Development (USAID).

FIGURE 4

Total TB R&D Funding by Funder Category, 2018
Total: $906,125,319

Increased TB spending at the NIH accounts for 37% of the US$134 million increase in total TB R&D funding observed between 2017 and 2018. NIH funding for TB researched jumped from US$248 million to US$297 million between 2017 and 2018. This reflects a combination of personal and political commitment to TB research among NIAID leadership and sizeable appropriations increases to the total NIH budget passed by the U.S. Congress in recent years. In September 2018, shortly before the HLM, NIAID released its *Strategic Plan for Tuberculosis Research*, meaning that the allocation of these new research dollars is guided by a comprehensive vision for advancing TB science.[5]

The United Kingdom is the second largest public sector funder, providing US$63 million (10% of all public sector funding). The European Union, India, Germany, Canada, and South Korea also invested over US$10 million in 2018. Although the public sector is the largest source of TB research funding, this area lacks diversity. The overwhelming majority of funds come from just a handful of countries: 85% of the public sector investment is from five countries. Janika Hauser from RESULTS UK points out that "BRICS and some of the middle-income countries are really going to play a key part in this. With burgeoning epidemics and also growing research communities, it makes twice as much sense for them to invest in TB research." Neither China nor the Russian Federation responded to requests to participate in this report, although both have significant TB research programs. Of the remaining BRICS countries, India is the only one to have contributed more than US$10 million (South Africa's investment was US$4.5 million).

The BRICS countries continue to deliberate on the formation of a BRICS TB Research Network, though detailed decisions on its structure, funding, mechanisms for community engagement, and access norms and principles have yet to be made. In November 2019, the leaders of the BRICS nations met in Brasilia and reiterated their support of joint TB research activities, stating: "We welcome. . .the Collaborative Research Program for TB, developed by BRICS TB Research Network in 2019, aimed at promoting new scientific, technological and innovative approaches to tackle the TB burden, by supporting scientific projects in a wide range of relevant issues related to TB."[6]

Of the 22 countries that reported over US$250,000 in TB research spending in both 2017 and 2018, a vast majority (16 of 22; 72%) increased their investments in 2018, an encouraging sign that the political declaration that emerged from the HLM was not just political showboating. These research funding commitments would have largely been made prior to the HLM. Notably, six countries decreased their investment in TB R&D over the last year: South Africa, Switzerland, Japan, Norway, Brazil, and New Zealand.

Annual fluctuations in countries' TB research investments illustrate one limitation of relying too heavily on national governments for funding without broader, community-driven coordination of the overall research agenda. Els Torreele, the executive director of the Médecins Sans Frontières (MSF) Global Access Campaign, commented on the need for what she called a "public-responsibility-driven R&D model," saying, "We really need to think about the collective governance mechanism to steer the R&D where the health impacts will be biggest and find some coordination [in priority setting]." Indeed, country accountability and oversight were conspicuously absent from the political declaration generated at the HLM. Continued engagement with community stakeholders will be key to ensuring that public sector funding decisions map onto community-based research priorities.

Trends in Philanthropic Funding

In 2018, philanthropic funding totaled US$159 million. Nearly 90% (US$141 million) of that money came from the Gates Foundation. As in previous years, the Gates Foundation provided the second largest investment in TB research across all funders (second only to the U.S. government). They provided more funds for TB research (US$141 million) than the private (US$85 million) and multilateral (US$42 million) sectors combined. An additional 13 philanthropic organizations invested in TB R&D. Of those 13, the Wellcome Trust is the only one that spent more than US$10 million on TB research.

Just over half (52%; US$83 million) of total philanthropic funding went to drug research. Philanthropic funding also provided substantial support for basic science research (16%; US$26 million) and vaccine research (15%; US$24 million). Operational, diagnostic, and infrastructure/unspecified spending rounded out philanthropic investments with expenditures of US$13 million, US$8.5 million, and US$3.6 million, respectively.

The composition of philanthropic funding has not seen major changes in recent years. Few new major foundations have stepped into the TB research space, though Tata Trusts in India and the Tahir Foundation in Indonesia have extended some support (unfortunately, neither foundation answered requests to participate in this year's survey).

The formation of the Gates Medical Research Institute (GMRI) represents the biggest shift in philanthropic funding for TB research in recent years. Fully funded by the Gates Foundation, the GMRI is a nonprofit biomedical research institute based in Boston that seeks to develop novel products to fight TB, malaria, and the major causes of maternal and newborn morbidity and mortality.[7] The GMRI is a wholly owned subsidiary of the Gates Foundation but is technically a separate entity. It remains to be seen whether the creation of the GMRI will lead to new and increased spending by the Gates Foundation, or whether it represents a pivot in strategy in which existing money for TB research at the Foundation will be channeled in a new direction. Currently, TB projects comprise over 50% of the GMRI portfolio and include both drug and vaccine development.[8] On the vaccine side, the GMRI is looking at whether revaccination with Bacillus Calmette–Guérin (BCG) can prevent TB infection in adolescents. On the drug side, the GMRI's work aims to accelerate the development of treatment-shortening regimens and help partners advance individual drug agents into regimen development.[9]

"The private sector is not going to be the savior . . . It needs to be a public-interest-driven public-private partnership. What we've often done is create public-private partnerships where we leave a lot of power and leeway to the private sector trying to still make it a viable business for them. In the situation of TB, even when buying the drugs, where does the money come from? Again, the public. So, let's take it toward a fully public-responsibility-driven R&D model."

—**Els Torreele, executive director of the MSF Access Campaign**

Trends in Private Sector Funding

In 2018, the private sector invested US$85 million, or 9% of total TB R&D funding. Twenty-four companies reported expenditures to TAG (four companies reported anonymously), although more are present in the TB R&D landscape. Only 10 of the 24 companies spent more than US$1 million, although two of the top 10 funders overall are pharmaceutical companies (Japan's Otsuka Pharmaceutical and "Company X," one of the anonymous reporters). The private sector invests heavily in drug development (US$73 million; 85% of total industry investment). Four companies spent a total of US$5 million in TB vaccines, and 11 companies reported a total of US$6 million in funding for diagnostics.

After declines in 2012, 2013, and 2014, private sector funding for TB R&D has remained static since 2015. In light of industry's failure to increase its investment in TB R&D—despite the development and marketing of new products—activists express strong skepticism that the private sector will play a lead role in ending TB. Kajal Bhardwaj describes the private sector as limiting access to TB treatment and diagnosis, calling attention to public sector funds used to generate products controlled by patent-protected monopolies: "Given the amount of public effort, funding, and contribution that have allowed accelerated approval of new treatments like bedaquiline, delamanid, and pretomanid, it is disheartening to see companies continue to retain complete control over who gets access to these medicines and how." Els Torreele shares Bhardwaj's frustration with the lack of public oversight on private sector research. Torreele explains that "what we've often done is create public-private partnerships where we leave a lot of power and leeway to the private sector. . . In the situation of TB, even when buying the drugs, where does the money come from? Again, the public. So, let's take it toward a fully public-responsibility-driven R&D model."

"Now, more than ever, researchers and scientists must use their voices as advocates to help break the stranglehold of corporate monopolies on TB treatment and diagnosis."

—**Kajal Bhardwaj, independent lawyer working on health and rights in India**

Trends in Multilateral Funding

"If I were to pick two entities out of the entire list that should be spending more, it would be the European Union and Unitaid."

—**Fifa Rahman, NGO delegation representative to the Unitaid Board**

After a significant increase in funding from 2016 to 2017, multilateral funding increased again in 2018, to US$42 million. Unitaid was the top multilateral funder, with an investment of US$26 million. Four additional funders—the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund); the Global Health Innovative Technology Fund (GHIT); the WHO; and the Stop TB Partnership—complete the multilateral funding landscape. Multilateral funders invested across most areas of TB R&D: primarily in operational research (US$24 million), but also in drugs (US$12 million) and diagnostics (US$6 million).

Most multilateral organizations working in TB research solicit funds from donors and distribute the funds via grants for projects related to the organization's mission. Unitaid funded US$215 million of TB projects (not limited to R&D) in 2018,[10] and from 2002 to August 2019, the Global Fund provided over US$6.7 billion in TB-related grants (see box for detail on the Global Fund's contributions to TB research).[11] This method of resource redistribution can provide centralized coordination and oversight. As calls for intensified collaboration in TB research increase in volume—not only from activists but also from governments and scientists themselves—multilateral agencies may play an increasingly important role in steering the TB research agenda.

Activists like Els Torreele with the MSF Access Campaign describe the TB research landscape as generally lacking such coordination. Torreele laments the "lack of a strategy towards the research portfolio. There should be a comprehensive research agenda. It's a pity, because I think we could be doing much more with what we have if we were better aligned towards what we're trying to achieve." Multilateral funding, by definition, builds connections across sectors. Increasing the proportion of funds disbursed via multilateral funders may be one way to increase funding for community-centered oversight. Fifa Rahman, from Unitaid's NGO delegation, explains: "One of the things we [the NGO delegation] brought up at the June [Unitaid] board meeting this year in Seoul was that Unitaid only spends 19% of its portfolio on TB. And while this is an increase from before, for us, it's an imbalance . . . Why is Unitaid only spending 19% of its portfolio on TB given that most people living with HIV are going to die of TB?"

Closer Look: Global Fund Support for TB Research

This year, for the first time in this report's history, the Global Fund was able to provide TAG with an estimate of its annual spending on TB operational research. (Previously, the Global Fund reported its cumulative expenditure on TB operational research since its inception in 2002.) The Global Fund reported spending US$10.5 million on TB operational research in 2018, making it the 17th largest funder of TB research overall.

The Global Fund generated this estimate by looking for research-related expenditures across the different modules and interventions that organize the Fund's grant-making. A detailed review of each country program might yield a more precise figure or uncover operational research funding not included in the US$10.5 million estimate reported here. Thus, readers should take this figure as a minimum estimate.

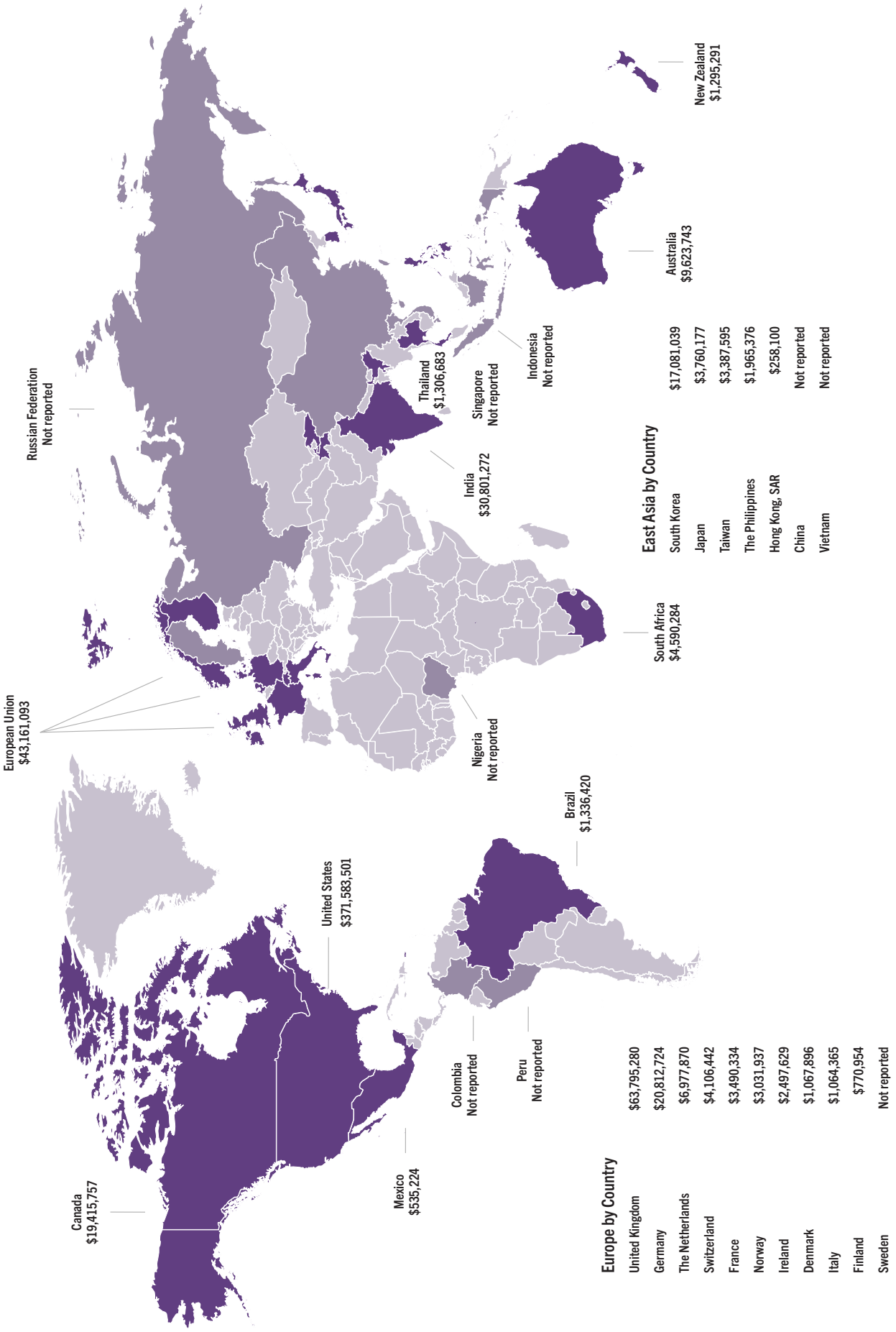
Interest in harnessing Global Fund resources to support TB operational research is high. A recent editorial in the *International Journal of TB and Lung Disease* highlighted the Global Fund's "vital role" in supporting operational research, calling on the Global Fund "to make OR [operational research] a priority for countries" by "supporting countries to request budgets for OR and to build national OR capacity."[12]

For its part, the Global Fund emphasized the importance of operational research in the "Tuberculosis Information Note" it issued in July 2019 to guide applicants requesting TB funding during the next grant cycle. The document plainly states: "Operational research is important to assess progress in program implementation and performance, identify challenges, [and] inform planning for improvement of quality and coverage of TB services."[13] The note also encourages applicants to think about the role of operational research "when implementing new, innovative interventions for which evidence of impact is incomplete." Indeed, operational research has proven critical to the rollout of new tools from GeneXpert for TB diagnosis to bedaquiline for the treatment of multidrug-resistant TB (MDR-TB).

In October 2019, the Global Fund's Sixth Replenishment Conference raised a record US$14 billion in pledges from donors to support the Global Fund's work over the next three years.[14]

FIGURE 5

Country Contributions to TB R&D, 2018



Fair Share

"I certainly support the call that 0.1% of overall investment in R&D go to TB. If countries would meet that target, we'd get close to closing the gap."

—**Wim Vandevelde, Global TB CAB member, Global Network of People Living with HIV/AIDS**

"Countries that don't contribute anywhere near appropriate levels are failing to deliver on the UN High-Level Meeting commitments but ultimately also doing a real disservice to the research and innovation landscapes in their countries."

—**Janika Hauser, parliamentary advocacy officer at RESULTS UK**

A key deliverable from the 2018 HLM was a political declaration, adopted by the UN's General Assembly in October 2018, that stated in no uncertain terms that "the world needs to refocus efforts on actions and investments, including in research, needed to achieve the Sustainable Development Goals target of ending the tuberculosis epidemic by 2030."[15] The 53 resolutions included in that declaration cover the range of issues related to TB—health inequity, the disproportionate impact of TB on people living with HIV, children's unique needs in TB diagnosis and treatment, and a call for increased multi- and cross-sectoral partnerships.

In this section of the report, we address a simple yet telling measure of countries' commitments to ending TB: the fair share target. Two-thirds of new TB infections occurred in eight countries—India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa—but meeting the global funding targets required to end TB will require every country to bear its share of the costs.[16] The fair share target is based on individual countries' total investment in all forms of R&D (gross domestic expenditure on research & development). Total global R&D spending comes out to US$2.0 trillion.[17] While it would require substantial shifts in funding priorities, if every country redistributed its research spending such that 0.1% of its overall spending on R&D went to TB research, we would achieve the goal of US$2 billion per year in TB research spending. Hence, a country's fair share of TB R&D is calculated as 0.1% of its overall spending on R&D.

Wim Vandevelde described the fair share targets as part of a larger effort to disaggregate global targets for TB prevention, diagnosis, and treatment made at the HLM into country-specific targets: "By having this data disaggregated for countries, local activists can go to decision makers, to politicians, to the press, and put some pressure. When you have very global targets, that doesn't have a lot of impact on local politicians."

Of the 25 countries with sufficient data available, only three met their fair share target: the Philippines, the United Kingdom, and South Africa. With an investment of nearly US$2 million in TB research, the Philippines achieved 281% of its fair share target. The UK surpassed its fair share target by US$23 million, reaching 157% of its target. Despite reducing its 2017 investment in TB research by nearly US$4 million, South Africa was again one of the only countries that met its fair share target.

A handful of countries—Taiwan, Ireland, the United States, New Zealand, and Canada—surpassed 70% of their fair share targets. (If general investments in non-TB-specific clinical trials infrastructure are included, the United States has also met its fair share target—see box.) India met two-thirds (66%) of its fair share target (the highest funding of any BRICS country). Denis Godlevskiy, an activist with International Treatment Preparedness Coalition in Eastern Europe and Central Asia (ITPCru), describes the relationship between increasingly nationalist governments in countries including Russia, the United States, France, and the UK and decreased TB research spending: "The political crisis is so obvious and it impacts the healthcare response; [populist leaders] are pushing health care to the bottom of the agenda. Health care is not an issue for them at all. They have this very strong tendency to soften the language and lessen commitments."

TABLE 1

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

RANK	COUNTRY	2018 FUNDING	ANNUAL FAIR SHARE TARGET	PERCENT OF TARGET MET IN 2018
1	United States	$371,583,501	$444,500,000	84%
2	United Kingdom	$63,795,280	$40,400,000	158%
3	India	$30,801,272	$46,500,000	66%
4	Germany	$20,812,724	$99,700,000	21%
5	Canada	$19,415,757	$25,300,000	77%
6	South Korea	$17,081,039	$64,000,000	27%
7	Australia	$9,623,743	$21,200,000	45%
8	The Netherlands	$6,977,870	$15,100,000	46%
9	South Africa	$4,590,284	$4,600,000	100%
10	Switzerland	$4,106,442	$13,400,000	31%
11	Japan	$3,760,177	$154,900,000	2%
12	France	$3,490,334	$55,400,000	6%
13	Taiwan	$3,387,595	$4,369,762	78%
14	Norway	$3,031,937	$5,300,000	57%
15	Ireland	$2,497,629	$3,300,000	76%
16	The Philippines	$1,965,376	$700,000	281%
17	Brazil	$1,336,420	$35,000,000	4%
18	Thailand	$1,306,683	$4,900,000	27%
19	New Zealand	$1,295,291	$1,800,000	72%
20	Denmark	$1,067,896	$7,500,000	14%
21	Italy	$1,064,365	$27,500,000	4%
22	Finland	$770,954	$7,100,000	11%
23	Mexico	$535,224	$10,300,000	5%
24	Hong Kong, SAR	$258,100	$9,900,000	3%
NA	China	Not reported	$305,600,000	---
NA	Indonesia	Not reported	$2,100,000	---
NA	Nigeria	Not reported	$7,000,000	---
NA	Pakistan	Not reported	$2,400,000	---
NA	Singapore	Not reported	$8,400,000	---
NA	Sweden	Not reported	$13,700,000	---
NA	Russian Federation	Not reported	$36,500,000	---
NA	Vietnam	Not reported	$1,300,000	---

Table includes countries that reported more than $250,000 in TB R&D funding to TAG and select other high-income or high-TB-burden countries.

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

With a few exceptions, nations have overwhelmingly failed to mobilize new funds for TB research, despite strong declarations of support issued by government leaders and delegates at last year's HLM. TB research spending in the majority of countries was dramatically under fair share target levels. Six countries were unable to meet even 10% of their fair share target, including Hong Kong (3%), Japan (2%), and Brazil (4%). As Janika Hauser puts it: "If the next Robert Koch or Sir John Crofton is currently living in countries like Brazil or France or Japan, we're going to have a really hard time finding them!"

Closer Look: U.S. Government Investments in TB Research

The U.S. government (USG) is the biggest contributor to TB research globally, investing more than every other government combined. Since 2009, USG agencies have spent US$2.8 billion on TB R&D—40% of the total US$6.9 billion spent from 2009 to 2018.

Despite this clear and substantial commitment, according to TAG's data, the United States has yet to reach its fair share target of spending at least US$444.5 million on TB R&D each year. By TAG's count, the USG spent US$371.6 million on TB research in 2018, satisfying 84% of its target.

A different method of assessing USG contributions to TB research suggests that the United States did meet its fair share target in 2018. In September 2019, USAID released a statement announcing that USAID, the NIH, the Centers for Disease Control and Prevention, and the Department of Defense "have collectively mobilized approximately US$491.5 million for TB R&D in fiscal year 2018, exceeding the US$444.5 million annual gross domestic expenditure on research and development target set at the 2018 United Nations General Assembly by the Treatment Action Group."[18]

The major difference in the two estimates can be traced to how TAG handles expenditure data from the NIH. The NIH posts detailed information on its spending via the Research Portfolio Online Reporting Tools (RePORT) system.[19] TAG carefully reviews RePORT data tagged as "tuberculosis" and assigns each award to one of the six research areas tracked by this report. During this process, we remove a handful of projects that upon close inspection are not related to TB. We also take out any awards that represent core support to clinical trials sites participating in the NIH Division of AIDS HIV Clinical Trials Networks. These networks—which include the AIDS Clinical Trials Group (ACTG) and the International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT)—study HIV and HIV-associated comorbidities, including TB.

Combined, these core awards to clinical trials sites add up to a substantial figure: US$114.8 million in 2018. The USG funding total cited by USAID includes this amount; historically, TAG has not included these figures as not every clinical trial site in each network engages in TB research.[20] So while RePORT classifies these awards as "tuberculosis," TAG removes them from our accounting to produce a more conservative estimate of USG TB R&D spending. (We do include protocol-specific spending by the ACTG and IMPAACT networks on TB clinical trials.)

If included in TAG's calculations, most of these excluded awards would be categorized as "infrastructure/unspecified projects" since they represent investments in clinical trials infrastructure, rather than funding for specific studies. In other words, adding these awards would have little impact on the funding totals reported for TB basic science, diagnostics, drugs, vaccines, and operational research.

In addition to this difference in handling NIH funding data, TAG's estimate of USG TB R&D funding includes spending by agencies not included in the USAID announcement, including the Food and Drug Administration, National Science Foundation, and Department of Veterans Affairs. United States support for TB research is truly a cross-government effort.

Regardless of the methodology used, one thing is clear: the USG's commitment to advancing TB research sets an example that other countries should emulate. TAG commends USAID for its leadership in measuring USG TB R&D spending in relation to the fair share target, and we urge all countries to follow through on commitments made at the HLM to invest their fair share in TB R&D. Ultimately, these targets set the floor—not the ceiling—for what countries must invest in research to end the world's deadliest infectious disease.

"Some of the countries who spend the vast lot of their resources on gathering political influence in TB are not investing any significant amount of money in R&D . . . Countries who have bigger burdens of TB should contribute more, and they're not paying their share."

—**Denis Godlevskiy, International Treatment Preparedness Coalition in Eastern Europe and Central Asia**

Burden-Investment Index

While the fair share targets link a country's share of TB spending to its overall R&D spending, these targets do not account for a country's TB burden. In 2017, TB activist Marcus Low came up with a second measure of countries' TB research investments: the Burden-Investment Index, or BII. To calculate the Burden-Investment Index, a country's share of the global TB burden is subtracted from its share of the total TB R&D investment (both numbers expressed as percentages). If a country's Burden-Investment Index score is positive, its share of total TB research funding is greater than its share of the TB burden; conversely, negative Burden-Investment Index scores indicate a country's investment in research is less than its share of the TB burden. Although Burden-Investment Index scores do not account for a country's overall wealth, they do provide a way to evaluate if countries with high TB burdens are contributing enough to TB research.

We had sufficient data to generate Burden-Investment Index scores for 25 countries. For the second year, the United States has the best score (0.600). Nineteen countries had a score of 0.000 or greater, meaning they are investing in TB R&D at least in proportion to their share of the TB burden. Three of the six countries with negative Burden-Investment Index scores (Mexico, Brazil, and Thailand) had scores greater than −0.010 but less than zero; in other words, while these countries' investments don't meet their share of TB incidence, they aren't falling too far behind.

India's Burden-Investment Index score remains at the bottom of the list (−0.223), practically unchanged from its 2017 score of −0.24. India bears over 27% of the global TB burden but accounts for less than 5% of research spending. It is critical for the countries with the highest TB burdens to invest in research, in part to ensure that R&D aligns with those countries' priorities.

We are three years into the Stop TB Partnership's five-year *Global Plan*, and the landscape of who funds TB research funding has not changed significantly during this period. Janika Hauser calls out countries that aren't meeting their burden, encouraging activists to hold governments accountable: "We can't let countries get away with arguing that the comparative weakness of the TB pipeline means that TB isn't worth investing in when that very weakness is the result of their failure to invest for so long." As noted in the conclusion of TAG's 2017 report, this year's figures provide a baseline against which we can measure whether countries will deliver on the commitments generated at the HLM. The evidence is stark: with a few notable exceptions, countries have not delivered the resources that will be required to end TB.

TABLE 2

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

Burden-Investment Index (BII) is a meaasure of a country's investment in TB research relative to its TB burden.

BII is calculated by subtracting a contry'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).

RANK	COUNTRY	SHARE OF GLOBAL TB BURDEN (%)	SHARE OF GLOBAL PUBLIC INVESTMENTS IN TB R&D (%)	BII SCORE 2018
1	United States	0.10%	60.13%	0.600
2	United Kingdom	0.05%	10.32%	0.103
3	India	26.90%	4.98%	-0.219
4	Germany	0.06%	3.37%	0.033
5	Canada	0.02%	3.14%	0.031
6	South Korea	0.34%	2.76%	0.024
7	Australia	0.02%	1.56%	0.015
8	The Netherlands	0.01%	1.13%	0.011
9	South Africa	3.01%	0.74%	-0.023
10	Switzerland	0.01%	0.66%	0.007
11	Japan	0.18%	0.61%	0.004
12	France	0.06%	0.56%	0.005
13	Taiwan	0.10%	0.55%	0.004
14	Norway	0.00%	0.49%	0.005
15	Ireland	0.00%	0.40%	0.004
16	The Philippines	5.91%	0.32%	-0.056
17	Brazil	0.95%	0.22%	-0.007
18	Thailand	1.06%	0.21%	-0.008
19	New Zealand	0.00%	0.21%	0.002
20	Denmark	0.00%	0.17%	0.002
21	Italy	0.04%	0.17%	0.001
22	Finland	0.00%	0.12%	0.001
23	Mexico	0.29%	0.09%	-0.002
24	Hong Kong, SAR	0.05%	0.04%	0.000
25	China	8.66%	NA	NA
26	Indonesia	8.45%	NA	NA
27	Nigeria	4.29%	NA	NA
28	Singapore	0.03%	NA	NA
29	Sweden	0.01%	NA	NA
30	Russian Federation	0.79%	NA	NA
31	Vietnam	1.74%	NA	NA

Table includes countries that repoted more than $200,000 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, 2005–2018 (in Millions)

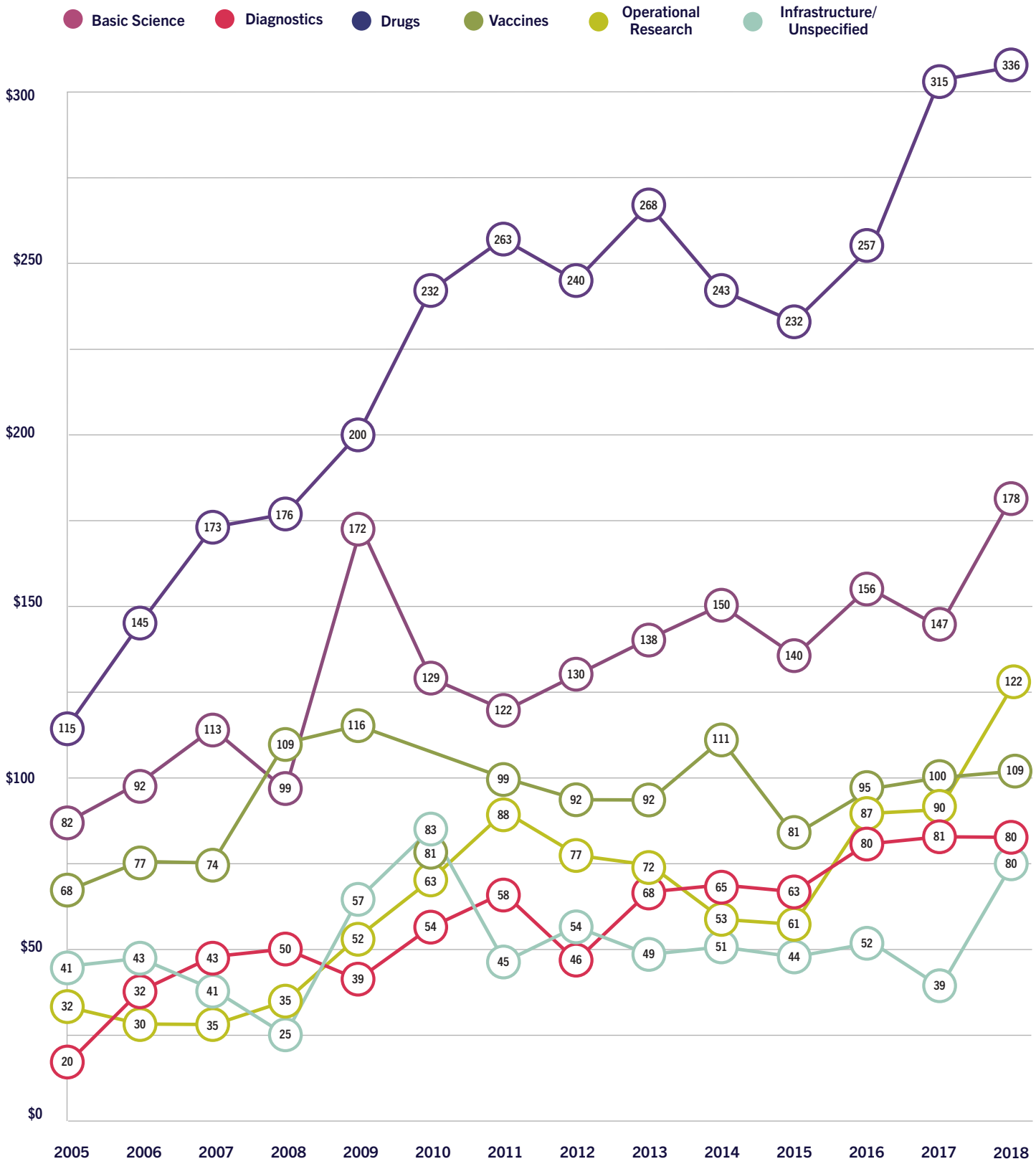
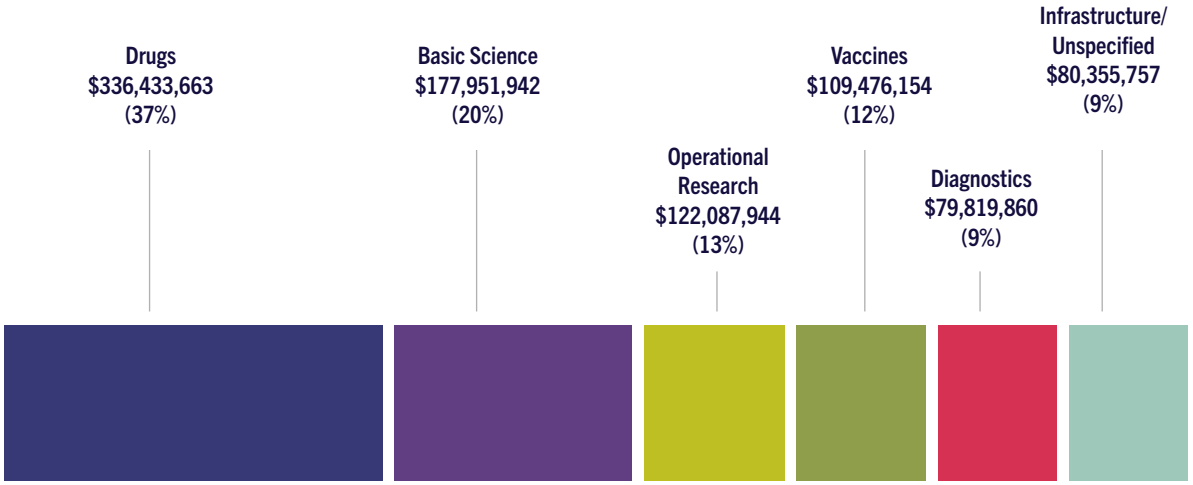


FIGURE 7

Total TB R&D Funding by Research Area, 2018
Total: $906,125,319



In 2018, TB drug research expenditures surpassed US$336 million and accounted for just over one-third (37%) of total TB R&D spending. Basic science, at US$177 million, accounted for 20% of the research portfolio, followed by operational research (US$122 million; 13%), vaccine research (US$109 million; 12%), and diagnostics and infrastructure/unspecified (US$79 million and US$80 million respectively; 9% each).

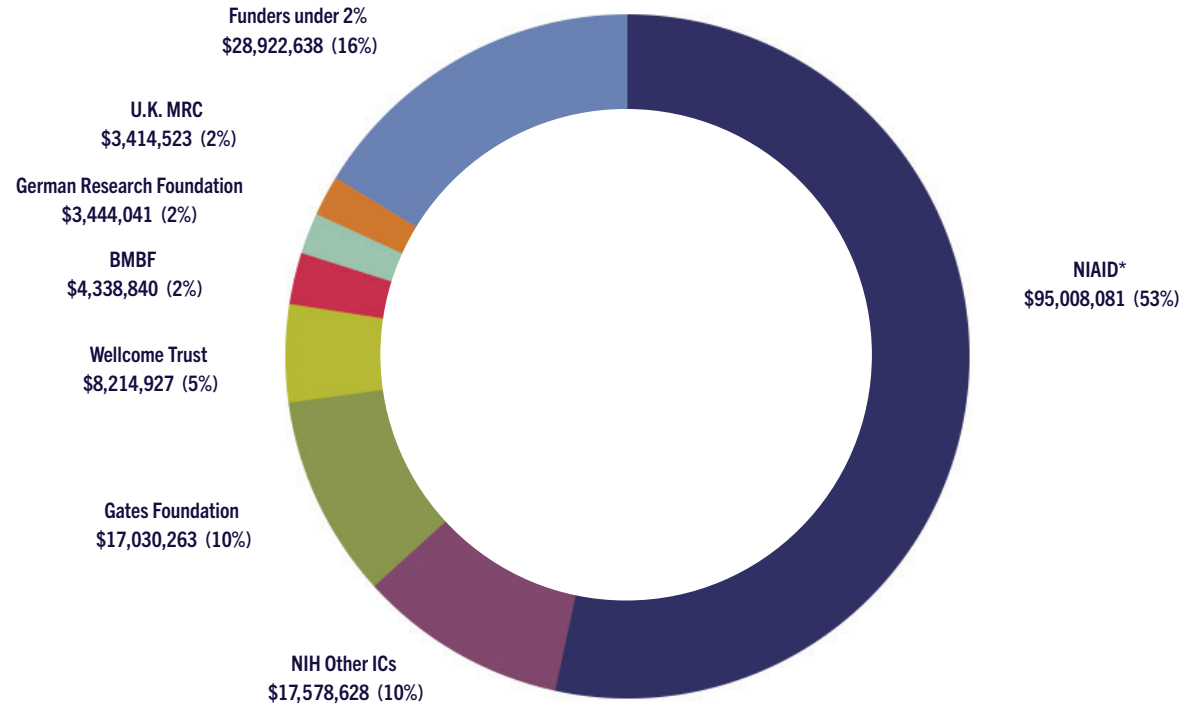
The 2018 distribution is similar to that in 2017, other than a sizable increase in the percentage of R&D spending categorized as infrastructure/unspecified research. At 208% of the 2017 figure, infrastructure/unspecified funding more than doubled. This may reflect changes in how funders report expenditures to TAG rather than increased spending in this area. The infrastructure/unspecified category includes everything from training programs for early-career scientists, clinical trials infrastructure, and miscellaneous projects funders are unable to categorize. It is difficult to tell whether the marked increase in infrastructure/unspecified funding in 2018 reflects greater investments in training and infrastructure, signals an uptick in interdisciplinary projects that do not fit neatly into other categories, or is simply an artefact of reporting.

Funding for operational and basic science research also increased when compared with the previous year (136% and 120% of 2017 amounts, respectively). Spending on drugs (106%), vaccines (109%), and diagnostics (98%) remained relatively flat when compared with 2017.

Basic Science

FIGURE 8

Basic Science: $177,951,942



Funders with investments under 2%

U.K. Biotechnology and Biological Sciences Research Council	$3,019,239
Swiss National Science Foundation (SNSF)	$2,698,512
Australian National Health and Medical Research Council (NHMRC)	$2,688,524
European Commission	$1,727,916
French National Research Agency (ANR)	$1,643,417
Canadian Institutes of Health Research (CIHR)	$1,406,826
Indian Council of Medical Research (ICMR)	$1,252,966
South African Department of Science and Technology	$1,090,950
Indian Ministry of Science and Technology	$959,322
Italian Ministry of Health	$787,740
Marsden Fund	$704,307
U.S. National Science Foundation (NSF)	$692,593
Swiss Federal Institute of Technology in Lausanne (EPFL)	$665,762
Taiwan Centers for Disease Control	$578,648
Academy of Finland	$566,439
Korean Ministry of Health and Welfare	$517,066
Natural Sciences and Engineering Research Council of Canada	$490,140
U.S. Department of Veterans Affairs	$481,255
Institut Pasteur	$453,396
South African Medical Research Council (SAMRC)	$445,324
Japan Agency for Medical Research and Development (AMED)	$415,380
Norwegian Agency for Development Cooperation (NORAD)	$397,177
Korean Ministry of Education	$396,654
U.K. Department for Business, Energy, and Industrial Strategy (BEIS)	$376,982
Norwegian Ministry of Education and Research	$369,656
Japan International Cooperation Agency (JICA)	$343,122
Science Foundation Ireland	$311,904
Korean Ministry of Science and ICT	$293,533
National Research Coucil of Thailand	$249,973

Thailand National Science and Technology Development Agency (NSTDA)	$241,110
Philippine Council for Health and Research Development	$235,603
Netherlands Organization for Health Research and Development (ZonMw)	$225,435
Mexico National Council for Science and Technology	$200,629
Health Research Council of New Zealand	$191,712
Philippine Commission on Higher Education	$187,400
Japanese Ministry of Health, Labour and Welfare	$183,309
Indian Council of Scientific and Industrial Research	$167,692
Hong Kong Health and Medical Research Fund	$165,569
Doris Duke Charitable Foundation	$123,750
Tata Trusts	$98,731
Public Health England	$92,483
Australian Research Council	$88,475
Thrasher Research Fund	$86,428
Human Frontier Science Program	$85,756
European Molecular Biology Organization	$82,847
National Research Foundation of Korea	$67,500
Korean Institute of Tuberculosis	$59,850
Norwegian Ministry of Health and Care Services	$53,970
Healthcare Infection Society	$46,242
U.K. National Centre for the 3Rs (UKRI)	$39,636
Japan BCG Laboratory	$38,461
Taiwan Ministry of Health and Welfare	$30,000
Japan Society for the Promotion of Science	$25,474
Indian Science and Engineering Research Board	$22,385
Public Health Agency of Canada	$18,853
Taipei City Government	$15,575
Nigerian Institute of Medical Research	$13,850
Independent Research Fund Denmark	$9,194

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

> "The work done to strengthen TB community advisory boards . . . is fantastic to see and ultimately also improves the quality of the research that's being conducted, because they [CABs] have that needs-driven point in mind from the start. I think engagement between academic and professional communities and civil society and affected communities should be strengthened even further."
>
> —**Janika Hauser, parliamentary advocacy officer, RESULTS UK**

In 2018, the U.S. government provided more than US$112 million of the US$177 million in funding for basic science research (63% of total basic science R&D funding). Other significant contributors to this area include the Gates Foundation, the Wellcome Trust, Germany, and the United Kingdom. Basic science funding reached a new high in 2018, surpassing the previous high of US$172 million set in 2009 and demonstrating substantial upward growth for the first time in eight years. Notably, all of the top funders of TB basic science in 2018 are institutions located in either the United States or Europe.

The resolutions that emerged from the HLM called specifically for innovation and collaboration in basic science.[21] For example, paragraph 42 of the HLM political declaration expresses the commitment of states "to advancing research for basic science, public health research, and the development of innovative products and approaches." While it is too soon to tell if the political momentum generated at the HLM will lead to more funding for basic science, the increase observed in 2018 almost certainly reflects the commitment of NIAID at the U.S. NIH to "expand fundamental knowledge of TB" through its new TB research strategic plan.[22]

NIAID's 2018 TB strategic plan identified five research priorities: improving fundamental knowledge of TB, improving diagnostic tools, improving TB prevention efforts, making progress in treatments for all age groups, and developing new tools and resources in each of these areas. Recognizing that basic science will have a role in each of these objectives, NIAID has increased its funding for basic research across its TB portfolio, with basic science and therapeutics accounting for 70% of NIAID's 2018 TB R&D spending.[23] As the top single funder of TB basic science research, NIAID's investments in this area will continue to shape the R&D field for years to come.

Although funding increased in this area over 2017, total investments in basic science amount to barely half (52%) of the total investment in TB drugs. To contextualize TB-related basic science spending, a 2013 analysis by TAG and AVAC reported HIV-related basic science funding of over US$838 million in 2011.[24] The comparatively small amount of basic science spending in TB research makes a coordinated research agenda even more urgent. To that end, NIAID identifies more than 25 existing clinical and basic research resources it intends to leverage toward its TB research agenda. Of note, none of the listed resources are advocacy groups, although some (like the HIV/AIDS Clinical Trials Networks) have strong community advisory components.

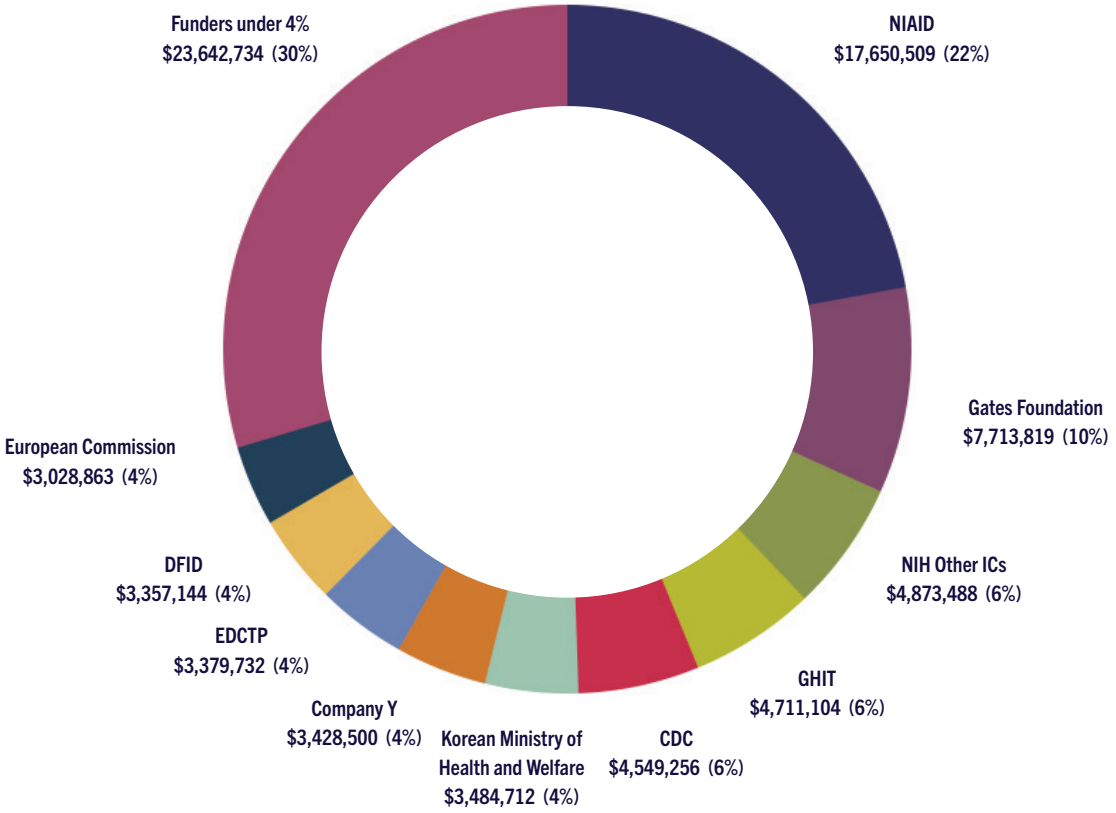
Basic science can be notoriously inaccessible to nonscientist activists. Ensuring that basic science aligns with community priorities will require the establishment of—and funding for—continued community engagement, education, and oversight. As Els Torreele of the MSF Access Campaign notes, "investigator-driven research that is not all aligned [with community needs] becomes problematic. If there's plenty of money and resources, a little bit of duplication or competition may not be harmful. But when the field is so small, it becomes wasteful."

One potential solution lies in the potential of community advisory boards (CABs) increasing their engagement in early stage research. Janika Hauser of RESULTS UK applauds the growth of various TB CABs, commenting that "the work done to strengthen TB community advisory boards both at the global and that individual level is fantastic to see and ultimately also improves the quality of the research that's being conducted, because they have that needs-driven point in mind from the start. I think engagement between academic and professional communities and civil society and affected communities should be strengthened even further."

Diagnostics

FIGURE 9

Diagnostics: $79,819,860



Funders with investments under 4%

Dutch Ministry of Foreign Affairs (formerly DGIS)	$2,592,280
U.S. Department of Defense Medical Research and Development Program	$2,163,098
U.K. Medical Research Council (U.K. MRC)	$1,844,511
Unitaid	$1,743,261
Genedrive	$1,597,319
German Federal Ministry of Education and Research (BMBF)	$1,549,721
Australian Department of Foreign Affairs and Trade (DFAT)	$1,388,063
Korean Ministry of SMEs and Startups	$998,417
Innovate UK (UKRI)	$931,118
U.K. National Institute for Health Research (NIHR)	$753,400
Science Foundation Ireland	$561,979
U.K. Engineering and Physical Sciences Research Council	$452,288
Bioneer	$434,465
Public Health Agency of Canada	$424,295
South African Medical Research Council (SAMRC)	$397,423
Korean Ministry of Science and ICT	$345,323
Australian National Health and Medical Research Council (NHMRC)	$322,656
U.K. Department for Business, Energy, and Industrial Strategy (BEIS)	$316,371
Norwegian Agency for Development Cooperation (NORAD)	$282,412
Roche	$270,144
Korea Foundation For International Healthcare	$270,000
Japan Agency for Medical Research and Development (AMED)	$254,646
Brazilian Ministry of Science, Technology, Innovation and Communication	$248,281
National Institute of Health Carlos III	$233,732
U.S. National Science Foundation (NSF)	$232,876
Company X	$230,000
Canadian Institutes of Health Research (CIHR)	$227,244
Finnish Institute for Health and Welfare	$204,516
Hain Lifescience	$194,331
Taiwan Centers for Disease Control	$181,985
The ELMA Foundation	$175,000
Independent Research Fund Denmark	$165,898
Indian Council of Medical Research (ICMR)	$127,175
Wellcome Trust	$124,406
Abbott	$124,376
Natural Sciences and Engineering Research Council of Canada	$123,175
Thrasher Research Fund	$118,978
Swiss National Science Foundation (SNSF)	$112,229
National Research Coucil of Thailand	$99,341
Qiagen	$90,000
Korean Ministry of Trade, Industry and Energy	$85,500
Health Research Council of New Zealand	$84,579
Thailand National Science and Technology Development Agency (NSTDA)	$77,847
World Health Organization	$65,000
European Centre for Disease Prevention and Control	$59,454
National Institute of Health—University of the Philippines Manila	$50,882
Philippine Council for Health and Research Development	$49,189
Korean Ministry of Education	$41,000
Grand Challenges Canada	$38,735
Institut Pasteur	$37,683
Médecins Sans Frontières	$27,157
Korea Atomic Energy Research Institute	$27,000
Damien Foundation Belgium	$23,373
AFI Corporation	$18,060
Tata Trusts	$17,566
Bouisson Bertrand Institute	$13,441
Indian Ministry of Health and Family Welfare (MOHFW)	$10,144
FUJIFILM Wako Pure Chemical Corporation	$4,876
Medical & Biological Laboratories Co.	$4,515

With R&D investments totaling over US$79 million, diagnostics is the only area of TB research that saw reduced funding in 2018 (a loss of US$1 million). Seven of the 10 biggest funders were from the public sectors of the US, EU, UK, and South Korea. NIAID spent over US$17 million on diagnostic research, while other NIH institutes and centers contributed an additional US$4.8 million. The Gates Foundation was the only philanthropic funder to contribute significantly to diagnostic research, providing nearly US$8 million.

Critically, improving diagnosis remains one of activists' key priorities in TB R&D. Activists want both new diagnostic technologies and increased access to already existing diagnostic tests. This discrepancy between activists' priorities and funders' financial commitments is emblematic of a larger disconnect between funding institutions and the communities who are intended to benefit from the results of TB R&D. Marie Theunissen, Community Research Advisors Group (CRAG) member and Desmond Tutu TB Centre CAB coordinator, put it bluntly: "I'm of the opinion that we do not engage with communities enough. Most of the decisions [about TB research] are made by people in the top positions, and they don't see what's going on in the community because they don't live in the community."

Without increasing funding for TB diagnostic research, we will be unable to develop new diagnostic tools or resolve the low uptake of existing diagnostic technologies. Evaline Kibuchi, chief national coordinator of the Stop TB Partnership—Kenya, described her disappointment with advances in diagnostics, saying, "The progress has been very slow. The only thing that we can take pride in the past 10 years is GeneXpert." Other activists pointed to the current and next-generation urine-based TB LAM tests as promising advances. Denis Godlevskiy described the existing TB LAM test as "good" but "far from ideal," especially in comparison to analogous tools designed for similar ease and point-of-care application such as HIV rapid tests or pregnancy tests. A next-generation LAM test made by FujiFilm has a higher sensitivity than the current test manufactured by Abbott and may, if endorsed by the WHO, make urine-based LAM testing a more widely accepted part of TB programs—but its approach to market has also been slower than expected.

In addition to TB LAM tests, Fifa Rahman shared her excitement about TrueNat, a molecular test developed in India that is similar to GeneXpert. In her view, "we can't rely on just one diagnostic." What the field really needs, in Rahman's opinion, are "multiplex platforms that can produce results quickly and at the point of care." Platforms such as GeneXpert that can run tests for multiple conditions (e.g., TB, hepatitis C virus, HIV viral load) hold tremendous potential, "but if we don't utilize these platforms for other diseases, we won't get the gain we want because of the comorbidities included with TB," commented Rahman.

In accordance with the views of Rahman, Godlevskiy, and Kibuchi, a comprehensive review of TB diagnostics in development published in October 2019 similarly named rapid molecular tests such as GeneXpert and TrueNat and urine-based LAM tests for diagnosing TB in people living with HIV as "the most significant areas of progress in the TB diagnostics pipeline" over the last decade. Looking forward, the review highlighted the promise of advances in rapid drug susceptibility testing for first- and second-line drugs, particularly "next-generation developments in targeted and whole genome sequencing for individualizing treatment regimens."[25]

Inadequate funding and a frustratingly slow pace of development are two limitations in TB diagnostic research; poor implementation of existing diagnostic technologies is a third. As Denis Godlevskiy puts it, "In a world where you still have pieces of old-fashioned health systems in place, you won't be able to apply new technologies with an old system of public health management." The WHO notes that many countries continue to use sputum microscopy to detect TB, although GeneXpert is quicker, is more accurate, and is able to detect resistance to first-line TB drug rifampicin.[26] The TBXpert Project—a partnership of the WHO Global TB Programme, the Stop TB Partnership, and Unitaid that provided 1.4 million GeneXpert instruments to 21 countries—is one example of a multilateral program intended to fill gaps in implementation.[27] However successful programs like the TBXpert Project may be at catalyzing initial uptake of a new tool, philanthropic and multilateral programs cannot replace public sector responsibility for public health. Part of this responsibility must include ensuring that public health systems have access to affordable and fair pricing. In the case of GeneXpert, the longstanding US$10 per cartridge price point should have fallen substantially, in sync with the increasing sales volumes and manufacturing efficiencies enjoyed by GeneXpert's manufacturer, Cepheid. Recognizing this, activists at the 50th Union World Conference on Lung Health called on Cepheid, to cut the price of the test to an all-inclusive US$5.[28]

"We are leaving behind the majority of patients. The majority of patients don't have MDR. The majority of patients are people with latent TB infection, and we've left them behind because we don't have good assessment tools; we don't have diagnostic tools that let you know for sure when [your infection] may be reactivated. So, we are fighting with our eyes blinded. And research is not moving as fast as it should be in that area. This is one of my major concerns."

—**Rosa Herrera, Global TB CAB member and TB physician**

"Communities can really be advocates for the uptake and rollout of new tools, if they are included from the beginning. And that doesn't always happen, especially if it's not in the trial design."

—**Wim Vandevelde, Global TB CAB member, GNP+**

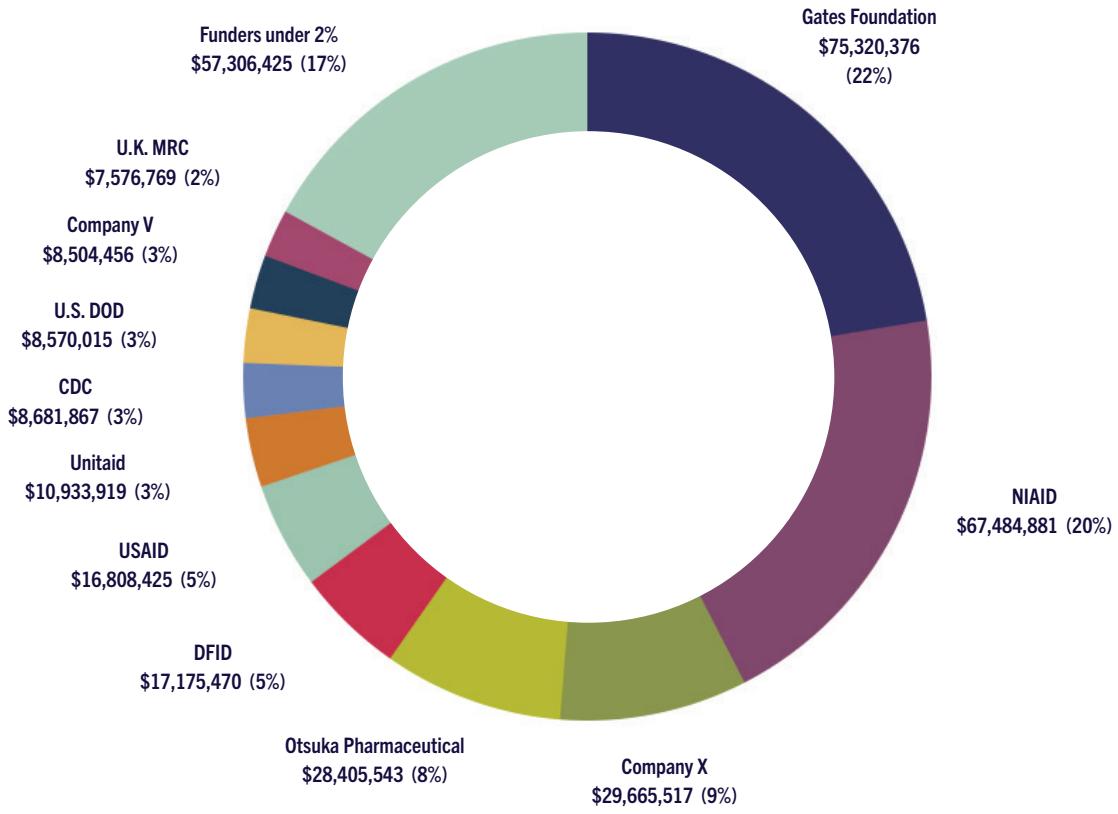
Both sputum microscopy and GeneXpert diagnose TB using sputum, making diagnosis particularly challenging for children and some adults, including people living with HIV and anyone with extrapulmonary TB.[29] Researchers and community stakeholders are eager for additional diagnostic tools based on samples other than sputum. The current diagnostic research portfolio includes tools like the urine-based TB-LAM and novel stool-based assays.[30,31] Better tests for TB infection—including ones able to predict which people with TB infection are most likely to progress to active disease—are another priority innovation for activists. These community priorities largely align with the WHO's list of high-priority TB diagnostic tools (called "target product profiles"). The WHO list includes 1) a triage test to rule out TB and to use for systematic screening; 2) a sputum-free rapid TB diagnostic test based on biomarkers; 3) next-generation drug-susceptibility testing that can be used at the microscopy center level of the health system; 4) treatment monitoring tests (i.e., to assess cure); and 5) predictive tests for TB infection.[32]

For Kibuchi, the lagging pace of diagnostic research is particularly egregious in pediatrics: "One of the priorities is diagnosis for children. That should be out by tomorrow. We keep saying, 'we love our children,' or 'we give them priority.' But it's unacceptable that adults have seen [improved] diagnosis but nobody has come up with something for children." Kibuchi remembers, "A while ago in Kenya, there was a diagnosis using stool. And the last time I checked, it has progressed very well. I've been waiting to hear about the progress of this at the global level but haven't heard." Unfortunately, while new diagnostic tools are often well described in academic literature, findings are not always relayed to the communities who made the research possible.

Drugs

FIGURE 10

Drugs: $336,433,663



Funders with investments under 2%

Médecins Sans Frontières	$5,442,820
German Federal Ministry of Education and Research (BMBF)	$5,282,491
U.S. National Institutes of Health, Other Institutes and Centers (NIH Other ICs)	$4,374,206
European and Developing Countries Clinical Trials Partnership (EDCTP)	$4,105,211
Dutch Ministry of Foreign Affairs (formerly DGIS)	$3,576,100
U.K. National Institute for Health Research (NIHR)	$2,977,456
Australian Department of Foreign Affairs and Trade (DFAT)	$2,776,125
European Commission	$2,264,555
Qurient	$2,250,000
Korea Drug Development Fund	$2,023,689
Macleods Pharmaceuticals	$2,000,000
Wellcome Trust	$1,982,541
Merck	$1,561,976
French National Research Agency (ANR)	$1,422,981
Global Health Innovative Technology Fund (GHIT)	$1,176,103
Irish Aid	$1,168,660
Korean Ministry of Science and ICT	$1,043,245
German Research Foundation (DFG)	$1,017,319
Korean Ministry of Health and Welfare	$1,014,407
Sequella	$1,000,000
U.S. Food and Drug Administration (FDA)	$946,590
Indian Council of Medical Research (ICMR)	$931,049
U.S. Department of Veterans Affairs	$813,871
Canadian Institutes of Health Research (CIHR)	$716,500
Public Health England	$614,353
U.K. Department for Business, Energy, and Industrial Strategy (BEIS)	$510,965
Australian National Health and Medical Research Council (NHMRC)	$471,475
U.K. Biotechnology and Biological Sciences Research Council	$385,287
Swiss Federal Institute of Technology in Lausanne (EPFL)	$332,881
Swiss National Science Foundation (SNSF)	$297,058
Health Research Council of New Zealand	$286,501
Japan Agency for Medical Research and Development (AMED)	$270,900
Netherlands Organization for Health Research and Development (ZonMw)	$259,291
Norwegian Ministry of Education and Research	$224,567
Norwegian Agency for Development Cooperation (NORAD)	$183,570
South African Medical Research Council (SAMRC)	$174,188
Damien Foundation Belgium	$162,855
Taiwan Centers for Disease Control	$157,392
Company L	$150,000
Legochem Biosciences	$140,213
Institut Pasteur	$116,636
French National Agency for AIDS Research (ANRS)	$100,675
Korean Rural Development Administration	$98,400
Hong Kong Health and Medical Research Fund	$92,531
Brazilian Ministry of Health	$92,275
Indian Council of Scientific and Industrial Research	$72,888
Stop TB Partnership (UNOPS)	$69,440
Individual donors to TB Alliance	$50,311
Indian Ministry of Science and Technology	$46,936
U.K. National Centre for the 3Rs (UKRI)	$39,636
Natural Sciences and Engineering Research Council of Canada	$24,757
Indian Ministry of Health and Family Welfare (MOHFW)	$9,648
Faber Daeufer	$2,000
Astellas Pharma Inc.	$903

> "Looking at the pipeline, which looks promising compared to what we observed 10 years ago, it looks like progress. But I prefer to compare the TB drug pipeline with the HIV field. And if you do that kind of comparison, we look pretty poor, actually."
>
> —**Denis Godlevskiy, ITPCru**

Totaling US$336 million, drug research receives the largest share of TB research funds. The U.S. and U.K. governments invested over one-third of these funds (US$126 million). The private sector, led by Company X and Otsuka Pharmaceutical, spent US$66 million on drug research. Fifty-three different funders who had expenditures under 2% of the total investment provided a combined 17% of all drug funding—just shy of the 20% investment (US$75 million) provided by the Gates Foundation.

Although drug research receives more funding than any other area of TB R&D, expenditures on drug development fall far short of need. Three years into the Stop TB Partnership's 2016–2020 *Global Plan*, funders have only met 21% of the US$4.15 billion funding goal for TB drug R&D. Still, it is important to acknowledge that the field has made tremendous progress over the past several years. As recently as 2016, phase I of the TB drug pipeline sat completely empty—a troubling sign given that most compounds that enter phase I testing will not advance to further development stages, much less obtain regulatory approval. Today, there are at least seven compounds undergoing phase I trials. A 2019 review of the TB treatment pipeline opened by calling attention to the number of "new compounds with novel mechanisms of action or advantaged properties" that have advanced to phase I and II clinical studies, "replenishing a clinical pipeline that has seemed bare for the greater part of the last decade."[33]

Is this replenished pipeline of sufficient size and diversity to hasten TB elimination? Probably not. Fifa Rahman of Unitaid's NGO Delegation questions whether the pipeline can even address the current epidemic, pointing out that "the number of antibiotics currently in the pipeline is not enough to deal with the burden that we have today." In other words, we are inadequately prepared to deal with the current TB epidemic, much less an epidemic with increasing proportions of MDR- and XDR-TB. If the incidences of MDR- and XDR-TB continue to rise, more people will need to be treated with limited options—a number of which, until recently, required long courses of injectable treatment. Hence, much of the research in the drug arena is focused on developing short-course and all-oral regimens for people with MDR- and XDR-TB. Following a sea change in WHO guidance in 2018, fully oral regimens are now the first choice for MDR-TB treatment—improving treatment outcomes as well as patients' quality of life by dropping the injectable drug agents that saddled patients with significant toxicities (e.g., permanent hearing loss) while contributing little to cure.[34]

Other activists, seeking metrics with which to evaluate recent progress, compared the pace of TB drug development to R&D in other diseases. Evaline Kibuchi of Stop TB Partnership—Kenya suggests, "Let's benchmark ourselves with HIV. HIV just came in the 80s, and we are almost doing away with it. TB has been here for how long? The only barrier is that we don't have an adequate political interest and commitment to R&D." Denis Godlevskiy also couched TB drug development in relation to progress seen in HIV therapeutics: "Looking at the pipeline, which looks promising compared to what we observed 10 years ago, it looks like progress. But I prefer to compare the TB drug pipeline with the HIV field. And if you do that kind of comparison, we look pretty poor, actually." In this vein, Global TB CAB member Wim Vandevelde describes the TB pipeline as "a rather modest pipeline. It's better than it was before. But compared to other diseases like cancer or HIV, where there are very busy pipelines, that is not the case in TB, and it has to do with underfunding—the historical underfunding and the political pressure on governments to step in where the pharmaceutical industry is not interested."

Indeed, a review of global investments in TB research commissioned by the WHO found that between 1970 and 2016, the TB field saw fewer new chemical entities approved than for HIV or malaria, and that among new treatments introduced, "most represented new formulations, indications, or combinations of products developed decades earlier."[35] In particular, the HIV treatment pipeline saw 47 new quality-assured treatment options brought to market during this period, compared to just 16 for TB.

That number can now be revised to 17. In August 2019, the FDA approved pretomanid, a drug developed by the TB Alliance, when used in combination with bedaquiline and linezolid for treatment of XDR-TB and treatment-intolerant forms of MDR-TB.[36] Pretomanid's approval stands as a landmark event for a field where only three other new TB drugs have been approved in the last 40 years (bedaquiline, delamanid, and rifapentine).

However, not all activists have celebrated pretomanid's approval unconditionally, illustrating how each R&D advance reveals more work to be done. Denis Godlevskiy describes how he was "hoping for so much more" from pretomanid's approval, citing concerns about the design of the trial that led to the approval, lack of full presentation of data on pretomanid from other trials, and concerns about the accessibility and affordability of the regimen.

On the topic of access, Kajal Bhardwaj, an activist and lawyer working in India, commented on the cozy relationship between TB Alliance and some of its private and public sector partners:[37] "The deal between TB Alliance and Mylan . . . for the production and supply of pretomanid-based combinations is evidently designed to limit access and not expand it. While the terms of the deal are not public, it is clear that not all countries will be able to access the generic medicines produced under this deal. This is extremely disheartening as this approach has been adopted by a 'not-for-profit' organization that is apparently not immune from objectives of some of its 'for-profit' partners." Case in point: the TB Alliance has filed for patent protection on the combination of bedaquiline, pretomanid, and linezolid in the BRICS countries, a move expected of for-profit pharma but unusual for a not-for-profit developer.

At the 50th Union World Conference on Lung Health, activists led multiple demonstrations on price and access targeting Johnson and Johnson, Otsuka, the TB Alliance, and diagnostic developer Cepheid. Although targeting different developers, these protests sprung from some common elements: a concern for equitable access, an expectation for transparency in pricing and commercial licensing arrangements, a demand for swifter registration of products with national regulatory authorities, an acknowledgement that public money played a pivotal role in developing many of these new products, and the pressing urgency of closing the deadly treatment-access gap in which only one-fourth of people with MDR-TB receive treatment.

Although these tensions point to some real areas of disagreement, they also indicate that, for the first time in decades, the TB drug pipeline has produced tangible advances that communities want to fight for. In some ways, this principled agitation is a testament to the more frequent returns on investment that TB drug development is starting to produce. Janika Hauser with RESULTS UK expressed her excitement about new treatment options. For Hauser, "It's really good to see that as investments increase, we are seeing new products come to market. So we can see that kind of gradual increase in investment is already having an impact." After her review of the preliminary funding data, Els Torreele of MSF Access Campaign commented that "there is much more momentum [in TB research] than what the figures show."

Despite differing perspectives expressed across the interviews, critiques raised by Bhardwaj, Godlevskiy, Vandevelde, Rahman, and others illustrate the key activist concerns related to the drug development pipeline: who funds the studies, who benefits from the studies, and ultimately, to whom is the research accountable? Many of the activists interviewed for this report issued calls for increased accountability in drug research—that is, for the research portfolio to better match community priorities, and for the treatment advances generated by that research to be shared more equitably.

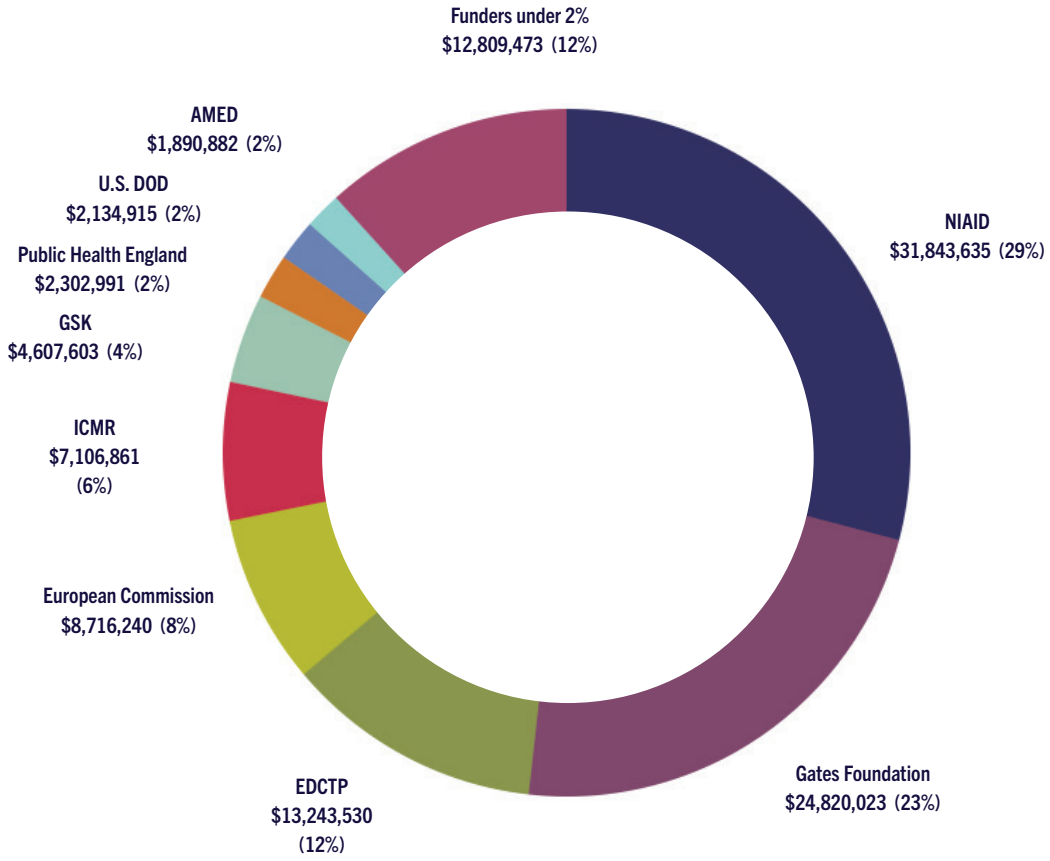
"It's really good to see that as investments increase, we are seeing new products come to market. So we can see that kind of gradual increase in investment is already having an impact."

—Janika Hauser, parliamentary advocacy officer at RESULTS UK

Vaccines

FIGURE 11

Vaccines: $109,476,154



Funders with investments under 2%

Korean Ministry of Health and Welfare	$1,690,840
German Federal Ministry of Education and Research (BMBF)	$1,615,061
U.S. National Institutes of Health, Other Institutes and Centers (NIH Other ICs)	$1,251,886
U.K. Department for International Development (DFID)	$1,056,952
Norwegian Agency for Development Cooperation (NORAD)	$1,031,281
Canadian Institutes of Health Research (CIHR)	$1,010,639
U.K. Biotechnology and Biological Sciences Research Council	$976,185
Independent Research Fund Denmark	$579,557
Butantan Institute	$500,000
Science Foundation Ireland	$455,086
Company X	$424,000
Korean Ministry of Science and ICT	$351,769
Japan BCG Laboratory	$285,649

U.S. Department of Veterans Affairs	$281,537
Brazilian Ministry of Health	$246,952
Norwegian Ministry of Education and Research	$232,277
U.K. National Centre for the 3Rs	$187,088
U.K. Department for Environment, Food and Rural Affairs	$171,755
Netherlands Ministry of Health, Welfare and Sport	$94,661
Natural Sciences and Engineering Research Council of Canada	$87,281
Korean Ministry of Education	$65,378
Taiwan Ministy of Science and Technology	$60,000
Archival Pharma	$58,433
U.K. Medical Research Council (U.K. MRC)	$57,208
South African Medical Research Council (SAMRC)	$25,456
Japanese Ministry of Health, Labour and Welfare	$12,542

> "I get more excited about vaccines than anything else because then a person doesn't have to go through agony at all . . . A vaccine is still that number one silver bullet. When I think about a vaccine I get excited, because it means TB could really be gone in my lifetime."
>
> **—Kate O'Brien, We Are TB**

Two funders—the U.S. government and the Gates Foundation—provided US$60 million of the US$109 million in total TB vaccine funding. Most vaccine R&D funding comes from the public sector; GlaxoSmithKline (GSK) and the Gates Foundation were the only two non-public-sector funders to invest more than US$2 million in vaccine research.

Although 2018 is the third year in which spending has increased, vaccine funding has not seen substantial increases since 2005. After increasing in 2008 and 2009, vaccine funding fell from 2010 through 2013. In 2014, spending returned to the 2008 level, followed again by a sharp decline the next year. Vaccine spending has been trending upward since 2015, but this year's funding remains below the peaks observed in 2009 and 2014.

This fitful up-down pattern may reflect the opening and closing of large clinical trials programs. For example, following negative results from a phase IIb trial of the TB vaccine candidate MVA85A in 2013, the field entered a period that some funders described as "going back to basics."[38] During this time, activity centered on smaller basic and translational science endeavors rather than large clinical studies. That period is ending: in October 2019, the *New England Journal of Medicine* published results of a phase IIb trial sponsored by GSK and funded by GSK and Aeras showing that the vaccine candidate M72/AS01E provided 50% protection against developing active TB disease to adults with TB infection.[39] This marks a major occasion for the field. It is the first demonstration that a vaccine can protect adults already infected with TB from developing TB disease; it provides proof of concept that a subunit vaccine such as M72/AS01E can protect against disease; and it affords the opportunity to investigate possible biomarkers that correlate with this protection.[40]

This positive finding has raised the need to advance M72/AS01E into late-stage development with "a sense of collaboration and urgency," to quote the WHO, which has hosted several meetings to raise support for further research on this promising candidate. A phase III trial of M72/AS01E would be an enormous undertaking and would require the kind of huge step-up in resources possible only when funders work together.[41]

Funding needs for TB vaccine research extend well beyond M72/AS01E. Currently, there are 15 candidate vaccines under active clinical development.[42] In October 2019, the GMRI opened enrollment into a second trial looking at whether revaccination with BCG—the only licensed TB vaccine, one given to infants at birth—can prevent TB infection among South African adolescents.[43] The study aims to confirm the positive efficacy signal found in a recently completed phase II study of BCG revaccination.[44] Phase IIb trials of other TB vaccine candidates, such as the whole-cell non-tuberculosis mycobacterial vaccine DAR-901, will return results in 2020.[45] In other words, M72/AS01E may soon have company as one of several TB vaccines looking for phase III funding.

As predicted, India's investment in vaccine development increased significantly for 2018, to over US$7 million. The Indian Council of Medical Research recently launched a phase III trial comparing two TB vaccine candidates (VPM1002 and MIP) to placebo in over 12,000 household contacts of people with TB.[46] The other BRICS countries for which we have data, Brazil and South Africa, funded significantly less research in this area. However, South Africa hosts the majority of the world's TB vaccine clinical trials activity, and South African scientists are recognized leaders in this field. South Africa's case reveals some of the complexities of tracking TB research funding. Funders are not always located in the same country that the research takes place in (or even in the same country as the scientists leading the research), skewing country-by-country analyses toward countries with higher overall spending on R&D. Vaccine research would not be possible without the contributions of trial participants from high-TB-burden communities in countries like South Africa, yet these crucial contributions are not reflected in South Africa's funding numbers.

A new safe and effective TB vaccine is the missing linchpin of TB prevention efforts. Developing an effective vaccine will require a substantial and sustained increase in funding. Rosa Herrera sees an urgent need to increase funding for TB prevention, including vaccines, stating, "We need to find the missing billions—the missing millions of dollars. We're not going to achieve goals without the proper funding . . . When we are talking about research . . . we need to think more about prevention and think about the base of the iceberg . . . because that is where the majority of people are." Rosa's image of the iceberg describes the fact that one-fourth of humanity is infected with TB, creating the base from which future cases of TB arise from reactivated infection. A vaccine that protects people already infected with TB from developing disease could have a powerful effect on reducing TB incidence,[47] but only if made available equitably, at scale, in a timely manner.

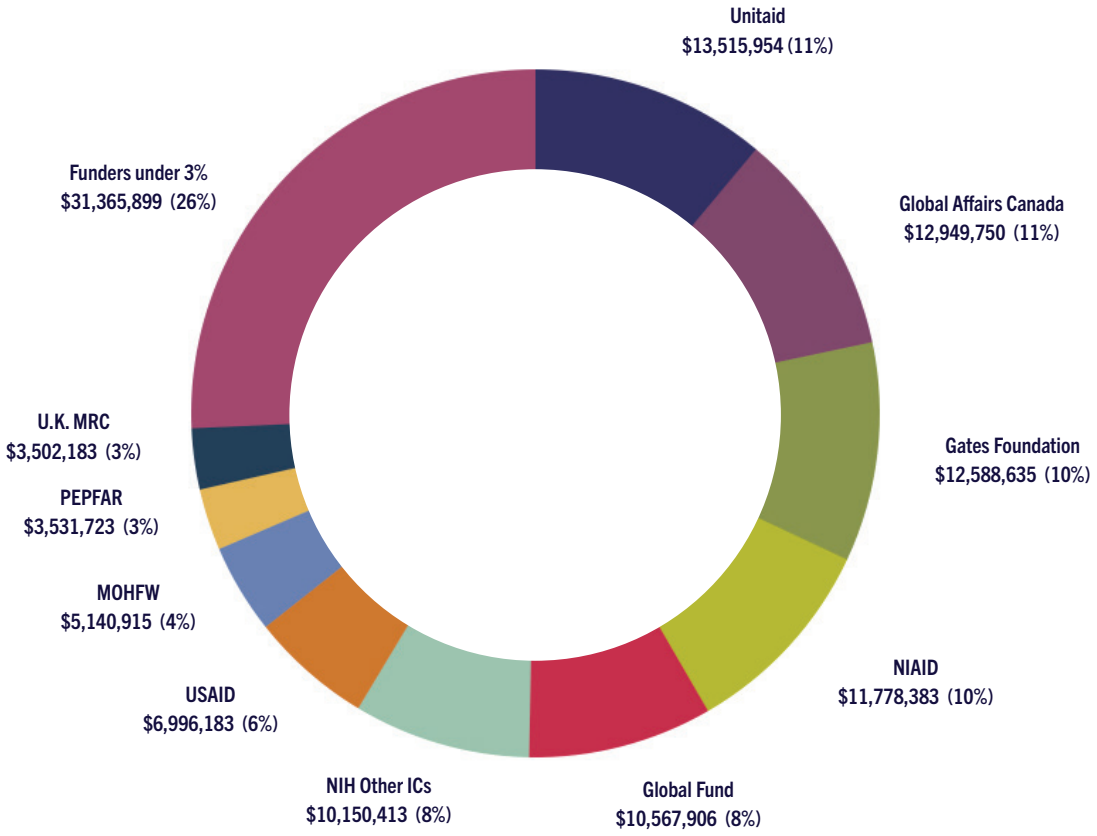
How much funding will be required to advance vaccines currently in the pipeline while continuing to support the discovery and preclinical work from which new candidates will emerge? A lot more than the world invests now. One useful benchmark is annual funding for HIV vaccine R&D. Funding for TB vaccines pales in comparison to spending on HIV vaccine research. Even with slight variations, annual HIV vaccine R&D spending has exceeded US$800 million every year since 2006, reaching a high of US$961 million in 2007 (TB vaccine funding reached its high of US$115 million in 2009). The 2018 HIV vaccine investment of US$842 million is more than 7.5 times the US$109 million TB vaccine investment.[48]

Delegates at 2018's HLM recognized the important role vaccines will play in ending TB, committing to "advancing the development of new vaccines and the provision of other tuberculosis prevention strategies."[49] However, this recognition did not come with clear and measurable targets for vaccine development. If the 2018 figures are an indication of countries' commitments, the HLM may have generated more talk than action.

Operational Research

FIGURE 12

Operational Research: $122,087,944



Funders with investments under 3%

U.K. Department for International Development (DFID)	$3,087,740
European Commission	$2,790,096
South African Medical Research Council (SAMRC)	$2,410,687
U.S. Centers for Disease Control and Prevention (CDC)	$2,336,736
European and Developing Countries Clinical Trials Partnership (EDCTP)	$2,298,316
Taiwan Centers for Disease Control	$2,102,003
Canadian Institutes of Health Research (CIHR)	$1,880,618
Indian Council of Medical Research (ICMR)	$1,691,713
U.K. National Institute for Health Research (NIHR)	$1,527,004
Australian Department of Foreign Affairs and Trade (DFAT)	$1,384,361
U.K. Biotechnology and Biological Sciences Research Council	$1,353,814
U.K. Department for Business, Energy, and Industrial Strategy (BEIS)	$1,300,215
National Institute of Health—University of the Philippines Manila	$937,790
National Research Coucil of Thailand	$638,412
U.K. Economic and Social Research Council	$574,715
Philippine Council for Health and Research Development	$504,511
Australian National Health and Medical Research Council (NHMRC)	$504,066
Médecins Sans Frontières	$466,804
Tata Trusts	$404,093

Mexico National Council for Science and Technology	$334,594
Initiative 5%	$323,260
Danish International Development Agency	$313,248
Italian Ministry of Foreign Affairs	$276,625
Taipei City Government	$261,992
Korean Ministry of Health and Welfare	$247,600
Norwegian Agency for Development Cooperation (NORAD)	$231,324
Netherlands Organization for Health Research and Development (ZonMw)	$230,104
Korean Ministry of Science and ICT	$213,200
Brazilian Ministry of Science, Technology, Innovation and Communication	$143,455
Doris Duke Charitable Foundation	$123,750
Brazilian Ministry of Health	$105,457
World Health Organization	$104,846
Indian Ministry of Science and Technology	$67,569
U.K. Natural Environment Research Council	$66,190
Japan Society for the Promotion of Science	$43,190
Japanese Ministry of Health, Labour and Welfare	$31,903
Health Research Council of New Zealand	$28,193
LHL International	$25,703

"When you do operational research, you are analyzing access and you figure out clearly what your barriers are . . . Once you do operational research, you figure [out] the barrier and how to solve it. So the same commitment made for diagnostics or drugs has to go to operational research. It's the only way we're going to move forward and create experiences that others can learn from."

—**Rosa Herrera, Global TB CAB member and TB physician**

In 2018, operational research accounted for 13% of all TB research spending, with a total investment of US$122 million. Unitaid was the largest funder, spending US$13 million, although both Global Affairs Canada and the Gates Foundation invested over US$12 million in this area (each is a major contributor to the Stop TB Partnership's flagship TB REACH program, which funds projects that bring TB services to vulnerable and hard-to-reach communities).[50] Altogether, 13 distinct public sector funders from the United States, United Kingdom, India, Taiwan, European Union, and South Africa reported operational research expenditures of over US$2 million. With 2018 spending of US$10 million, the Global Fund was the fifth largest funder of operational research, making up 9% of the total.

Overall operational research expenditures increased to 137% of their 2017 amount. This represents an all-time high. Funding for operational research is more evenly spread across funders than any other area of TB research. No single funder accounted for more than 11% of the operational research total, and spending by donors whose expenditures were less than 3% of total spending accounted for more than one-quarter (26%) of all operational research funding. Since operational research intends to analyze and fill gaps in implementation—the causes for which vary regionally and demographically—it is perhaps appropriate that the funding responsibility is shared more evenly.

Evaline Kibuchi describes missed opportunities in operational research. For Kibuchi, "the biggest problem is stigma. This has not been adequately researched, and we implement [stigma campaigns] without being informed by data from research. Recently, the community did a stigma index study, and the results have been informing quite a lot of implementation around addressing stigma . . . We keep saying TB has greater stigma than HIV, but there's no documented evidence to say what are the major sources of stigma, what populations perpetuate stigma, and so forth. So even interventions [that address stigma] are random, anecdotal." Even though funders like the Global Fund invest in programs to reduce stigma and discrimination, activists working on the ground perceive a discrepancy between funders' research priorities and the complexities of real-world implementation in this regard.

Likewise, Wim Vandevelde from the Global TB CAB describes the potential role operational research can play in addressing actual, as opposed to ideal, circumstances. As Vandevelde explains, "Research for TB drugs happens under relatively ideal circumstances. That's not the state of real-life situations in which the drugs are approved. So it's important also to check what is actually happening when the drugs are rolled out and course correct when necessary."

Given their focus on real-world uptake, operational and implementation research projects have traditionally demonstrated an openness to community input and direction. The WHO reports the development of formal processes for community input into TB guidelines,[51] and the two multilateral funders that invest significantly in operational research (the Global Fund and Unitaid) include representatives of communities affected by TB and nongovernmental organization representatives on their executive boards.[52,53]

In the view of Global TB CAB member Rosa Herrera, "The same commitment made for diagnostics and drugs has to go to operational research. It's the only way we're going to move forward and create experiences that others can learn from." In this vein, the research-related resolutions within the HLM political declaration look beyond product development, calling on member states to support "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." With this political recognition, operational research should become a core part of the TB research agenda and not the mere afterthought of product development or basic discovery.

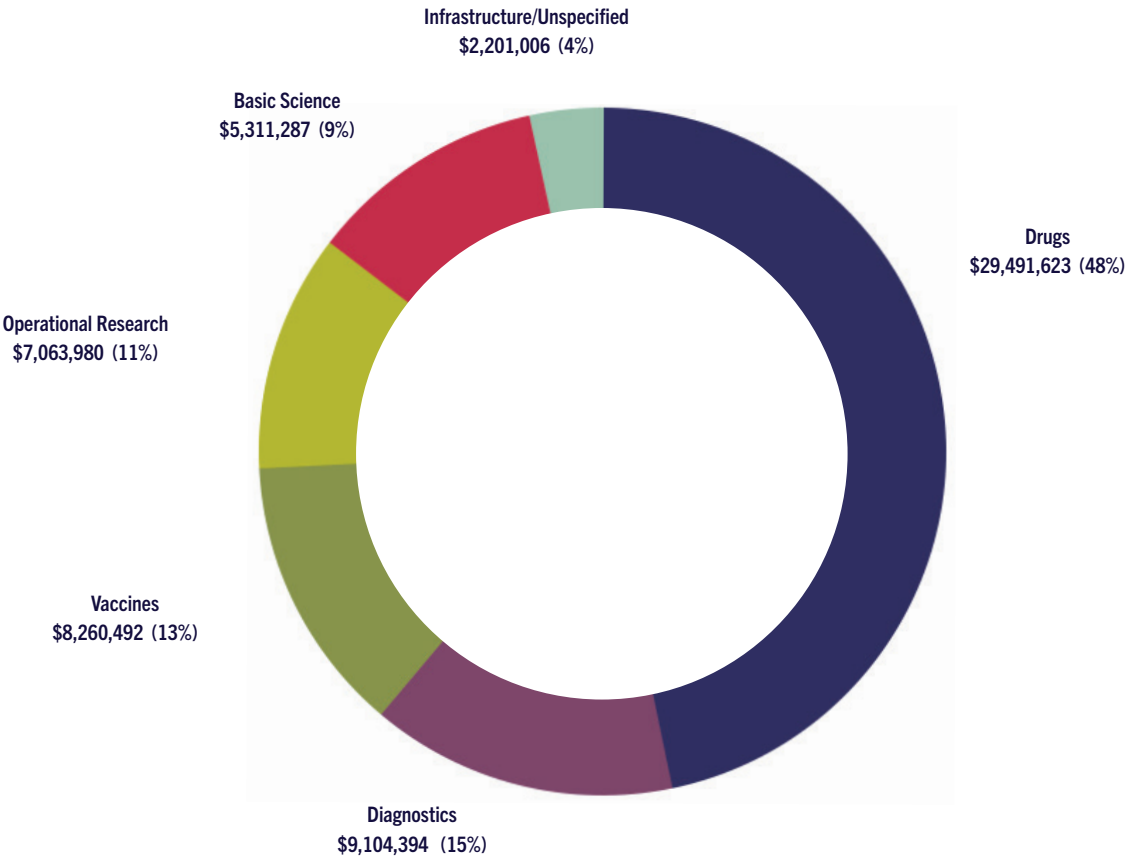
"Research for TB drugs happens under relatively ideal circumstances. That's not the state of real-life situations in which the drugs are approved. So it's important also to check what is actually happening when the drugs are rolled out and course correct when necessary."

—**Wim Vandevelde, Global TB CAB member, GNP+**

Pediatric TB Research

FIGURE 13

Pediatric TB R&D Funding by Research Area, 2018
Total: $61,432,780



"We need to demand that in every single target of research they [researchers] include at least a tiny cohort of children and pregnant women. Because they also need the development and research—they need to benefit from the funding that is raised for tuberculosis worldwide."

—**Rosa Herrera, Global TB CAB member and TB physician**

Pediatric TB funding increased for a second year in 2018, surpassing US$60 million for the first time since TAG began tracking pediatric-related research spending in 2012. These two years of increased funding come after three years of relatively flat funding in 2014, 2015, and 2016. Spending on pediatric TB research equaled US$61.4 million in 2018. Almost half (US$29 million; 48%) of this funding went to drug research. Diagnostics received 15% (US$9 million), pediatric vaccine research 13% (US$8 million), operational research 11% (US$7 million), and basic science 9% (US$5 million). The remaining 4% was reported as infrastructure/unspecified funding.

The European and Developing Countries Clinical Trials Partnership (EDCTP) was the largest single funder of pediatric research, investing nearly US$10 million. USAID spent US$9 million in the areas of pediatric drug and operational research. Company X reported a US$6 million investment in pediatric drug research, and Macleods Pharmaceuticals invested US$2 million in its pediatric TB drug program.

TABLE 3

Pediatric TB R&D Funders by Rank, 2018

2018 RANK	FUNDING ORGANIZATION	FUNDER TYPE	2018 FUNDING	PERCENTAGE
1	European and Developing Countries Clinical Trials Partnership (EDCTP)	P	$9,824,493	16.0%
2	U.S. Agency for International Development (USAID)	P	$9,199,933	15.0%
3	U.S. National Institutes of Health, National Institute of Allergy and Infectious Diseases (NIAID)	P	$8,928,097	14.5%
4	Company X	C	$6,300,000	10.3%
5	U.S. National Institutes of Health, Other Institutes and Centers (NIH Other ICs)	P	$4,820,423	7.8%
6	U.K. National Institute for Health Research (NIHR)	P	$4,807,873	7.8%
7	U.K. Medical Research Council (U.K. MRC)	P	$3,839,430	6.2%
8	Unitaid	M	$2,598,261	4.2%
9	Macleods Pharmaceuticals	C	$2,000,000	3.3%
10	U.S. President's Emergency Plan for AIDS Relief (PEPFAR)	P	$1,540,479	2.5%
11	Wellcome Trust	F	$1,497,933	2.4%
12	South African Medical Research Council (SAMRC)	P	$829,111	1.3%
13	Norwegian Agency for Development Cooperation (NORAD)	P	$573,187	0.9%
14	Bill & Melinda Gates Foundation	F	$562,206	0.9%
15	Butantan Institute	P	$500,000	0.8%
16	Company V	C	$391,501	0.6%
17	Indian Ministry of Science and Technology	P	$386,139	0.6%
18	Public Health Agency of Canada	P	$342,788	0.6%
19	Initiative 5%	P	$323,260	0.5%
20	Indian Council of Medical Research (ICMR)	P	$301,126	0.5%
21	Academy of Finland	P	$287,988	0.5%
22	Japan Agency for Medical Research and Development (AMED)	P	$254,646	0.4%
23	Philippine Council for Health and Research Development	P	$222,511	0.4%
24	German Federal Ministry of Education and Research (BMBF)	P	$210,359	0.3%
25	Thrasher Research Fund	F	$205,406	0.3%
26	Médecins Sans Frontières	F	$184,623	0.3%
27	The ELMA Foundation	F	$175,000	0.3%
28	Australian National Health and Medical Research Council (NHMRC)	P	$121,459	0.2%
29	Public Health England	P	$80,593	0.1%
30	Other funders with expenditures less than $50,000		$123,956	0.2%
	Total		$61,432,780	

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

Otsuka Pharmaceutical notified TAG that it cannot disaggregate pediatric expenditures from its overall investment and is therefore not listed in the table.

The United States, United Kingdom, and European Union contributed 69% of the public sector R&D funding earmarked for pediatric TB research. No other country invested more than US$1 million in pediatric research. India, with a total TB research investment of over US$30 million, allocated just under US$700,000 for pediatric research (2.3%). Similarly, only 2% of Canada's total TB research funding went to pediatric R&D (though Global Affairs Canada does not specify the percentage of its funding for the Stop TB Partnership's TB Reach program which goes toward pediatric-related research activities).

By and large, the pediatric TB research agenda has centered on how to use existing technologies and treatments with and in children. However, as noted in the briefing note "Research Priorities for Paediatric Tuberculosis," developed by TAG and the WHO Child and Adolescent TB Working Group, children have unique needs that will require a specific, pediatric-oriented research agenda.[54]

With regard to diagnosis, over 95% of pediatric TB-related deaths occur in children who are not being treated for TB; in other words, these children have been missed by existing diagnostic tests and campaigns.[55] Widely used diagnostic tools (like GeneXpert and sputum microscopy) are less accurate in pediatric populations, making alternative methods of diagnosis a priority. Kate O'Brien with We Are TB shared her excitement around innovations in pediatric diagnostics: "When people talk about being able to test TB from urine, that blows my mind. Stool! I was pregnant when I had tuberculosis and there's so many children who get tuberculosis . . . It is great to think about being able to use stool, or to [test for TB] with urine." Pediatric-focused diagnostics are clearly an urgent need, and enthusiasm for these technologies is high. Unfortunately, with an investment of only US$9 million in 2018, improving pediatric TB diagnosis will likely remain an unfinished part of the pediatric TB research agenda for the foreseeable future.

The majority of pediatric TB treatment research has focused on optimizing doses of existing and new drugs for use in children. This strategy is a pragmatic way to leverage existing products and health care infrastructures. However, adjusting dosages alone will not be sufficient to address the full spectrum of pediatric treatment needs. Children—especially children under five years of age who require higher per-weight dosages than older children—also need formulations that are easier to administer.[56]

Projects like STEP-TB—funded by Unitaid and implemented by the TB Alliance—developed child-friendly formulations of first-line drug-sensitive TB drugs. [57] In addition, the Global Drug Facility has helped build a market for new pediatric second-line drug formulations, many of which were developed by Macleods Pharmaceuticals, which reported spending US$2 million on pediatric drug development in 2018. Still, access to available pediatric TB medications remains far below need. Marie Theunissen, CRAG member and coordinator of the Desmond Tutu TB Centre CAB, recounted her feelings of excitement and disappointment over pediatric TB drugs, sharing that "we had a launch of a dissolvable TB medication. What excited me was that this was for children and adolescents—the most difficult population for taking medications. It's a soluble tablet, which can be dissolved in very little water and cuts the amount of water they have to use . . . But I'm concerned about the time that it's taken to gather the data together and make these findings known to the public and to the participants. That needs to improve because people are not dying in five years' time; people are dying here and now. And people need to access medication, here and now!" As Theunissen astutely notes, development efforts are only useful if research findings are accessible.

Delegates at 2018's HLM acknowledged the need for expanded pediatric TB treatment, committing in the political declaration to "successfully treating 40 million people with tuberculosis from 2018 to 2022, including 3.5 million children, and 1.5 million people with drug-resistant tuberculosis, including 115,000 children."[58] Measurable progress toward achieving this target would entail treating an average of 700,000 children for TB each year and 23,000 children with drug-resistant TB. Meeting these targets will require political mobilization and significantly increased investments across pediatric TB—including pediatric TB research.

Discussion

The months leading up to last year's HLM generated increased energy and community mobilization aimed at ending TB. Advocates addressed the HLM on behalf of TB-affected communities and organized meetings between civil society and country missions to the UN, national political leaders, and donors. This concerted mobilization showed that global TB advocacy has produced well-informed networks of activists who are no longer willing to accept research that does not speak to community priorities.

The HLM generated a comprehensive political declaration that addressed many of advocates' priorities. This year's funding numbers provide the baseline against which we will measure whether governments back up the commitments laid out in the HLM political declaration with real monetary investments. Total TB R&D funding in 2018 surpassed US$906 million dollars—a remarkable funding increase over the course of a year given historic trends. Now that the bar has been raised, the challenge for funders is to reach even greater investment heights moving forward.

However, skepticism that the HLM generated anything beyond empty promises is beginning to emerge among activists. Janika Hauser with RESULTS UK commented that "there's still time for countries to prove that they can walk their talk on research financing, but that time is running out really quickly." Funding is a key piece of the puzzle. Yet, no influx of money can adequately address the structural factors that have perpetuated the global TB epidemic unless that money is matched by the political will to combat inequity.

Four themes emerge from this year's funding report: 1) the need to conduct rigorous research capable of generating quality data to inform implementation, 2) the imperative to increase access at every stage of research, and not just during implementation, 3) the importance of increasing investment in community engagement with research, and 4) the necessity of improving collaboration and coordination across the TB research landscape. Each of these themes also appears in the UN HLM political declaration. It will be difficult to achieve any of these goals without advocacy and accountability measures.

Rigorous Research and Quality Data

Many of the activists TAG spoke with this year stressed the need to call for rigorous research as opposed to simply more research. Activists pointed to quality of data as one important factor underlying rigor. Citing the need for quality data in drug research, Wim Vandevelde of the Global TB CAB and GNP+ expressed concern that for some of the new regimens being tested, "we don't have sufficient data on the efficacy of the different parts of the regimen. We see that now with the [regimen that led to pretomanid's approval], where we have little data on pretomanid . . . We don't even know how effective it is because the other two components [of the regimen]—bedaquiline and linezolid—are very strong, and the drug sponsor didn't invest in teasing out what each drug contributes to the regimen. So we need to be advocating for trials with new regimens where we firmly understand the regimen."

For some, the problem lies with misaligned and misdirected incentives for drug development. Els Torreele of the MSF Access Campaign pointed to the examples of bedaquiline and delamanid: "What the companies did to satisfy the regulators and get regulatory approval as soon as possible was actually not at all what we need for clinical practice." Torreele explained how Johnson and Johnson and Otsuka each studied bedaquiline and delamanid as add-ons to existing regimens without combining the two compounds or studying their potential to shorten treatment. The resulting "disconnect between studies a company does to get . . . regulatory approval [and] what the community needs for using new tools in clinical practice," to quote Torreele, requires fixing.

One solution outlined by Torreele would entail conducting extensive phase II studies to optimize dose, duration, and drug combinations before launching phase III trials. Current incentives supporting drug development, however, do not always encourage this approach. "If you develop a new drug, you want to get to the market and get your priority review voucher as soon as possible," said Torreele, referring to an incentive program at the FDA that rewards companies that register drugs for certain neglected diseases with a so-called priority review voucher (PRV). Companies that receive a PRV can either apply it to fast track the approval of other products (allowing them to beat competitors to market) or sell it to another company (PRVs

"Commit to mobilize sufficient and sustainable financing, with the aim of increasing overall global investments to 2 billion dollars, in order to close the estimated 1.3 billion dollar gap in funding annually for tuberculosis research, ensuring that all countries *contribute appropriately* to research and development, to support *quality* research and development of new and the effective implementation of recently approved health technologies . . ."

—UN HLM political declaration, para. 47 excerpted [emphases added]

"[. . . reaffirming the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) [which] notes the need for *appropriate incentives* in the development of new health products . . ."

—UN HLM political declaration, para. 19 excerpted [emphasis added]

"[. . . aim to achieve effective universal access to quality diagnosis, treatment, care, and adherence support . . . with a special focus on reaching those who are vulnerable . . ."

—UN HLM political declaration, para. 24 excerpted

have sold for between US$68 million and US$350 million).[59] An unanticipated consequence of this powerful incentive program is that instead of doing robust phase II work, "there is the rush to go to marketing authorization" to quote Torreele.

Other incentives that apply to TB drug development actually lower evidentiary standards for new drug approvals. For example, in the United States, the FDA's Limited Population Pathway for Antibacterial and Antifungal Drugs aims to facilitate drug development for "serious or life-threatening infections in limited populations of patients with unmet needs." The program pursues this aim by, in part, relaxing evidentiary requirements for new drug approvals. Patient groups, including TAG, have warned that this could lead to cutting corners in research by expediting drugs to market with limited data on safety and efficacy. In testimony to the FDA on this new scheme, TAG emphasized that "we need appropriate incentives that facilitate development and promote rigorous science, not merely more incentives."[60]

Still other incentives (e.g., the U.S. Orphan Drug Act) encourage product development by granting developers extended periods of marketing exclusivity, essentially lengthening the life of patent protection.[61] Incentives that bolster monopolies over new tools to fight TB make little sense given that more than two-thirds of total TB research funding comes from governments, and that most TB products in the pipeline have benefitted from public funding. In this context, what matters is shifting the efforts of governments from creating additional incentives to creating appropriate incentives—ones that generate quality data able to answer questions of clinical relevance, set fair access terms with private developers, and acknowledge the role of public funding in creating public goods.

Equitable Access

Too often, conversations about access occur during implementation—*after* a new tool has been developed. Many of the activists we spoke to this year underscored the importance of considering access, including but not limited to pricing, during—not after—development. Otherwise, new and improved drugs, vaccines, and diagnostics will remain out of reach for many who need them. Fifa Rahman of the Unitaid NGO Delegation explains that "without [community] voices on those projects early on, you're just not going to get the same emphasis on access, affordability, or equity."

The 3HP regimen is a perfect example of the struggles to make publicly financed TB innovations equitably accessible. The two drugs in the 3HP regimen—rifapentine and isoniazid—were both discovered decades ago; isoniazid was never patented, and the primary patent on rifapentine expired long ago. Moreover, publicly funded clinical trials generated the data demonstrating the safety and efficacy of 3HP in preventing TB. Despite this, access to rifapentine remained circumscribed by the high price set by the French pharmaceutical company Sanofi—until intervention by two publicly financed multilateral agencies. In November 2019, Unitaid and the Global Fund inked a deal with Sanofi to discount the price of the rifapentine component of the 3HP regimen by 66%. This greatly improved the regimen's

affordability for public programs in the 100 countries eligible for the discount, but without that intervention by two large multilateral donors, rifapentine would likely have remained prohibitively expensive until the entry of generic competition. Evaline Kibuchi summarizes the controversy over 3HP pricing, noting that "affordability has been an issue. The prices [pharma] comes with, definitely the average citizen in the country—most cannot afford it. So in most cases, you have to find somebody who comes in between to negotiate affordable prices."

Many activists note that profit, rather than access or affordability, remains the guiding force in the development of new TB technologies. This contradicts the expressed aim of UN member states in the HLM political declaration to "promote tuberculosis research and development efforts aiming to be needs driven, evidence based and guided by the principles of affordability, effectiveness, efficiency and equity and which should be considered as a shared responsibility."[62] As an independent lawyer working on intellectual property and human rights, Kajal Bhardwaj is well aware of the competing interests at work in TB drug development—and the human impact of these negotiations. As she explains, "Patients and governments have to traverse a complex maze of so-called access programs to get ahold of the new TB drugs. Prices vary widely, and it remains unclear which countries can access which prices." Generic production is a powerful tool to increase access to new drugs. Bhardwaj calls on governments to increase their efforts to expand access to generics: "It is imperative the governments now step in and ensure that affordable and quality generic competition for TB drugs takes place to ensure a predictable and sustainable government response to MDR-TB," including through the use of legal interventions (e.g., flexibilities contained in the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights).

Access to innovations—in prevention, diagnostics, and treatment—remains a key goal of TB research. As Janika Hauser puts it, "The final objective for public financing of TB research has to be getting the product to the person who needs it. So, we have to be really uncompromising about access provisions" to make access a priority.

"Commit to create an environment conducive to research and development of new tools for tuberculosis, and to enable timely and effective innovation and affordable and available access to existing and new tools and delivery strategies . . ."

—UN HLM political declaration, para. 43 excerpted

"We need to orient our strategies towards freeing newly approved TB treatment, prevention, and diagnostic [tools] of monopolistic barriers for all patients in all countries and avoid creating or supporting complicated pathways to access that are being dictated by companies instead of communities."

— Kajal Bhardwaj, independent lawyer working on health and rights in India

Community Engagement

Producing data and products with real-world utility requires meaningful community engagement. Marie Theunissen, CAB coordinator with the Desmond Tutu TB Centre, explains, "people in the community in high-TB-burden areas are the very people who will be able to tell us what works and what doesn't—and how money should be spent." Theunissen observes that research priorities are rarely determined by people in the hardest-hit communities—a flaw in the system that limits both the relevance and accessibility of research findings.

For Theunissen, community education is a key step to building a community that is able to participate meaningfully in research priority setting. Theunissen observes that when researchers have prioritized ongoing conversation with community members, the community has responded with increased engagement:

"Commit to providing special attention to the poor, those who are vulnerable . . . and communities especially at risk of and affected by tuberculosis, in accordance with the principle of social inclusion, especially through ensuring strong and meaningful engagement of civil society and affected communities in the planning, implementation, monitoring and evaluation of the tuberculosis response . . ."

—UN HLM political declaration, para. 38 excerpted

"People in the community in high-TB-burden areas are the very people who will be able to tell us what works and what doesn't—and how money should be spent."

—**Marie Theunissen, Community Research Advisors Group member and Desmond Tutu TB Centre community advisory board coordinator**

"Commit to enable and pursue multisectoral collaboration at the global, regional, national and local levels, across health and nutrition, finance, labour, social protection, education, science and technology, justice, agriculture, the environment, housing, trade, development and other sectors, in order to ensure that all relevant stakeholders pursue actions to end tuberculosis and leave no one behind . . ."

—**UN HLM political declaration, para. 39 excerpted**

"Further commit to advancing that new research and innovation environment through global collaboration, including through . . . strengthening research capacity and collaboration through improving tuberculosis research platforms and networks across the public and private sectors . . ."

—**UN HLM political declaration, para. 44 excerpted**

"You get community who are willing to contribute to any discussion that you might have. And that makes it more robust, and they will be willing to go out and get more input from other community members, so that it doesn't just become the opinions of the few that represent the community. The community is willing to engage, to go back and discuss with the larger community, and to bring that back to the researchers."

Activists recognize that meaningful community engagement is not just about more money for community work but will also require internal accountability measures. As Denis Godlevskiy asks, "How do we make community engagement a really legitimate voice of those who are in need? I think that's the question that needs a lot of work." Activists must continue to ask themselves the same questions they ask of R&D—including who is determining research priorities and to whom is the research ultimately accountable.

Rosa Herrera, a doctor, TB CAB member, and herself a TB survivor, calls for the global advocacy community to do better in terms of accessibility. As Herrera describes, "All the interviews, all the messages, all the participation in big [meetings]—applications for these things are in English, and the regular patient doesn't have access to another application from developing countries . . . So I think we need to be more inclusive about language and have translation services in order to have real patients speak loud and clear—to give them those platforms."

However, the burden of increasing the accessibility of R&D processes and outputs cannot fall solely on activists. Wim Vandevelde expresses his desire for R&D funders to prioritize community engagement, stating "[It] would be great if there was more funding for engagement in research." Indeed, for research to ultimately succeed, the funders who invest in TB research must also continue to invest in community engagement. This investment must be accompanied by a commitment among research funders and developers to move beyond mere inclusion to engage communities meaningfully and on their own terms. "It's [community engagement] very often just checking a box. You know WHO or others say you have to have community engagement or community advisory boards, but their hearts are not really in it," reflected Vandevelde.

Community engagement is not only an ethical imperative; it also represents a smart investment on the part of research funders. In a published interview with two other leaders of community engagement in TB research, Vandevelde reflected on the ways community engagement has contributed to TB R&D. Community advisory boards have successfully lobbied for changes to the design of key studies, helped disseminate trial findings to communities, secured the inclusion of key populations such as people living with HIV and children in clinical trials, built trust in research among TB-affected communities, and advocated for the uptake of new innovations, to name just a few areas of positive impact cited by Vandevelde.[63]

Collaboration and Coordination

The HLM political declaration acknowledged the breadth of the TB research portfolio, calling for improved and expanded diagnostics, shorter and more effective treatments, and a scaling up of implementation programs. Additionally, while this report tracks and disaggregates R&D funding by research area, in practice it can be difficult to clearly separate these tracks. Diagnostics are improved through operational research, basic science depends on local infrastructure, pediatric research reaches into all areas, and so on. It is clear that multilateral organizations will play a key role in both funding and conducting future TB research. What remains less clear is how—and by whom—the global TB research agenda will be determined, and who will support R&D coordination efforts.

Private and philanthropic funders determine R&D spending according to their own interests. Those sectors have demonstrated varying degrees of responsiveness to community engagement, but multilateral organizations will be instrumental in the public-private-commercial partnerships that will be required to address the breadth of research needs. Multilateral organizations are poised to act on the overlaps between TB R&D and TB health care delivery systems. For RESULTS UK's Janika Hauser, "Big conversations about coordination without the investment to back it up really don't cut the mustard." Hence, it is imperative that multilateral funders support—financially and politically—the priorities of TB-affected communities.

A consensus seems to exist among activists that TB research could be—and should be—more accountable to the public. Most of the activists we interviewed describe a dangerous status quo where political grandstanding is not always backed by funds, pharmaceutical companies pursue profit above people, and multilateral organizations are so busy filling implementation gaps that they cannot build stable systems of community engagement. This status quo needs to change—but how? Els Torreele proposes collective governance of TB research, arguing, "Given the massive public and philanthropic—but mostly public—investment, we really need to think about the collective governance mechanism to steer the R&D to where the health impacts will be biggest, and find some coordination."

With two years remaining in Stop TB Partnership's five-year *Global Plan*, coordination becomes increasingly urgent. TB research funding has increased each of the last three years, and at over US$906 million, financial commitments to TB research reached an all-time high in 2018. Still, TB funding falls short on every metric—absolute spending, inflation-adjusted spending, fair share spending, and Burden-Investment Index scores. The gap in TB research funding is more accurately characterized as a gulf. However, if 2018's rate of increase can be maintained for the next two years, we may be able to make more significant progress toward closing that gap. As Kate O'Brien reminds us, "people with TB are people and their suffering is important. Even if they can be cured, reducing their suffering is important. And it's possible."

"I'm tired of the situation where the only time you get government actively involved is at these huge meetings."

—Marie Theunissen, Community Research Advisors Group member and Desmond Tutu TB Centre community advisory board coordinator

"Given the massive public and philanthropic—but mostly public—investment, we really need to think about the collective governance mechanisms to steer the R&D to where the health impacts will be biggest and find some coordination."

—Els Torreele, MSF Access Campaign executive director

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Appendix 1: Methodology

TAG tracks global funding for TB R&D by surveying public, philanthropic, private, and multilateral organizations with known or potential investments in TB research. The survey asks recipients to report expenditures on TB research in a given fiscal year and categorize spending by six research areas: basic science, diagnostics, drugs, vaccines, operational research, and infrastructure/unspecified projects. Surveyed institutions may report spending by individual projects or aggregate expenditures by research area. Within these categories, the survey asks recipients to indicate any funding for pediatric TB research. Respondents report expenditures according to the parameters of their fiscal year, so the funding reported here does not align with calendar year 2018 perfectly.

TAG surveyed 202 organizations for this year's report and received 124 surveys in return. From these, we identified 139 institutions funding TB research in 2018. Nine organizations that returned surveys reported spending no money on TB R&D in 2018, and three groups declined to participate.

The TAG survey asks organizations to report TB research spending in local currencies, which TAG converts into U.S. dollars using the July 1, 2018, 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 2018, rather than commitments, pledges, 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 assiduously reviews each returned survey for completeness. We take careful measure 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 funder. For 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 10 qualitative interviews with activists representing civil society, community-based organizations, and TB -affected communities. Each was asked to assess the current state of TB research in relation to available versus required funding and to comment on the extent to which community priorities are reflected in the global TB research agenda. Each interviewee received an embargoed copy of preliminary survey findings in early September 2019 with a list of open-ended questions. We interviewed nine individuals over the phone, and one submitted answers in writing. Each phone interview was recorded and transcribed. We pulled quotations from the transcripts and written response, 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 provided interviewees the opportunity to review the selected quotations prior to publication.

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 fund 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's report. The high degree of concentration of TB research funding means that the top 30 donors typically comprise over 90% of total spending, and the composition of this group has remained remarkably stable over time. This year, all of the top 30 funders from 2017 participated in the survey.

A number of funders with known investments in TB research did not return surveys this year (see Table 4). TAG received no information from entities in Russia and China. In the case of China, officials at the Chinese Center for Disease Control and Prevention indicated to TAG they could provide data if the request came from an official UN channel such as the WHO Country Office. Unfortunately, repeated appeals to the WHO office in Beijing went unanswered. A request to WHO headquarters to facilitate reporting by the Russian Federation also went unacknowledged. 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 and that international institutions such as WHO will play an active role in supporting such reporting.

TAG encourages all funders not listed here to participate in future report rounds. Please contact TAG at tbrdtracking@treatmentactiongroup.org with any 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 124 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.

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, teen, natal, 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 TB infection or disease in children directly. Some funders have told TAG that they cannot disaggregate pediatric research funding from overall expenditures on TB R&D. Otsuka, for example, did not report how much of the US$28.4 million it spent on TB drug development in 2018 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 children. TAG encourages all funders to develop ways of disaggregating pediatric TB research spending from within larger funding totals to support more accurate estimation in this area.

Research areas tracked by TAG:

1. Basic science: undirected, investigator-initiated research to discover fundamental knowledge about *Mycobacterium tuberculosis* and closely related mycobacterial organisms.
2. Diagnostics: preclinical and clinical trials and evaluations of diagnostic technologies and algorithms.
3. Drugs: preclinical and clinical research on treatments and treatment strategies for *Mycobacterium tuberculosis* 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 categorize.

Table 4: Funders with known investments in TB research that did not report

ORGANIZATION	SURVEY OUTCOME
Alere/Abbott	Did not return survey
Anhui Zhifei Longcom	Did not return survey
Carlos III Health Institute	Did not return survey
Eli Lilly and Company	Did not return survey
Fondation Mérieux	Did not return survey
Institute Pasteur Korea	Did not return survey
Max Planck Institute for Infection Biology	Did not return survey
Serum Institute of India	Did not return survey
Swedish Research Council	Did not return survey
Singapore Agency for Science, Technology and Research (A*STAR)	Did not return survey
National Agency for Research on AIDS and Viral Hepatitis (ANRS)	Did not return survey
Novartis	Did not return survey
Institute of Tropical Medicine Pedro Kourí Cuba	Did not return survey
Ospedale San Raffaele	Did not return survey
Innovations Fonden Denmark	Did not return survey
National Research Foundation of South Africa	Did not return survey
Tata Trusts/India Health Fund	Did not return survey
Molbio	Did not return survey
LegoChem Biosciences	Did not return survey
Vakzine Projekt Management	Did not return survey
French National Institute of Health and Medical Research (INSERM)	Did not return survey
Qiagen	Declined to participate
Singapore National Medical Research Council	Declined to participate
Tahir Foundation	Declined to participate

Appendix 2

TB R&D Funders by Rank, 2018

2018 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
1	U.S. National Institutes of Health, National Institute of Allergy and Infectious Diseases (NIAID)†	P	$253,434,034
2	Bill & Melinda Gates Foundation†	F	$141,115,233
3	U.S. National Institutes of Health, Other Institutes and Centers (NIH Other ICs)†	P	$43,946,795
4	U.S. Agency for International Development (USAID)†	P	$36,735,190
5	Company X†	C	$30,319,517
6	Otsuka Pharmaceutical†	C	$28,405,543
7	Unitaid	M	$26,193,134
8	U.K. Department for International Development (DFID)†	P	$24,677,306
9	European and Developing Countries Clinical Trials Partnership (EDCTP)†	P	$24,491,122
10	Indian Council of Medical Research (ICMR)	P	$24,243,814
11	European Commission†	P	$18,527,670
12	U.S. Centers for Disease Control and Prevention (CDC)†	P	$17,619,008
13	U.K. Medical Research Council (U.K. MRC)†	P	$16,395,195
14	German Federal Ministry of Education and Research (BMBF)	P	$16,351,364
15	Global Affairs Canada	P	$12,949,750
16	U.S. Department of Defense Medical Research and Development Program (DMRDP)	P	$12,868,028
17	Global Fund to Fight AIDS, Tuberculosis and Malaria	M	$10,567,906
18	Wellcome Trust†	F	$10,321,874
19	Company V	C	$8,504,456
20	U.K. National Institute for Health Research (NIHR)	P	$7,644,833
21	Korean Ministry of Health and Welfare	P	$7,153,744
22	Dutch Ministry of Foreign Affairs (formerly DGIS)†	P	$6,168,379
23	Médecins Sans Frontières	F	$5,936,781
24	Global Health Innovative Technology Fund (GHIT)	M	$5,887,207
25	U.K. Biotechnology and Biological Sciences Research Council	P	$5,734,525
26	Australian Department of Foreign Affairs and Trade (DFAT)	P	$5,548,549
27	Canadian Institutes of Health Research (CIHR)†	P	$5,258,772
28	Indian Ministry of Health and Family Welfare (MOHFW)	P	$5,220,666
29	GlaxoSmithKline (GSK)	C	$4,607,603
30	German Research Foundation (DFG)	P	$4,461,360
31	Korean Ministry of Science and ICT	P	$4,167,351
32	Australian National Health and Medical Research Council (NHMRC)	P	$3,986,720
33	U.K. Department for Business, Energy, and Industrial Strategy (BEIS)	P	$3,820,815
34	U.S. President's Emergency Plan for AIDS Relief (PEPFAR)‡	P	$3,531,723

C = Corporation/Private Sector; F = Foundation/Philanthropy; M = Multilateral; P = Public-Sector Agency; † 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
$95,008,081	$17,650,509	$67,484,881	$31,843,635	$11,778,383	$29,668,545
$17,030,263	$7,713,819	$75,320,376	$24,820,023	$12,588,635	$3,642,118
$17,578,628	$4,873,488	$4,374,206	$1,251,886	$10,150,413	$5,718,174
$0	$0	$16,808,425	$0	$6,996,183	$12,930,582
$0	$230,000	$29,665,517	$424,000	$0	$0
$0	$0	$28,405,543	$0	$0	$0
$0	$1,743,261	$10,933,919	$0	$13,515,954	$0
$0	$3,357,144	$17,175,470	$1,056,952	$3,087,740	$0
$0	$3,379,732	$4,105,211	$13,243,530	$2,298,316	$1,464,334
$1,252,966	$127,175	$931,049	$7,106,861	$1,691,713	$13,134,049
$1,727,916	$3,028,863	$2,264,555	$8,716,240	$2,790,096	$0
$0	$4,549,256	$8,681,867	$0	$2,336,736	$2,051,149
$3,414,523	$1,844,511	$7,576,769	$57,208	$3,502,183	$0
$4,338,840	$1,549,721	$5,282,491	$1,615,061	$0	$3,565,251
$0	$0	$0	$0	$12,949,750	$0
$0	$2,163,098	$8,570,015	$2,134,915	$0	$0
$0	$0	$0	$0	$10,567,906	$0
$8,214,927	$124,406	$1,982,541	$0	$0	$0
$0	$0	$8,504,456	$0	$0	$0
$0	$753,400	$2,977,456	$0	$1,527,004	$2,386,973
$517,066	$3,484,712	$1,014,407	$1,690,840	$247,600	$199,119
$0	$2,592,280	$3,576,100	$0	$0	$0
$0	$27,157	$5,442,820	$0	$466,804	$0
$0	$4,711,104	$1,176,103	$0	$0	$0
$3,019,239	$0	$385,287	$976,185	$1,353,814	$0
$0	$1,388,063	$2,776,125	$0	$1,384,361	$0
$1,406,826	$227,244	$716,500	$1,010,639	$1,880,618	$16,945
$0	$10,144	$9,648	$0	$5,140,915	$59,960
$0	$0	$0	$4,607,603	$0	$0
$3,444,041	$0	$1,017,319	$0	$0	$0
$293,533	$345,323	$1,043,245	$351,769	$213,200	$1,920,281
$2,688,524	$322,656	$471,475	$0	$504,066	$0
$376,982	$316,371	$510,965	$0	$1,300,215	$1,316,283
$0	$0	$0	$0	$3,531,723	$0

Appendix 2

TB R&D Funders by Rank, 2018 (continued)

2018 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
35	South African Medical Research Council (SAMRC)	P	$3,499,334
36	Company Y	C	$3,428,500
37	Swiss National Science Foundation (SNSF)	P	$3,107,799
38	French National Research Agency (ANR)	P	$3,066,398
39	Taiwan Centers for Disease Control	P	$3,020,028
40	Public Health England	P	$3,009,828
41	Japan Agency for Medical Research and Development (AMED)	P	$2,831,808
42	Qurient	C	$2,250,000
43	Norwegian Agency for Development Cooperation (NORAD)	P	$2,125,765
44	Korea Drug Development Fund	P	$2,023,689
45	Macleods Pharmaceuticals	C	$2,000,000
46	Korean Ministry of Land, Infrastructure and Transport	P	$1,855,556
47	Genedrive	C	$1,597,319
48	U.S. Department of Veterans Affairs	P	$1,576,663
49	Merck	C	$1,561,976
50	Science Foundation Ireland	P	$1,328,969
51	Irish Aid	P	$1,168,660
52	South African Department of Science and Technology	P	$1,090,950
53	Indian Ministry of Science and Technology	P	$1,073,828
54	Sequella	C	$1,000,000
55	Swiss Federal Institute of Technology in Lausanne (EPFL)	P	$998,643
56	Korean Ministry of SMEs and Startups	P	$998,417
57	National Institute of Health—University of the Philippines Manila	P	$988,673
58	National Research Coucil of Thailand	P	$987,726
59	U.S. Food and Drug Administration (FDA)†	P	$946,590
60	Innovate UK	P	$931,118
61	U.S. National Science Foundation (NSF)	P	$925,469
62	Norwegian Ministry of Education and Research	P	$826,500
63	Philippine Council for Health and Research Development	P	$789,304
64	Italian Ministry of Health	P	$787,740
65	Independent Research Fund Denmark	P	$754,649
66	Natural Sciences and Engineering Research Council of Canada	P	$725,353
67	Netherlands Organization for Health Research and Development (ZonMw)	P	$714,830
68	Marsden Fund	P	$704,307
69	U.K. Economic and Social Research Council	P	$625,067

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

BASIC SCIENCE	DIAGNOSTICS	DRUGS	VACCINES	OPERATIONAL RESEARCH	INFRASTRUCTURE/ UNSPECIFIED
$445,324	$397,423	$174,188	$25,456	$2,410,687	$46,256
$0	$3,428,500	$0	$0	$0	$0
$2,698,512	$112,229	$297,058	$0	$0	$0
$1,643,417	$0	$1,422,981	$0	$0	$0
$578,648	$181,985	$157,392	$0	$2,102,003	$0
$92,483	$0	$614,353	$2,302,991	$0	$0
$415,380	$254,646	$270,900	$1,890,882	$0	$0
$0	$0	$2,250,000	$0	$0	$0
$397,177	$282,412	$183,570	$1,031,281	$231,324	$0
$0	$0	$2,023,689	$0	$0	$0
$0	$0	$2,000,000	$0	$0	$0
$0	$0	$0	$0	$0	$1,855,556
$0	$1,597,319	$0	$0	$0	$0
$481,255	$0	$813,871	$281,537	$0	$0
$0	$0	$1,561,976	$0	$0	$0
$311,904	$561,979	$0	$455,086	$0	$0
$0	$0	$1,168,660	$0	$0	$0
$1,090,950	$0	$0	$0	$0	$0
$959,322	$0	$46,936	$0	$67,569	$0
$0	$0	$1,000,000	$0	$0	$0
$665,762	$0	$332,881	$0	$0	$0
$0	$998,417	$0	$0	$0	$0
$0	$50,882	$0	$0	$937,790	$0
$249,973	$99,341	$0	$0	$638,412	$0
$0	$0	$946,590	$0	$0	$0
$0	$931,118	$0	$0	$0	$0
$692,593	$232,876	$0	$0	$0	$0
$369,656	$0	$224,567	$232,277	$0	$0
$235,603	$49,189	$0	$0	$504,511	$0
$787,740	$0	$0	$0	$0	$0
$9,194	$165,898	$0	$579,557	$0	$0
$490,140	$123,175	$24,757	$87,281	$0	$0
$225,435	$0	$259,291	$0	$230,104	$0
$704,307	$0	$0	$0	$0	$0
$0	$0	$0	$0	$574,715	$50,352

Appendix 2

TB R&D Funders by Rank, 2018 (continued)

2018 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
70	Institut Pasteur	F	$607,715
71	Health Research Council of New Zealand	P	$590,984
72	Academy of Finland	P	$566,439
73	Korean Ministry of Education	P	$544,032
74	Mexico National Council for Science and Technology	P	$535,224
75	Tata Trusts	F	$520,390
76	Butantan Institute	P	$500,000
77	U.K. Engineering and Physical Sciences Research Council	P	$452,288
78	Brazilian Ministry of Health	P	$444,684
79	Public Health Agency of Canada	P	$443,148
80	Bioneer	C	$434,465
81	Japanese Ministry of Health, Labour and Welfare	P	$415,489
82	Brazilian Ministry of Science, Technology, Innovation and Communication	P	$391,736
83	Japan International Cooperation Agency (JICA)	P	$343,122
84	Japan BCG Laboratory	C	$324,110
85	Initiative 5%	P	$323,260
86	Thailand National Science and Technology Development Agency (NSTDA)	P	$318,957
87	Danish International Development Agency	P	$313,248
88	Taipei City Government	P	$277,567
89	Italian Ministry of Foreign Affairs	P	$276,625
90	Roche	C	$270,144
91	Korea Foundation For International Healthcare	F	$270,000
92	U.K. National Centre for the 3Rs	P	$266,360
93	Hong Kong Health and Medical Research Fund	P	$258,100
94	Doris Duke Charitable Foundation	F	$247,500
95	Indian Council of Scientific and Industrial Research	P	$240,579
96	National Institute of Health Carlos III	P	$233,732
97	Thrasher Research Fund	F	$205,406
98	Finnish Institute for Health and Welfare	P	$204,516
99	Hain Lifescience	C	$194,331
100	Philippine Commission on Higher Education	P	$187,400
101	Damien Foundation Belgium	F	$186,228
102	The ELMA Foundation	F	$175,000
103	U.K. Department for Environment, Food and Rural Affairs	P	$171,755
104	World Health Organization	M	$169,846
105	Company L	C	$150,000

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

† Organization has reported to TAG each year since 2005

BASIC SCIENCE	DIAGNOSTICS	DRUGS	VACCINES	OPERATIONAL RESEARCH	INFRASTRUCTURE/ UNSPECIFIED
$453,396	$37,683	$116,636	$0	$0	$0
$191,712	$84,579	$286,501	$0	$28,193	$0
$566,439	$0	$0	$0	$0	$0
$396,654	$41,000	$0	$65,378	$0	$41,000
$200,629	$0	$0	$0	$334,594	$0
$98,731	$17,566	$0	$0	$404,093	$0
$0	$0	$0	$500,000	$0	$0
$0	$452,288	$0	$0	$0	$0
$0	$0	$92,275	$246,952	$105,457	$0
$18,853	$424,295	$0	$0	$0	$0
$0	$434,465	$0	$0	$0	$0
$183,309	$0	$0	$12,542	$31,903	$187,736
$0	$248,281	$0	$0	$143,455	$0
$343,122	$0	$0	$0	$0	$0
$38,461	$0	$0	$285,649	$0	$0
$0	$0	$0	$0	$323,260	$0
$241,110	$77,847	$0	$0	$0	$0
$0	$0	$0	$0	$313,248	$0
$15,575	$0	$0	$0	$261,992	$0
0	0	0	0	276625.328	0
$0	$270,144	$0	$0	$0	$0
$0	$270,000	$0	$0	$0	$0
$39,636	$0	$39,636	$187,088	$0	$0
$165,569	$0	$92,531	$0	$0	$0
$123,750	$0	$0	$0	$123,750	$0
$167,692	$0	$72,888	$0	$0	$0
$0	$233,732	$0	$0	$0	$0
$86,428	$118,978	$0	$0	$0	$0
$0	$204,516	$0	$0	$0	$0
$0	$194,331	$0	$0	$0	$0
$187,400	$0	$0	$0	$0	$0
$0	$23,373	$162,855	$0	$0	$0
$0	$175,000	$0	$0	$0	$0
$0	$0	$0	$171,755	$0	$0
$0	$65,000	$0	$0	$104,846	$0
$0	$0	$150,000	$0	$0	$0

Appendix 2

TB R&D Funders by Rank, 2018 (continued)

2018 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
106	Legochem Biosciences	C	$140,213
107	Abbott	C	$124,376
108	Research Institute of Tuberculosis/Japan Anti-Tuberculosis Association	P	$101,093
109	French National Agency for AIDS Research (ANRS)	P	$100,675
110	Korean Rural Development Administration	P	$98,400
111	Netherlands Ministry of Health, Welfare and Sport	P	$94,661
112	Qiagen	C	$90,000
113	Australian Research Council	P	$88,475
114	Human Frontier Science Program	F	$85,756
115	Korean Ministry of Trade, Industry and Energy	P	$85,500
116	European Molecular Biology Organization	P	$82,847
117	Stop TB Partnership (UNOPS)	M	$69,440
118	Japan Society for the Promotion of Science	P	$68,664
119	National Research Foundation of Korea	P	$67,500
120	U.K. Natural Environment Research Council	P	$66,190
121	Taiwan Ministy of Science and Technology	P	$60,000
122	Korean Institute of Tuberculosis	P	$59,850
123	European Centre for Disease Prevention and Control	P	$59,454
124	Archival Pharma	C	$58,433
125	Norwegian Ministry of Health and Care Services	P	$53,970
126	Individual donors to TB Alliance	F	$50,311
127	Healthcare Infection Society	F	$46,242
128	Grand Challenges Canada	P	$38,735
129	Taiwan Ministry of Health and Welfare	P	$30,000
130	Korea Atomic Energy Research Institute	P	$27,000
131	LHL International	P	$25,703
132	Indian Science and Engineering Research Board	P	$22,385
133	AFI Corporation	C	$18,060
134	Nigerian Institute of Medical Research	P	$13,850
135	Bouisson Bertrand Institute	F	$13,441
136	FUJIFILM Wako Pure Chemical Corporation	C	$4,876
137	Medical & Biological Laboratories Co.	C	$4,515
138	Faber Daeufer	C	$2,000
139	Astellas Pharma Inc.	C	$903
	TOTAL		$906,125,319

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

† Organization has reported to TAG each year since 2005

BASIC SCIENCE	DIAGNOSTICS	DRUGS	VACCINES	OPERATIONAL RESEARCH	INFRASTRUCTURE/ UNSPECIFIED
$0	$0	$140,213	$0	$0	$0
$0	$124,376	$0	$0	$0	$0
$0	$0	$0	$0	$0	$101,093
$0	$0	$100,675	$0	$0	$0
$0	$0	$98,400	$0	$0	$0
$0	$0	$0	$94,661	$0	$0
$0	$90,000	$0	$0	$0	$0
$88,475	$0	$0	$0	$0	$0
$85,756	$0	$0	$0	$0	$0
$0	$85,500	$0	$0	$0	$0
$82,847	$0	$0	$0	$0	$0
$0	$0	$69,440	$0	$0	$0
$25,474	$0	$0	$0	$43,190	$0
$67,500	$0	$0	$0	$0	$0
$0	$0	$0	$0	$66,190	$0
$0	$0	$0	$60,000	$0	$0
$59,850	$0	$0	$0	$0	$0
$0	$59,454	$0	$0	$0	$0
$0	$0	$0	$58,433	$0	$0
$53,970	$0	$0	$0	$0	$0
$0	$0	$50,311	$0	$0	$0
$46,242	$0	$0	$0	$0	$0
$0	$38,735	$0	$0	$0	$0
$30,000	$0	$0	$0	$0	$0
$0	$27,000	$0	$0	$0	$0
$0	$0	$0	$0	$25,703	$0
$22,385	$0	$0	$0	$0	$0
$0	$18,060	$0	$0	$0	$0
$13,850	$0	$0	$0	$0	$0
$0	$13,441	$0	$0	$0	$0
$0	$4,876	$0	$0	$0	$0
$0	$4,515	$0	$0	$0	$0
$0	$0	$2,000	$0	$0	$0
$0	$0	$903	$0	$0	$0
$177,951,942	$79,819,860	$336,433,663	$109,476,154	$122,087,944	$80,355,757

Appendix 3

TB Activists Interviewed by TAG

1	Kajal Bhardwaj	Independent lawyer working on health and rights in India
2	Denis Godlevskiy	International Treatment Preparedness Coalition in Eastern Europe and Central Asia (ITPCru)
3	Janika Hauser	Parliamentary advocacy officer, RESULTS UK
4	Rosa Herrera	TB physician and Global TB Community Advisory Board member (Global TB CAB)
5	Evaline Kibuchi	Chief national coordinator, Stop TB Partnership—Kenya
6	Kate O'Brien	We Are TB
7	Fifa Rahman	Board member for NGOs, Unitaid executive board
8	Marie Theunissen	Community Research Advisors Group member, Desmond Tutu TB Centre community advisory board coordinator
9	Els Torreele	Executive director, Médecins Sans Frontières Access Campaign
10	Wim Vandevelde	Global TB CAB member, Global Network of People Living with HIV/AIDS (GNP+)

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