TAG
Treatment Action Group

Stop TB Partnership

2016 Report on Tuberculosis Research Funding Trends, 2005–2015: No Time to Lose

October 2016
Treatment Action Group
By Mike Frick

ACKNOWLEDGMENTS

Treatment Action Group is grateful to all of the participating TB R&D funders that make this report possible and to the Stop TB Partnership, the Stony Wold-Herbert Foundation, and the TB Alliance for supporting the writing of this report. TAG would like to thank the TB scientists, funders, and activists who agreed to be interviewed for this report, many of whom are members of the Stop TB Partnership's New Tools Working Groups. Mike Frick thanks Audrey Kaem for providing the calm space in Boerum Hill, Brooklyn, New York, where this report was written.

ABOUT TAG

Treatment Action Group is an independent AIDS research and policy think tank fighting for better treatment, a vaccine, and a cure for AIDS.

TAG works to ensure that all people with HIV 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 AIDS.

TB/HIV PROJECT

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

Mike Frick is a TB/HIV senior project officer at TAG. He holds a bachelor's degree in international studies and Chinese from Kenyon College and a master of science degree in global health and population from the Harvard School of Public Health.

CONTACT TAG

Treatment Action Group

90 Broad Street, Suite 2503

New York, NY 10004 USA

Tel 1.212.253.7922

Fax 1.212.253.7923

tag@treatmentactiongroup.org

www.treatmentactiongroup.org

ISBN 978-0-9905242-8-1

Layout by Hollander Snow Studio, Inc.

2016 Report on Tuberculosis Research Funding Trends, 2005–2015: No Time to Lose

OCTOBER 2016

TREATMENT ACTION GROUP

BY MIKE FRICK

EDITED BY MARK HARRINGTON AND ERICA LESSEM

DEDICATION

In memory of Stephen Lawn

We dedicate this report to Professor Stephen Lawn, accomplished and passionate TB and HIV researcher and wonderful human being. May his words spoken in Cape Town on December 4, 2015, inspire us all:

"The science is there. We know what the interventions are. But we need a new attitude . . . it's outrageous that so many people have this fatal disease and we just make out 'this is just too difficult to do.' Let's just get on and do it."

—Stephen Lawn, London School of Hygiene & Tropical Medicine and University of Cape Town

TABLE OF CONTENTS

Executive Summary

The dearth of resources for tuberculosis research and development (TB R&D) is by now widely known. The 11th annual *Report on Tuberculosis Research Funding Trends* from Treatment Action Group (TAG) only further demonstrates this dismal truth. In 2015, funding for TB R&D fell by US$53.4 million from 2014, landing at $620,600,596—its lowest level since 2008. This is not the first time funding for TB research has fallen—TAG reported a $36.5 million decrease in 2012 and a $12.3 million drop in 2014—but it marks the biggest decline since TAG began tracking global funding for TB R&D 11 years ago. And the timing of this decline is inauspicious, coming at the opening of a new era of global action against TB in which the goalposts frame a more ambitious vision of the future: a world free of TB.

Every beginning also marks an end, in this case the end of the Stop TB Partnership's *2011–2015 Global Plan to Stop TB (2011–2015 Global Plan)*, a roadmap for expanding and strengthening the implementation of TB services and intensifying R&D to make possible the diagnostic tests, preventive interventions, and combination treatments that together could end TB as a public health threat. By tracking annual spending on TB research since 2005, TAG has sought to create accountability for meeting the *Global Plan*'s targets for R&D. With data on 2015 funding now in hand, we can comprehensively review the successes and setbacks of the last five years. The summary judgment looks bleak: actual funding has fallen far short of the *2011–2015 Global Plan* targets in every area of TB R&D, from basic science to the development of new diagnostics, drugs, and vaccines to operational research on the implementation of new and existing tools (figure 1). The $3.29 billion funders invested in TB R&D over 2011–2015 amounted to only one-third of the $9.84 billion target.

This is far from what the authors of the *2011–2015 Global Plan* envisioned. In stating their goals for TB research, the developers of the plan sought more than just a high dollar figure; they were seeking tangible scientific progress. The R&D section of the *2011–2015 Global Plan* mixed two very distinctive vocabularies. In certain places, it spoke in an activist voice of achieving "radical transformation" in TB prevention, diagnosis, and treatment by approaching research in an "entirely new way." In other places, the chapter borrowed metaphors from physics and the natural sciences—for example, its opening call for a "quantum leap" in TB research. These two ways of speaking—part activist, part technocrat—met in the chapter's closing reference to a "TB research movement." This movement referred both to the social mobilizations and global solidarity campaigns that have underpinned rapid scientific advances against the HIV pandemic and to physical movement—the forward leaps in financial resources required to take TB R&D to a higher plane of innovation and productivity.

Social mobilizations to support TB R&D made significant strides over the past five years in terms of raising awareness about the shortfall in funding and pressuring governments and the global community to fill this deficit. One of the most memorable steps reverberated with the footfalls of the hundreds of people who marched with the Treatment Action Campaign in Cape Town, South Africa, on December 3, 2015, under the rallying cry "invest in TB R&D." Many of the marchers carried signs emblazoned with the words "we die of TB," an unforgettable reminder to political leaders that funding TB research is necessary to uphold the human rights to life, health, and scientific progress. The marchers called on leaders of the BRICS nations (Brazil, Russia, India, China, and South Africa) plus Indonesia to triple funding for TB research and asked for sizeable investment increases from developed countries, including Germany and the United States. Thanks to these activists and others, the lack of funding for TB research is now understood as a human rights issue in need of a collective, political solution.

Unfortunately, the amount of money available for TB research has not grown apace with community demands. Total TB R&D funding stayed relatively flat over 2011–2015, ranging from a high of $686.3 million in 2013 to a low of $620.6 million in 2015. Movement in TB research funding has been governed principally by inertia, and even then, funding has not always moved in the right direction. Decreases in TB R&D spending in 2012, 2014, and 2015 offer reminders that a flat trend can easily turn into a falling one. (In fact, the

FIGURE 1

2011–2015 *Global Plan* Funding Targets versus Actual Funding

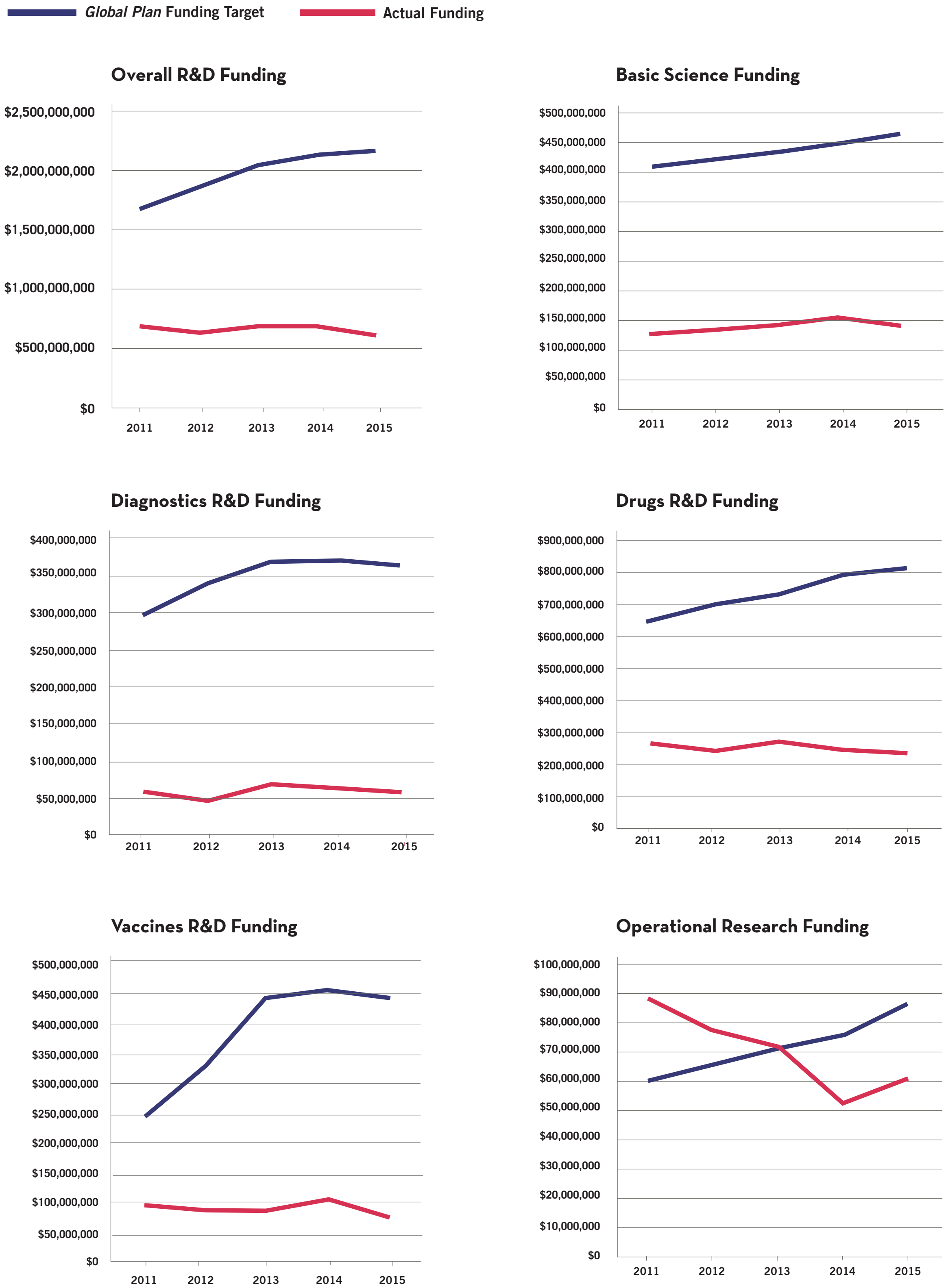
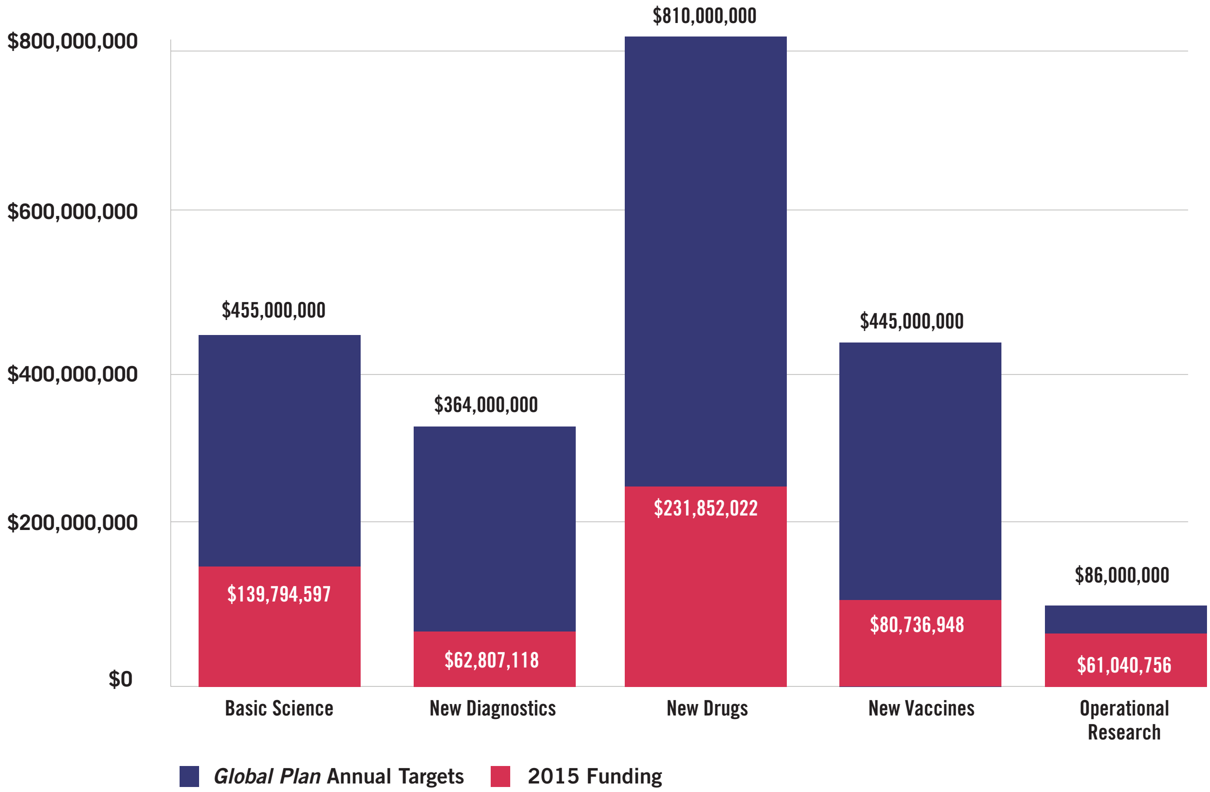


FIGURE 2

Annual *Global Plan* Research Funding Targets versus 2015 Funding



flat line that represents funding from 2011 to 2015 masks a negative slope when the numbers are adjusted for inflation.) The concentration of funding among a few donors from a few countries (the United States government and the Bill & Melinda Gates Foundation [Gates Foundation] together accounted for 57 percent of TB R&D funding over this period) reveals the lack of solidarity underpinning the TB research cause. The *2011–2015 Global Plan* acknowledged that high-income countries would need to contribute as much as half of the necessary resources, but it also called on TB-endemic countries, especially the BRICS nations, to "mobilize the rest internally." With the exception of modest investments from India ($11.1 million in 2015) and South Africa ($3.9 million in 2015), BRICS countries have not mobilized in support of TB research.

This report is a report card, not a postmortem exam. While the data we present here diagnose a serious shortage of resources for TB research, the problems identified are not irreparable. By design, report cards are retrospective. But they are only useful if, in summarizing past performance, they also give a direction for future improvement. Aside from TB having regained its pre-1990 position as the world's leading infectious killer, one of the strongest arguments in support of expanding TB R&D may be how much the field's scientists have accomplished with so little. Insufficient investment does not mean that TB research is a bad investment. The opposite is true. With just a third of the *2011–2015 Global Plan* funding target in hand, the TB research field made several historic advances:

- the conditional approval of two new drugs from novel classes to treat drug-resistant TB, the first in over four decades;
- the development of a shorter regimen for treating TB infection that is safe and efficacious in children and people with HIV;
- the development of several new diagnostic tests, including a rapid and robust alternative to smear, a simple test that can identify TB in people with HIV with very low CD4+ T-cell counts,

and several options for diagnosing first- and second-line drug resistance faster than conventional culture; and

- the beginnings of a true paradigm shift in fundamental understandings of the biology of *Mycobacterium tuberculosis* (MTB), the causative agent of TB, as it interacts with its human host along what is now seen as a continuum of infection and disease.

TB researchers have upturned old dogmas, introduced new tools and strategies, organized more meaningful engagement of communities in clinical trials, and generated a folio of new ideas and revised approaches that merit investigation over the next five years. It will take a massive step up in funding to break the inertia that kept the TB R&D field from experiencing the full promise of this upward trajectory.

In solidarity,

Introduction

"Limited funding is impacting everything in our TB work. First, it impacts the speed at which new tools can become available. Second, it impacts the pipeline. It also impacts advocacy efforts. Fourth, the annual decline in research funding will be translated into failures in reaching any target in the *Global Plan to End TB*, WHO End TB Strategy, and Sustainable Development Goals."

—Lucica Ditiu, Executive Director, Stop TB Partnership

Between 2011 and 2015, global funding for TB R&D totaled $3.29 billion. The *2011–2015 Global Plan* estimated that the world needed to spend $9.84 billion on TB R&D over this five-year period to enable the scientific advances in TB prevention, diagnosis, and treatment required to end TB as a public health threat.[1] Instead, combined spending by governments, private-sector corporations, charitable organizations, and multilateral institutions amounted to just one-third of this target. The period opened on a relatively high note in 2011 when donors gave $675.3 million to TB R&D but closed on a much lower one when funding dropped to $620.6 million in 2015, the lowest level of spending since 2008.

This 11th consecutive *Report on Tuberculosis Research Funding Trends* by TAG presents new data on TB research funding in 2015, the fifth and final year of the *2011–2015 Global Plan,* and, in closing out the reporting period, serves as a report card on the plan's goals for R&D. The report reviews scientific progress in relation to funding overall and within each of the six research areas tracked by TAG: basic science, diagnostics, drugs, vaccines, operational research, and research related to pediatric TB. (TAG collects information on a seventh category—infrastructure and unspecified projects—but does not provide an in-depth analysis of this area due to its miscellaneous nature.) Quotations from interviews TAG conducted with leading TB researchers and activists about the state of TB research and funding for it appear throughout the report and offer firsthand perspectives on how available funding affected progress and shaped opportunities over the past five years.

Interviewees overwhelmingly expressed disappointment that funding failed to measurably increase over the past five years, but many also highlighted the significant advances made in each area of research despite the scarcity of financial resources. From basic science to operational research, scientists met specific obstacles and challenges—some anticipated, others not—whose solutions required embracing new approaches, theories, or tools. Gilla Kaplan, director of the tuberculosis program at the Gates Foundation, articulated this idea when she told TAG, "we've seen a great amount of progress. One of the biggest achievements has been an expanding recognition that focused, problem-solving R&D can help us better understand the basic science behind TB and develop smarter tools to impact the trajectory of the disease." Instead of unleashing a flood of new products on the market, developers of new TB diagnostics, drugs, and vaccines more often found themselves carrying findings from clinical trials back to the lab to engage basic scientists working to clarify fundamental understandings of the biology of TB infection and disease.

While basic scientists and product developers spent a large part of the period piecing together a more nuanced picture of TB at the level of the cell and in the human host, epidemiologists and public health professionals continued to track the magnitude of the TB epidemic globally. TB incidence continued its slow decline of 1.2% per year from 2011 to 2015, but this miniscule decline was countered by increases in human population, and developments within and outside of the TB field offered few reasons to celebrate

TABLE 1

Changes in TB R&D Funding, 2005-2015

YEAR	TOTAL TB R&D INVESTMENT	CHANGE OVER PREVIOUS YEAR	CHANGE OVER PREVIOUS YEAR (%)	CHANGE OVER 2005	CHANGE OVER 2005 (%)
2005	$358,476,537	N/A	N/A	N/A	N/A
2006	$418,928,300	$60,451,763	16.86	$60,451,763	16.86
2007	$478,343,421	$59,415,121	14.18	$119,866,884	33.44
2008	$494,576,235	$16,232,815	3.39	$136,099,698	37.97
2009	$636,979,349	$142,403,113	28.79	$278,502,812	77.69
2010	$643,360,390	$6,381,042	1.00	$284,883,853	79.47
2011	$675,328,887	$31,968,497	4.97	$316,852,350	88.39
2012	$638,783,272	-$36,545,615	-5.41	$280,306,735	78.19
2013	$686,303,295	$47,520,023	7.44	$327,826,758	91.45
2014	$674,036,492	-$12,266,804	-1.79	$315,559,955	88.03
2015	$620,600,596	-$53,435,896	-7.93	$262,124,059	73.12

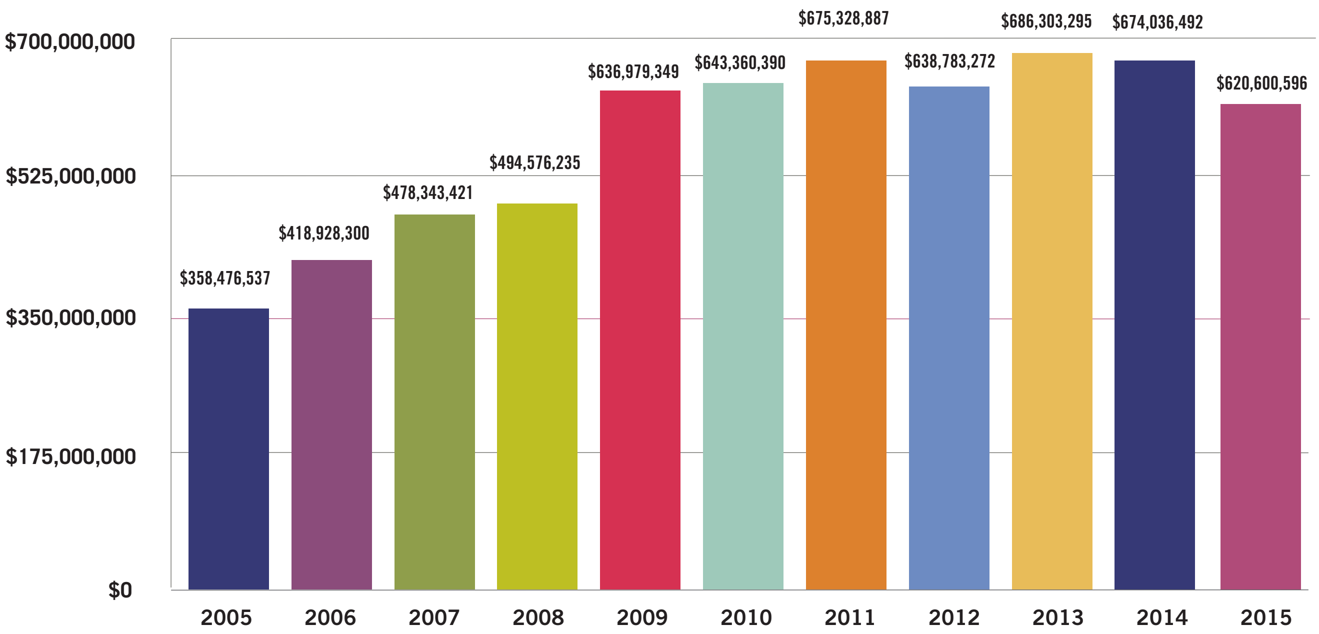
"There has been a tendency over the years to take R&D for granted, as though the medicines and diagnostics somehow miraculously appear when necessary. But in truth, ignoring the importance of R&D is disastrous when combatting an infectious disease like TB. We learned in HIV that R&D, once unleashed, has saved millions of lives. The same can and must be true of TB."

—Stephen Lewis,
Co-Director, AIDS-Free World

this modest pace. A prevalence survey in Indonesia uncovered double the number of TB cases than previously acknowledged, leading the World Health Organization (WHO) to upwardly revise its estimate of TB incidence.[2] A first-time analysis of drug-resistant TB (DR-TB) trends from 2008 to 2013 confirmed that DR-TB poses a serious threat to global health, with an estimated 500,000 new cases occurring every year.[3] These epidemiological shifts occurred against a backdrop of global instability. Economic stumbles and wavering political will in the BRICS nations dissipated any impression that middle-income countries could be counted on to fully finance the response to TB in the absence of international support.[4] Many countries and regions

FIGURE 3

Total TB R&D Funding, 2005-2015



also experienced unprecedented rates of internal and external migration.[5] Alongside these governmental challenges, structural shifts in the pharmaceutical industry revealed the risks of relying on the private sector to conduct infectious disease research. Between 2012 and 2014, three pharmaceutical companies left TB drug development as part of a larger, industry-wide pivot away from anti-infectives R&D.[6,7,8] All of these threats to progress formed the backdrop to the WHO's striking announcement in 2015 that TB had overtaken HIV as the world's leading cause of death due to a single infectious agent, a finding that threw the need for intensified research and innovation into stark relief.[9]

"Within the Southern Africa region, funding for HIV, TB, and malaria is likely to shift over the coming years from international donors to regular national budgets as countries graduate into middle-income-country status. Southern African countries need to start addressing the challenges faced in financing R&D, and advocacy is needed to push this agenda."

—Lynette Mabote, Team Leader, Regional HIV, TB and Human Rights Programmes, AIDS and Rights Alliance for Southern Africa

Methodology

"The good news is that in 2011 global R&D funding was almost doubled compared to 2005, with a steady increase from 2005 'til 2009. However, since 2009, we can see a plateau . . . indicating a rather worrying stagnation in global TB R&D funding. Considering that the methodology of the TAG report has improved with an increasing number of donors contributing to the survey, and that there seem to be newcomers, then this plateau may even shadow a slight decrease in global R&D funding."

—Christian Lienhardt, Team Leader, Research for TB Elimination, World Health Organization Global TB Programme

Each year since 2005, TAG has tracked global funding for TB R&D using an electronic survey sent to public, private, philanthropic, and multilateral organizations with known or potential investments in TB research. The survey asks recipients to enumerate the amount of money spent on TB R&D in a given year and classify spending by six categories corresponding to the research areas in the *2011–2015 Global Plan*. Following publication of the first-ever *Roadmap for Childhood Tuberculosis* in 2013, TAG began asking organizations to report funding for pediatric TB research across the same six categories (see note on TAG's pediatric TB research resource-tracking methodology).

RESEARCH AREAS TRACKED BY TAG:

1. Basic science: undirected, investigator-initiated research to discover fundamental knowledge about MTB and closely related mycobacterial organisms.

2. Diagnostics: preclinical and clinical trials of diagnostic technologies and algorithms.

3. Drugs: preclinical and clinical research on treatments and treatment strategies for TB infection and 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 tools and strategies to guide their effective implementation in program settings. Operational research may include randomized trials, surveillance, and epidemiological and observational studies.

6. Infrastructure/unspecified projects: TB research that the donor is unable to further classify.

For this year's report, TAG surveyed 194 organizations. We received 100 surveys in return and, from these, identified 111 organizations funding TB research. Fourteen organizations that returned surveys reported spending no money on TB R&D in 2015. Many funders reported investments in local currencies, which TAG converted into U.S. dollars using the July 1, 2015, 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. (However, we performed all calculations using unrounded data.) Dollar figures represent disbursements, or the actual transfer of funds made in 2015, rather than commitments or budgetary allocations for future years.

TAG takes careful measures to avoid double-counting awards reported by more than one donor. Multiple circumstances can give rise to double counting, including the fact that many organizations that receive funding for some projects serve as a source of funding for others (e.g., by issuing grants or making sub-awards using funds received under a larger parent grant). To address this situation, our survey asks recipients to note whether spending represents funding given to others, funding received from others, or self-funded research. Any awards listed by more than one survey participant enter our database as reported by the original-source donor. For collaborative projects supported by more than one organization, we ask funders to report only their contribution to the project, not total costs. In addition, TAG tracks spending by product development partnerships (PDPs) such as Aeras and the TB Alliance separately, since PDPs do not act as original-source donors.

To supplement the financial information, TAG conducted qualitative interviews with 11 TB experts; interviewees included scientists working in each area of TB research plus distinguished activists, community leaders, policymakers, and funders (see appendix 2 for a list of people interviewed by TAG). Each interviewee received an advance copy of preliminary survey findings in early September 2016 with a list of open-ended questions. We interviewed six individuals over the phone; the remaining five interviewees submitted answers in writing. Phone interviews lasted approximately 30–60 minutes and were recorded and transcribed verbatim. We grouped quotations from the transcripts and written responses into common themes, from which we selected the contributions that appear within and alongside the text of this report. TAG checked all quotations from phone interviews with the speakers prior to publishing. In some places, TAG edited quotations for length and clarity.

PEDIATRIC TB RESEARCH RESOURCE TRACKING METHODOLOGY

TAG's survey asks all funders to delineate support for pediatric TB research and assign any spending to one of the six core research areas. TAG further identifies research related to pediatric TB by conducting a keyword search of titles and abstracts contained in returned surveys using the following search terms: pediatric, paediatric, infant, child, kid, adolescent, and pregnant. While this methodology provides a reasonable estimate, it overlooks research that informs the development of pediatric products without enrolling children or studying TB infection or disease in them directly. Some funders have notified TAG that they lack the means to disaggregate pediatric research funding from their overall expenditure on TB R&D. Otsuka, for example, did not report how much of the $29 million it spent on TB drug development in 2015 went to pediatric delamanid studies. Donors supporting clinical trials, cohort studies, and epidemiological surveys that include people of all age groups can rarely specify the proportion of funds devoted to younger age groups. TAG urges all funders to develop ways of identifying and disaggregating pediatric TB research spending from within larger totals.

TABLE 2

TB R&D Funders by Rank, 2015

2015 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
1	U.S. National Institutes of Health, National Institute of Allergy and Infectious Diseases (NIAID)†	P	$178,686,059
2	Bill & Melinda Gates Foundation†	F	$110,985,743
3	U.S. National Institutes of Health, Other Institutes and Centers (NIH Other ICs)†	P	$34,920,532
4	U.S. Agency for International Development (USAID)†	P	$34,053,650
5	Otsuka Pharmaceuticals†	C	$29,042,414
6	U.K. Department for International Development (DFID)†	P	$23,034,975
7	GlaxoSmithKline (GSK)	C	$17,645,266
8	U.S. Centers for Disease Control and Prevention (CDC)†	P	$14,072,846
9	European Commission†	P	$13,775,984
10	UNITAID	M	$13,746,000
11	U.K. Medical Research Council (U.K. MRC)†	P	$10,692,435
12	Indian Council of Medical Research (ICMR)	P	$8,951,412
13	Company X†	C	$8,788,399
14	Company V	C	$8,332,778
15	Company Y†	C	$6,850,000
16	Wellcome Trust†	F	$6,653,184
17	German Federal Ministry of Education and Research (BMBF)	P	$6,501,534
18	Australian Department of Foreign Affairs and Trade (DFAT)	P	$5,139,706
19	Swiss National Science Foundation (SNSF)	P	$4,874,818
20	Qiagen	C	$4,870,000
21	Australian National Health and Medical Research Council (NHMRC)	P	$4,734,126
22	European and Developing Countries Clinical Trials Partnership (EDCTP)†	P	$4,650,743
23	Macleods Pharmaceuticals	C	$3,500,000
24	Public Health England	P	$3,260,041
25	Eli Lilly†	C	$2,750,000
26	Max Planck Institute for Infection Biology	P	$2,640,000
27	Canadian Institutes of Health Research†	P	$2,631,348
28	Norwegian Agency for Development Cooperation (NORAD)	P	$2,613,222
29	Institut Pasteur†	F	$2,441,449
30	Global Health Innovative Technology Fund (GHIT)	M	$2,430,526
31	French National Agency for Research (ANR)	P	$2,362,871
32	Swiss Federal Institute of Technology in Lausanne (EPFL)	P	$2,301,582
33	U.S. President's Emergency Plan for AIDS Relief (PEPFAR)††	P	$1,948,342
34	French National Agency for AIDS Research (ANRS)	P	$1,940,408
35	Dutch National Postcode Lottery*	P	$1,856,013
36	Statens Serum Institut	P	$1,830,784
37	Singapore Ministry of Health, National Medical Research Council (Singapore NMRC)	P	$1,815,489
38	Japanese Ministry of Health, Labour and Welfare	P	$1,722,841
39	Swiss Initiative in Systems Biology (SystemsX.ch)*	P	$1,654,844

P = Public-Sector R&D Agency; C = Corporation/Private Sector; M = Multilateral; F = Foundation/Philanthropy;
* New Donor; † Organization has reported to TAG each year since 2005
†† PEPFAR's total only includes funding for operational research (implementation science) sponsored by PEPFAR agency headquarters and does not include country-level funding used for operational research. As a result, this number likely significantly underestimates PEPFAR's support for TB research.

TABLE 2

TB R&D Funders by Rank, 2015 (continued)

2015 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
40	Singapore Agency for Science, Technology and Research (A*STAR)*	P	$1,645,314
41	Swedish Research Council	P	$1,588,852
42	National Philanthropic Trust*	F	$1,500,000
43	Indian Ministry of Health and Family Welfare (MOHFW)	P	$1,493,809
44	South African Medical Research Council (SAMRC)	P	$1,345,066
45	Japan International Cooperation Agency (JICA)	P	$1,222,657
46	South African Department of Health	P	$1,159,795
47	Irish Aid	P	$1,118,080
48	Taiwan Centers for Disease Control	P	$1,102,570
49	Innovative Medicines Initiative	P	$1,080,119
50	U.S. National Science Foundation	P	$996,557
51	Company R*	C	$880,133
52	Biofabri	C	$838,238
53	Médecins Sans Frontières	F	$801,991
54	National Research Foundation, South Africa	P	$731,142
55	Korea Drug Development Fund	P	$712,000
56	Qurient	C	$712,000
57	Indian Ministry of Science and Technology, Department of Biotechnology	P	$641,740
58	South African Department of Science and Technology (DST)	P	$637,937
59	World Health Organization (WHO)	M	$618,189
60	Irish Health Research Board	P	$584,257
61	Serum Institute of India*	C	$569,033
62	Netherlands Organization for Health Research and Development (ZonMw)	P	$559,040
63	Japan BCG Laboratory	C	$499,350
64	U.S. Food and Drug Administration (FDA)†	P	$463,978
65	Korean Ministry of Health and Welfare	P	$439,972
66	Company W	C	$438,300
67	Japan Agency for Medical Research and Development (AMED)*	P	$423,124
68	Science Foundation Ireland*	P	$417,774
69	Danish Council for Independent Research	P	$391,718
70	BioDuro	C	$337,500
71	Australian Research Council	P	$297,852
72	Fondation Total*	F	$279,520
73	Health Research Council of New Zealand	P	$274,570
74	Damien Foundation Belgium	F	$239,828
75	Korean Ministry of Science, ICT and Future Planning	P	$225,170
76	Foundation Jacqueline Beytout	F	$208,699
77	Cepheid	C	$200,000
78	QuantaMatrix	C	$178,000

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

TABLE 2

TB R&D Funders by Rank, 2015 (continued)

2015 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
79	Korea Centers for Disease Control and Prevention	P	$169,909
80	Swiss Lung Foundation*	F	$157,452
81	Research Council of Norway	P	$139,788
82	Lundbeck Foundation*	F	$127,901
83	SK Telecom*	C	$125,490
84	LG Life Sciences	C	$115,700
85	Southeastern Norway Regional Health Authority	P	$115,134
86	Colombia Department of Science, Technology and Innovation	P	$108,800
87	Howard Hughes Medical Institute	F	$100,000
88	Norwegian Public Health Association	P	$92,768
89	European Molecular Biology Organization*	F	$73,067
90	Somalogic	C	$71,741
91	Thrasher Research Fund	F	$63,786
92	U.K. National Institute for Health Research	P	$59,760
93	Innovation Fund Denmark	P	$55,727
94	LHL International	P	$53,111
95	Colombia National Institute of Health	P	$51,300
96	YD Diagnostics*	C	$50,000
97	International Union of Immunological Societies	F	$48,918
98	National Research Council of Thailand*	P	$40,000
99	Stop TB Partnership	M	$39,500
100	Norwegian Institute of Public Health	P	$32,538
101	Global BioDiagnostics	C	$31,774
102	Taiwan Ministry of Science and Technology	P	$30,000
103	Else Kröner-Fresenius Foundation*	F	$25,000
104	National Health Laboratory Service Research Trust, South Africa	P	$20,445
105	National University Health System, Singapore	P	$16,334
106	Faber Daeufer	C	$10,000
107	Foundation CHU Sainte-Justine*	F	$6,455
108	Individual donors to TB Alliance	F	$4,908
109	Colombian Ministry of Health and Social Protection	P	$4,630
110	Firland Foundation	F	$2,200
111	Philippine Tuberculosis Society*	F	$221

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

The Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) informed TAG that it can only report its cumulative expenditure on TB operational research between 2002 to 2015, which totaled $120.2 million. The Global Fund recently introduced a new measurement framework which should enable it to report its annual spending on TB research moving forward.

Organizations that previously supported TB research but reported no new spending in 2015: Danish International Development Agency (DANIDA), Global Affairs Canada (CIDA), Swedish International Development Cooperation Agency (SIDA), Swiss Agency for Development Cooperation (SDC), U.S. Department of Defense Medical Research and Development Program (DMRDP), Dutch Directorate-General for International Cooperation (DGIS), Spanish Agency for International Development Cooperation (AECID), and Grand Challenges Canada.

Limitations

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, as the true number of TB research funders worldwide is unknown. TAG takes several steps to ensure the report's comprehensiveness. First, we cast a wide net by adding new organizations to our survey list each year; most of these organizations do not have known TB R&D investments but either support health research generally or have a record of investing in related diseases. Second, the small size of the TB research field, and the high degree of concentration of funding, allows us to judge the success of our efforts by tracking the participation of the 30 largest funders of TB research year to year. The composition of the top 30 list has remained remarkably stable over time. This year, 29 of the top 30 funders from 2014 participated in the survey, producing a 96 percent yield among this core sample. Staff changes at the French National Institute of Health and Medical Research (INSERM) precluded its participation this year.[10] In 2014, INSERM ranked 26th and gave $3.3 million to TB R&D—all going toward basic science research—which comprised less than 0.5% of last year's total.

To expand the reach of our survey in under-represented regions, TAG had all survey materials translated into French, Spanish, Russian, Chinese, and Portuguese. Policies and practices governing data release to nongovernmental organizations such as TAG vary widely by country political contexts. To overcome the special challenges of securing data from Russia and China, TAG requested assistance from WHO country offices and, in the case of China, approached the U.S. embassy in Beijing. Despite these efforts, TAG did not receive any information from entities in either China or Russia. We believe both countries invest significantly in TB research. In China, most funds probably come from the Ministry of Science and Technology and the Chinese Academy of Sciences.[11] In Russia, we expect that the Ministry of Health and the Central TB Research Institute of the Russian Academy of Medical Sciences contribute the majority of TB research funds.[12] A few funders with known investments in TB research did not return surveys this year, including the Howard Hughes Medical Institute, which supports the KwaZulu-Natal Research Institute for TB-HIV in South Africa.

Rede TB (the Brazilian Network for Research in Tuberculosis) submitted information after our database locked but before this report went to press. Rede TB members—which include public, private, and not-for-profit organizations in Brazil—reported investing $1.9 million in TB research in 2015. Their investments are not included in the published figures that follow. In addition, the Canadian Institutes of Health Research (CIHR) and Company V provided TAG with supplementary data not included in their original submissions after the database locked. CIHR reported an additional $1,846,143 in funding, and Company V reported an additional $2,795,201. If added to the amounts originally reported to TAG, these numbers would raise CIHR's total 2015 TB R&D funding to $4.5 million and Company V's to $11.1 million. These corrections, and any others submitted to TAG, will enter print in next year's report. Please contact TAG at tbrdtracking@treatmentactiongroup.org if you have other information or corrections to share.

Resource tracking is a collaborative endeavor, and TAG is grateful to the funding institutions across the world that participate in our survey each year. TAG makes every effort to minimize the reporting burden on participating organizations, but even so, completing the survey takes considerable time and effort on the part of dozens of funding officers and administrative staff, each of whom has our special thanks. Table 2 acknowledges organizations that have reported to TAG every year since 2005 with a dagger (†) appearing next to their names.

Results

“The top donors, the Bill & Melinda Gates Foundation and NIAID, give almost 50 percent of the total funding. The involvement of other actors and sectors is very low, depicting very low commitment to fund TB research. TB R&D has been shelved by other actors; it is not their priority area.”

—Dorothy Namutamba, Programs Manager, International Community of Women Living with HIV Eastern Africa, and Co-Chair, Community Research Advisors Group

In 2015, global funding for TB R&D totaled $620,600,596, a decline of $53.4 million (8%) from 2014 and the lowest level of funding since 2008. This amount falls $1.6 billion short of the *2011–2015 Global Plan*’s target of $2.2 billion in 2015.

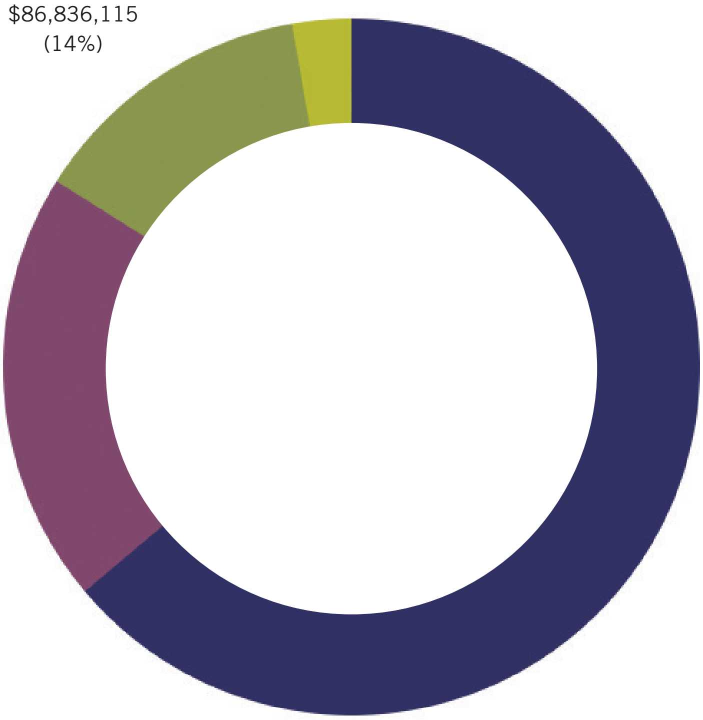
Several factors contributed to this significant drop in spending. First, many organizations indicated that the year 2015 either fell in between the milestones of grant payment schedules or marked a transitional year between the stop and start of major award programs. For example, the European Commission (EC) spent $13.8 million in 2015, $21 million less than the $34.9 million it gave in 2014. The EC Directorate-General for Research and Innovation attributed this gap to the EC’s 18-month payment cycle, meaning that projects last paid in late 2014 will not receive their next installment until 2016.[13] This affected two large TB vaccine projects; in addition, a new collaborative TB drug discovery initiative supported by the EC opened in 2015 but will not receive its first payment until 2016. Several development agencies—including Global Affairs Canada (formerly the Canadian International Development Agency), the Dutch Directorate-General for International Cooperation, and the Danish International Development Agency—reported zero investments in 2015 but indicated new TB research grants would start in 2016.[14,15]

However, grant cycles do not tell the whole story. Japanese pharmaceutical company Otsuka, the developer of new TB drug delamanid, has ranked as the third-largest donor to TB R&D since 2008. In 2015, Otsuka dropped to fifth place with investments of $29 million, a $24.2 million (45%) decrease from the $53.2 million it spent in 2014. This decline partly reflects the maturation of delamanid’s development program; delamanid’s phase III trial has completed enrollment, and Otsuka plans to publish results in 2018.[16] Otsuka’s lower total is also the product of macroeconomic policies that caused the Japanese yen to depreciate significantly against the U.S. dollar.[17] On July 1, 2015, the day TAG uses to convert foreign currencies into U.S. dollars, the yen-to-dollar exchange rate was near its lowest point in three years.[18] When denominated in yen, Otsuka’s 2015 investment of ¥3.6 billion is still lower than the ¥5.4 billion the company spent in 2014, but only by 34 percent.

On an aggregate level, funding for TB research declined across all sectors, except among multilateral institutions, where funding increased from $8.2 million in 2014 to $16.8 million in 2015. The doubling in multilateral funding is solely attributable to global-health financing mechanism UNITAID, which gave $9.5 million to the endTB project, a joint effort by Partners In Health (PIH), Médecins Sans Frontières (MSF), and Interactive Research & Development (IRD) to identify optimal combinations of new and repurposed TB drugs. Funding from public agencies and philanthropic organizations declined by around $25 million each, while funding from the private sector decreased by nearly $12 million. The relative contributions of different sectors to TB research, however, remain unchanged. Public-sector funding of $393 million accounted for 63 percent of total spending, followed by the philanthropic sector with $124 million (20%), the private sector with $86.8 million (14%), and multilateral institutions with $16.8 million (3%).

FIGURE 4

Total TB R&D Funding by Funder Category, 2015
Total: $620,600,596



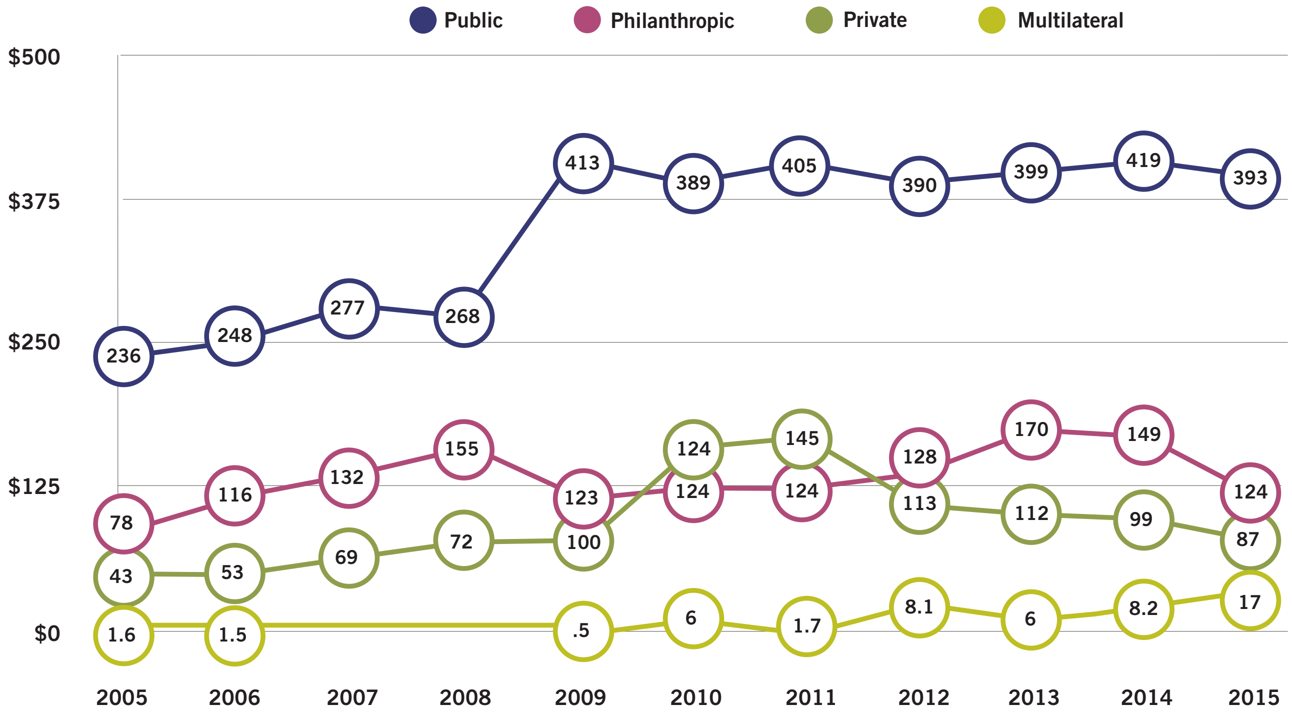
Funders spent the most money on TB drug R&D ($231.9 million), followed by basic science ($139.8 million), vaccines ($80.7 million), diagnostics ($62.8 million), operational research ($61.0 million), and infrastructure/unspecified projects ($44.4 million). Each category of research saw a decline in spending compared with 2014, with the exception of operational research, where funding increased by $8.2 million. With a decline of $30.6 million, TB vaccine R&D suffered the biggest drop and returned to a level of spending it last saw in 2010. This marked the second consecutive year of declining funding for TB drug development. Although the $11.5 million decrease between 2014 and 2015 was smaller than the $24.5 million drop between 2013 and 2014, funding for TB drug R&D has returned to its lowest level since 2010. Funding for TB basic science fell $10.3 million, pulling even with the $138 million it received in 2013. TB diagnostics funding posted the smallest decline ($2.6 million), but this was enough to knock diagnostics back to its lowest level of funding since 2012. In short, 2015 will be remembered for the strong feelings of déjà vu it summoned. The decreases in spending in 2015 were large enough to roll back smaller gains made over the last three years, leaving funding at the end of the *2011–2015 Global Plan* right back where it started at the beginning.

"It is clear to us that without adequate funding, the global community will not have the tools to control and eliminate TB. The levels of funding in 2015 are simply not enough. And sadly, the HIV community is starting to understand that if the world doesn't deal with TB, [their] efforts will remain unsuccessful."

—Jérôme St-Denis, Senior Advocacy and Resource Mobilization Officer, FIND

FIGURE 5

Total TB R&D Funding by Funder Category, 2005-2015 (in Millions)



"How is it possible that in 2015, every category of research has declined or is static in funding with the exception of operational research? Even more inexplicable is the fact that 2015 is the lowest year in financial terms since 2008. Even the recession period of 2009 was $30 million ahead of 2015. Something has gone dreadfully wrong. The continued decline speaks to one-and-a-half million deaths from TB a year."

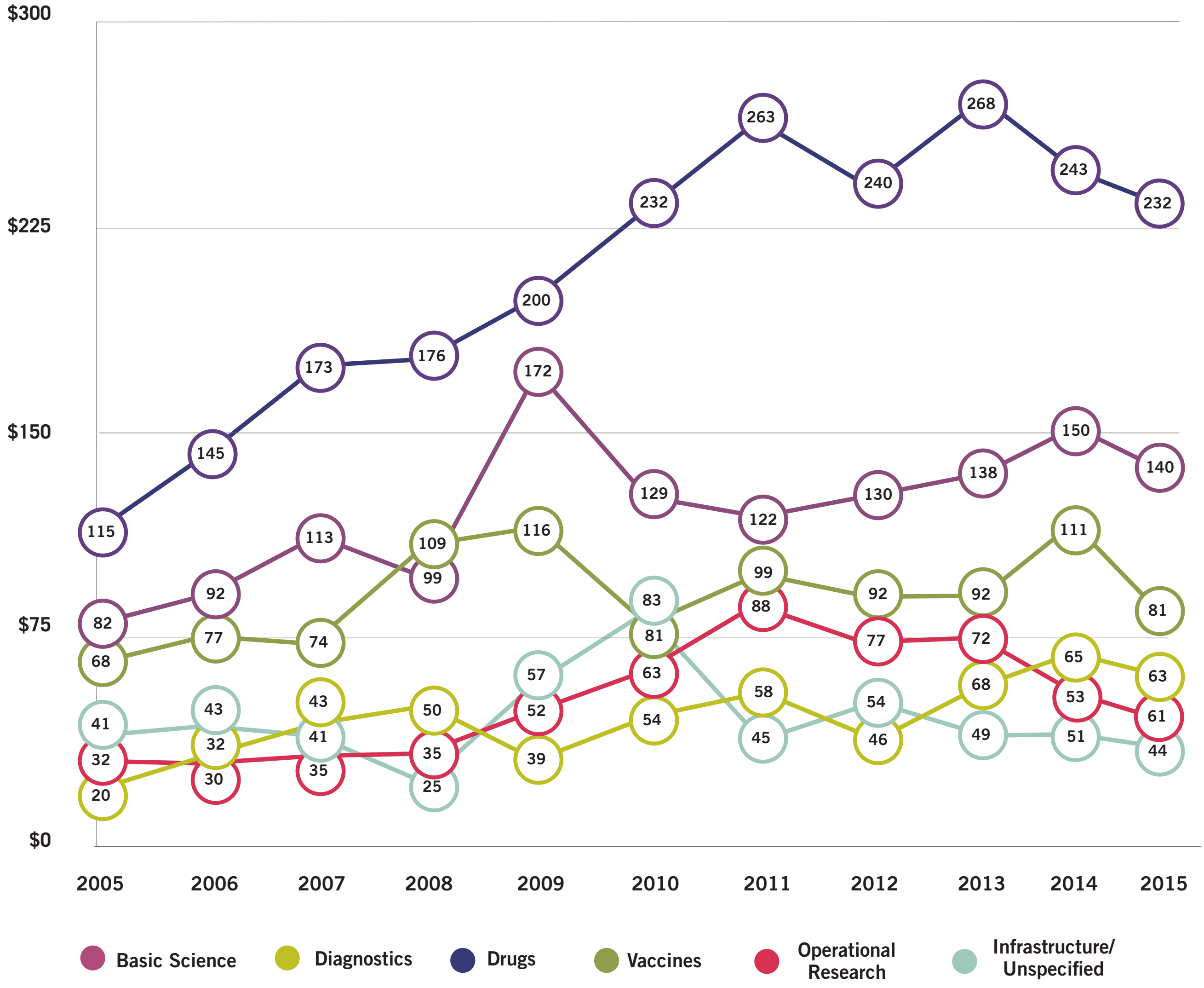
—Stephen Lewis, Co-Director, AIDS-Free World

This return to past funding levels drew condemnation from some of the TB experts whom TAG interviewed. "Financially, we cannot speak of any progress in R&D. If anything, we see this decrease in the financing trends," said Lucica Ditiu, executive director of the Stop TB Partnership. This decrease in funding led Stephen Lewis, co-director of AIDS-Free World, to ask, "how is it possible that in 2015, every category of research has declined or is static in funding with the exception of operational research? Even more inexplicable is the fact that 2015 is the lowest year in financial terms since 2008. Even the recession period of 2009 was $30 million ahead of 2015. Something has gone dreadfully wrong."

This backsliding also sparked concern among TB scientists. "As a scientist in the field who's been involved in TB research for many years, the fact that there was less investment in TB research in 2015 than in 2009—I consider it to be indefensible in light of what we now know: TB is now the leading infectious disease killer. Indefensible. That's all I can say, that's the word I've got," said Valerie Mizrahi, director of the Institute of Infectious Disease and Molecular Medicine, University of Cape Town.

FIGURE 6

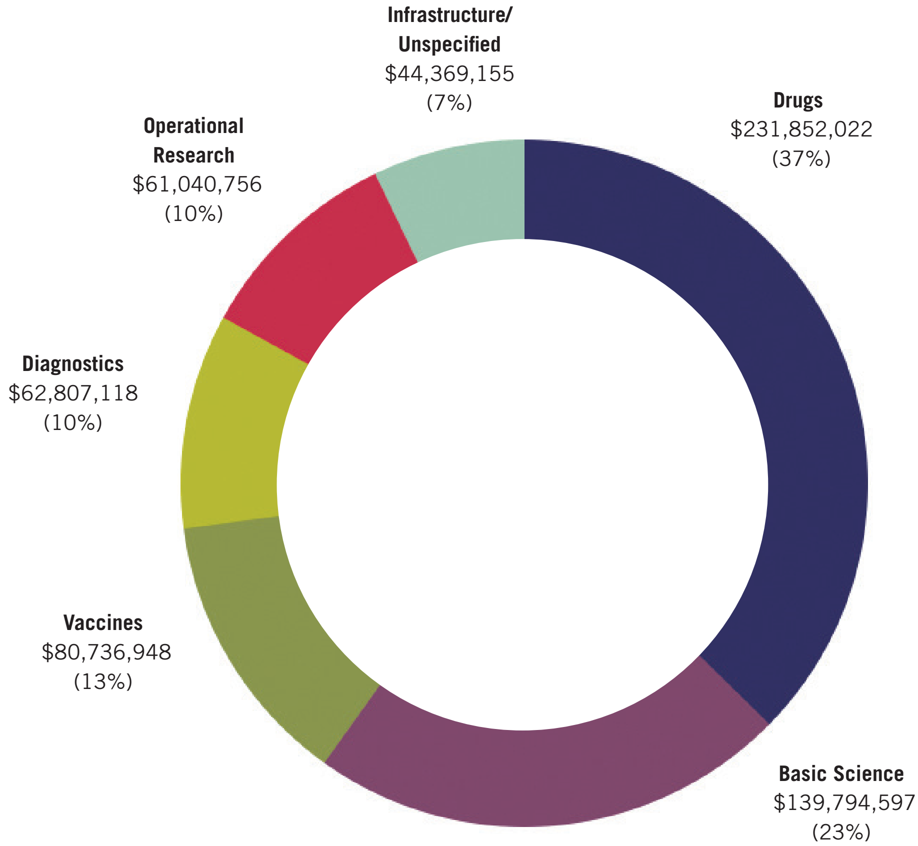
Total TB R&D Funding by Research Category, 2005–2015 (in Millions)



Funding sources for each area of research remain highly concentrated among one or two institutions. The U.S. National Institutes of Health (NIH) continued to contribute the lion's share of funding for TB basic science research with $95.4 million, 68 percent of the total. Within the NIH, the National Institute of Allergy and Infectious Diseases (NIAID) alone accounted for 58 percent of all basic science funding. NIAID also emerged as the largest funder of TB diagnostic R&D, where it gave $13.8 million (22%), followed by the Gates Foundation with $11.1 million (18%). The Gates Foundation and NIAID traded the top spots in TB drug development, where the Gates Foundation gave $48.1 million (21%) and NIAID $44.5 million (19%). The Gates Foundation was the biggest supporter of TB vaccine R&D, where its contribution of $26.9 million comprised one-third of total spending. A familiar ordering applied to operational research, where the Gates Foundation and NIAID gave a respective $17.7 million (29%) and $12.0 million (19%).

FIGURE 7

Total TB R&D Funding by Research Category, 2015
Total: $620,600,596



Dorothy Namutamba, program manager at the International Community of Women Living with HIV Eastern Africa and co-chair of the Community Research Advisors Group, pointed out that the dominance of NIAID and the Gates Foundation within each category of research also applied to overall TB R&D spending: "The top donors, the Bill & Melinda Gates Foundation and NIAID, give almost 50 percent of the total funding. The involvement of other actors and sectors is very low, depicting very low commitment to fund TB research. TB R&D has been shelved by other actors; it is not their priority area." Together, spending by NIAID and the Gates Foundation comprised 47 percent of global funding for TB R&D in 2015. The top five donors gave 63 percent of the total, the top 10 gave 76 percent, and the top 30 gave 92 percent. This degree of concentration has ruled the entire *2011–2015 Global Plan* period, indicating that the TB R&D funding base has not broadly expanded.

Basic Science

"At a high level, progress overall in the basic sciences has been impressive. I think that I've seen a much greater emphasis on actually studying human disease using the tools of basic science. This is not easy, but there have been significant advances in that area, and that stands out as something that distinguishes these five years compared to what happened before."

—Valerie Mizrahi, Director, Institute of Infectious Disease and Molecular Medicine, University of Cape Town

The *2011–2015 Global Plan* called for $455 million in funding for TB basic-science research in 2015 and $2.1 billion over the five-year period. In 2015, funders gave $139.8 million to TB basic science, resulting in a total of $678 million for basic science research from 2011 to 2015. These numbers leave an annual gap of $315 million and a five-year gap of $1.4 billion.

NIAID remained the uncontested giant of TB basic science, giving $80.9 million to this area—nearly 60 percent of the total. Combined, other NIH institutes and centers followed NIAID in second place with $14.5 million (10%). Other major supporters of TB basic science in 2015 included national science foundations in Switzerland, the United Kingdom, and Australia, as well as private charities such as the Wellcome Trust and the Gates Foundation. Over the 2011–2015 period, the NIH (NIAID plus all other institutes and centers) accounted for over 60 percent of all money spent on TB basic science research.

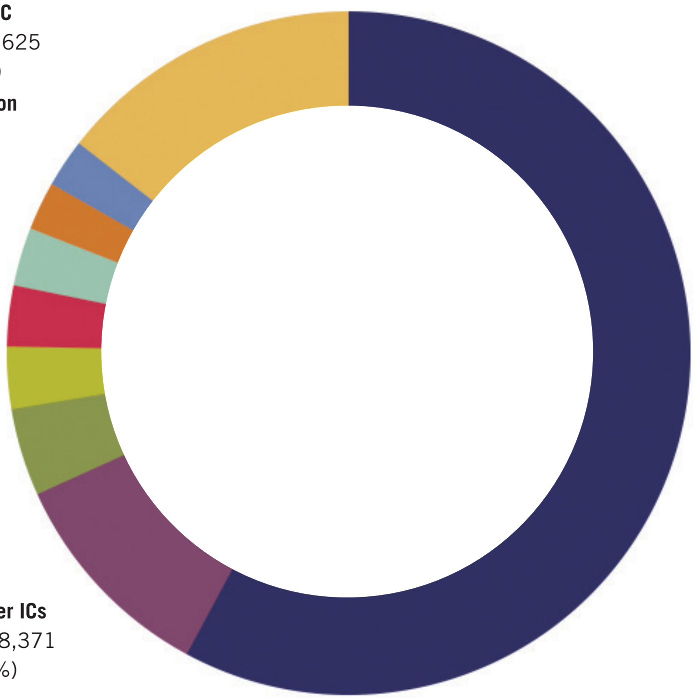
The *2011–2015 Global Plan* described basic science as "an integral part of an aggressive, transformational response to TB underpinning the development of new diagnostics, drugs, and vaccines" and outlined three priorities in this area: 1) improving the characterization of human TB; 2) understanding key features of host/pathogen interactions; and 3) defining critical questions that must be addressed to expedite the development of new tools.[19] Despite the shortfall of resources, scientists have made significant progress on all three fronts—although, as is often the case with fundamental discovery, progress has raised more questions than answers.

In the view of Valerie Mizrahi, "at a high level, progress overall in the basic sciences has been impressive." In particular, she singled out increased efforts to study TB disease in humans: "I think that I've seen a much greater emphasis on actually studying human disease using the tools of basic science. This is not easy, but there have been significant advances in that area, and that stands out as something that distinguishes these five years compared to what happened before."

Efforts to better characterize TB disease in humans have benefitted from new investment strategies that encourage a more reciprocal, iterative, and mutually reinforcing relationship between basic discovery and product development. The most prominent example of this approach is the Gates Foundation's "shift-to-left" strategy in TB vaccine R&D. Rather than concentrate resources on a limited number of expensive, late-stage phase IIb/III vaccine trials, the Gates Foundation is placing more resources in basic discovery, preclinical development, and phase I and II trials (events located on the left side of the clinical development pipeline).[20] Similar efforts are underway to inform TB drug development after three late-stage trials showed that fluoroquinolone-based therapy could not shorten treatment for drug-susceptible TB while maintaining the same rates of relapse-free cure as the six-month standard of care. "At the Gates Foundation, we have recognized that there is a need to go back to the drawing board, to invest more in R&D to better understand the complexity of TB," said Gilla Kaplan. "Why does treatment work for some people and fail for others? What's the structure and immune status of the granuloma, the TB lesion in the lung, that makes it difficult to treat for six weeks rather than six months? We've realized that answering some of these fundamental questions will be key to accelerating progress on TB."

FIGURE 8

Basic Science: $139,794,597



FUNDERS WITH INVESTMENTS UNDER 2%

German Federal Ministry of Education and Research (BMBF)	$1,670,180
Swiss Initiative in Systems Biology (SystemsX.ch)	$1,654,844
Canadian Institutes of Health Research	$1,571,528
Max Planck Institute for Infection Biology	$1,540,000
Institut Pasteur	$1,468,894
French National Agency for Research (ANR)	$1,441,141
Swedish Research Council	$1,413,257
Public Health England	$1,085,108
Swiss Federal Institute of Technology in Lausanne (EPFL)	$1,074,520
Singapore Agency for Science, Technology and Research (A*STAR)	$831,566
South African Medical Research Council (SAMRC)	$824,974
National Research Foundation, South Africa	$682,074
South African Department of Health	$571,741
Singapore Ministry of Health, National Medical Research Council (Singapore NMRC)	$566,059
Japanese Ministry of Health, Labour and Welfare	$463,925
Indian Ministry of Science and Technology, Department of Biotechnology	$451,510
Norwegian Agency for Development Cooperation (NORAD)	$387,213
U.S. National Science Foundation	$350,921
Australian Research Council	$297,852
Japan Agency for Medical Research and Development (AMED)	$294,120
Indian Council of Medical Research (ICMR)	$275,294
Health Research Council of New Zealand	$244,727
Korean Ministry of Science, ICT and Future Planning	$225,170
Research Council of Norway	$139,788
French National Agency for AIDS Research (ANRS)	$126,943
Southeastern Norway Regional Health Authority	$115,134
Howard Hughes Medical Institute	$100,000
Korea Centers for Disease Control and Prevention	$80,909
European Molecular Biology Organization	$73,067
Somalogic	$71,741
U.K. National Institute for Health Research (NIHR)	$59,760
Taiwan Ministry of Science and Technology	$30,000
Else Kröner-Fresenius Foundation	$25,000
National Health Laboratory Service Research Trust, South Africa	$20,445
Foundation CHU Sainte-Justine	$6,456

“For the resources TB gets, the scientists have done a pretty phenomenal job.”

—David Lewinsohn, Professor of Pulmonary and Critical Care Medicine, Oregon Health & Science University, and Chair, Stop TB Partnership Working Group on New TB Vaccines

Already this shift is changing the way product developers conduct clinical trials. In TB vaccine R&D, this has taken the form of nesting small experimental medicine studies in larger clinical trials.[21] Experimental medicine studies take advantage of the opportunity to work in humans to probe specific scientific questions designed to advance understanding of the biological mechanisms underlying TB infection and disease to guide product development.[22] In TB drug R&D, researchers have placed greater emphasis on biomarker and pharmacokinetic analyses to monitor response to treatment and track the differential penetration of TB drugs into lung lesions and other tissue sites.[23] Crucially, the study of the human has not come at the expense of better understanding MTB itself; host *and* pathogen (and the dynamic interaction between the two) have received increased attention. To take one example: advances in molecular imaging and genetic barcoding have made it increasingly possible to distinguish the locations and behaviors of different MTB cell types over the course of infection and disease (e.g., the persister organisms thought to underlie the lengthy duration of TB treatment and the risk of relapse that lingers after completion of therapy).[24]

These advances in TB basic science occurred despite a difficult funding environment, and there is a concern that similar success cannot be sustained without an infusion of new resources—and talent. “I’m not gloomy about the quality of the research,” said David Lewinsohn, professor of pulmonary and critical care medicine at Oregon Health & Science University and chair of the Stop TB Partnership’s Working Group on New TB Vaccines. “It’s more the quantity, and maybe the bigger issue over time is going to be getting young, talented people to go into TB research.” Valerie Mizrahi offered a stark assessment in the same vein: “Well, I must tell you, if I were 30 years younger today I would look at this and say, this is not a field that I want to go into. This is a field where it’s going to become increasingly difficult to secure funding. Is that the message we want to be conveying to our best young researchers?”

Diagnostics

> "The funds invested in TB R&D in 2015 are nowhere close to meeting the need. Contrary to HIV and malaria, there is no simple, affordable, point-of-care test—but that's not for lack of trying."
>
> **—Jérôme St-Denis, Senior Advocacy and Resource Mobilization Officer, FIND**

The *2011–2015 Global Plan* called for $364 million in funding for TB diagnostics R&D in 2015 and $1.7 billion over the five-year period. In 2015, funders gave $62.8 million to TB diagnostics, resulting in a total of $300 million from 2011 to 2015. These numbers leave an annual gap of $301 million and a five-year gap of $1.4 billion.

NIAID and the Gates Foundation retained their positions as the first- and second-largest funders for TB diagnostics R&D with respective spending of $13.8 million (22%) and $11.1 million (18%). The other top-five funders of TB diagnostics R&D were Company Y with $6.9 million (11%) and the U.S. Centers for Disease Control and Prevention (CDC) and Qiagen, each with $4.9 million (8%).

If fully funded, the *2011–2015 Global Plan* envisioned that "a portfolio of new and improved diagnostic tests for the detection of TB in all age groups, including DR-TB and latent TB infection" would be available by the end of 2015. Specifically, diagnostics developers set out to create tests for drug-sensitive (DS-) and DR-TB that could be used at the peripheral level of health systems, plus a test capable of identifying people with TB infection most likely to progress to active TB disease.[25] None of these goals were achieved in full, although the WHO did recommend new tests for DS- and DR-TB. Jérôme St-Denis, senior advocacy and resource mobilization officer at FIND, summarized the 2011–2015 period this way: "Over the past five years, one of the major advances has been the rapid uptake of GeneXpert MTB/RIF. Another major milestone has been the prioritizing of target product profiles to ensure the community [of diagnostics developers] is clear about the needs and the characteristics of products that would be adequate to answer those needs."

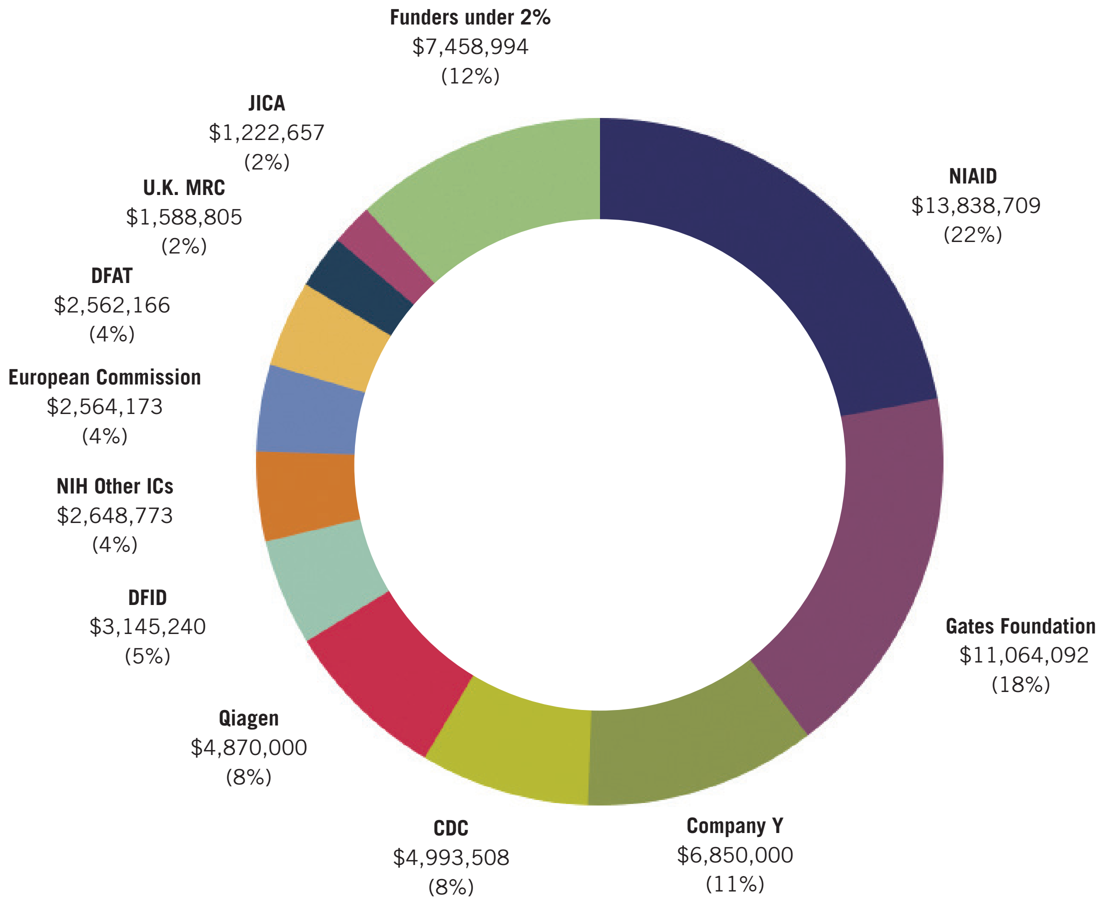
Developers entered the *2011–2015 Global Plan* years flying high with the WHO's recommendation in 2010 of Cepheid's GeneXpert MTB/RIF for the detection of rifampicin-resistant TB and HIV-associated TB.[26] But momentum stalled when the expected "fast followers" to GeneXpert either failed to show up or performed poorly in field evaluations. Activity picked up again in late 2015 when the WHO approved Alere's TB lipoarabinomannan (TB LAM) test, a noninvasive, inexpensive, urine dipstick test for diagnosing TB in people with HIV with severe immunosuppression (CD4+ T-cell counts <100 cells/mm^3).[27] Due to its low sensitivity, even in people with HIV, TB LAM is a rule-in test, meaning that a negative result must be followed by other testing to rule out TB. Even with this caveat, TB LAM offers a valuable tool for rapidly diagnosing TB in the group most at risk of dying from the disease. Many other TB diagnostic tests perform poorly in people with HIV, especially those with low CD4+ T-cell counts, and many people with HIV who succumb to TB die with their TB undiagnosed.[28] Notably, TB LAM is the first TB diagnostic test to show a mortality benefit in a clinical trial and is currently the only true rapid point-of-care test for TB.[29]

The middle stretch of the *2011–2015 Global Plan*, between the WHO's approval of GeneXpert in 2010 and TB LAM in 2015, saw another advance—not a new tool, but a powerful new advocacy narrative conveying the importance of improving TB diagnosis: the missing three million. The 2013 WHO *Global TB Report* revealed that three million individuals (one in three people who fall ill with TB each year) are either never diagnosed or never have their diagnosis reported to a public health system and thus go missing from the official record of the TB response.[30] This gap in TB diagnosis and reporting was not a new phenomenon, but by presenting familiar data in a new way, the WHO crafted a haunting message about the urgency of accelerating both the development of new diagnostics and the scale-up of existing ones.

Developers also made progress in diagnosing DR-TB, although rapid, universal drug susceptibility testing for individuals in need of evaluation for DR-TB remains a faint mirage on the horizon of future discovery. In late 2015, the WHO recommended two line probe assays to detect TB and resistance to rifampicin in smear-positive samples: GenoType MTBDR*plus* (manufactured by Hain Lifescience) and the Nipro Assay (manufactured by the Nipro Corporation). While an important step forward, these tools fall short of the

FIGURE 9

Diagnostics: $62,807,118



FUNDERS WITH INVESTMENTS UNDER 2%

Australian National Health and Medical Research Council (NHMRC)	$1,098,572
German Federal Ministry of Education and Research (BMBF)	$878,425
U.S. National Science Foundation	$645,636
European and Developing Countries Clinical Trials Partnership (EDCTP)	$582,815
Japanese Ministry of Health, Labour and Welfare	$430,886
Science Foundation Ireland	$417,774
Korean Ministry of Health and Welfare	$386,572
Singapore Agency for Science, Technology and Research (A*STAR)	$371,235
Norwegian Agency for Development Cooperation (NORAD)	$359,975
Médecins Sans Frontières	$256,574
Wellcome Trust	$243,346
Institut Pasteur	$218,955
Cepheid	$200,000
QuantaMatrix	$178,000
Indian Council of Medical Research (ICMR)	$174,406
SK Telecom	$125,490
LG Life Sciences	$115,700
Korea Centers for Disease Control and Prevention	$89,000
Damien Foundation Belgium	$83,856
Taiwan Centers for Disease Control	$80,900
World Health Organization (WHO)	$69,967
Canadian Institutes of Health Research	$69,062
French National Agency for Research (ANR)	$66,861
Thrasher Research Fund	$63,786
Indian Ministry of Science and Technology, Department of Biotechnology	$55,366
YD Diagnostics	$50,000
Indian Ministry of Health and Family Welfare (MOHFW)	$44,761
South African Department of Science and Technology (DST)	$43,863
Global BioDiagnostics	$31,774
South African Department of Health	$16,336
National University Health System, Singapore	$8,910
French National Agency for AIDS Research (ANRS)	$194

“With GeneXpert, I’m concerned that there is a narrative that the new technology is improving TB detection, but it actually doesn’t help a whole lot for children . . . It makes me concerned that potential developers won’t even go into the field because they think there’s not a need. It is terrific to have that new test, but we actually need multiple tests that are relevant to different types of patients. And tests developed specifically for children.”

—Mercedes Becerra, Professor of Global Health and Social Medicine, Harvard Medical School

desired revolution in DR-TB diagnosis. They also illustrate the long timelines slowing TB diagnostics development; Hain and Nipro each launched their respective assays in 2011 and then took five years to optimize and fully evaluate them.[31]

Positive recommendations from the WHO expanded diagnostic options during 2011–2015, but just as importantly, the WHO also issued negative recommendations to protect people with TB from misdiagnosis. In 2011, the WHO recommended against using serological (blood) tests to diagnose active TB.[32] Widely available at the time in the commercial sector in many countries, including India, these serological tests detect anti-TB antibodies or MTB antigens found in circulating blood. However, variability in antibody responses to TB among those with the disease, and antigenic similarity between MTB and other mycobacterial organisms, makes these serological tests much less reliable than microbiological or molecular tests, putting individuals at risk of misdiagnosis.[33] The WHO also warned that interferon gamma release assays (IGRAs) should not be used to predict the likelihood that latent TB infection will progress to active TB disease.[34] While IGRAs can diagnose TB infection and offer some advantages over older technologies like tuberculin skin testing, they cannot reliably predict which individuals with latent infection will go on to develop active, symptomatic disease.

TB Diagnostics R&D Progress Report

2011–2015 *Global Plan* Indicators of Success	Target (2015)	Reality (2015)
Number of new tests for the diagnosis of active TB that can be used in district labs	2	2
Number of new tests for active TB in peripheral labs	2	1
Number of new point-of-care tests for the diagnosis of active TB in peripheral health centers	2	1*
Number of new tests for the diagnosis of DR-TB in district labs	2	2
Number of new tests for the diagnosis of DR-TB in peripheral-level labs	1	0
Number of new tests for the diagnosis of DR-TB in health center	1	0
Number of new tests for LTBI and prediction of the risk of progression to TB disease	1	0**

* Plus a negative recommendation against using serological tests (2011).

** Plus a negative recommendation against using IGRAs to predict progression from infection to disease (2011).

Drugs

> "There's been some encouraging progress in the drug discovery space over the last few years. We've found new targets. Very frustrating, however, is that the pace of drug discovery is slow and critically related to the underfunding of the endeavor. But at the level of basic science, we are finding . . . interesting compounds that could potentially be developed into new drugs."
>
> **—Valerie Mizrahi, Director, Institute of Infectious Disease and Molecular Medicine, University of Cape Town**

The *2011–2015 Global Plan* called for $810 million in funding for TB drug R&D in 2015 and $3.7 billion over the five-year period. In 2015, funders gave $231.9 million to TB drug development, resulting in a total of $1.2 billion for drug R&D from 2011 to 2015. These numbers leave an annual gap of $578 million and a five-year gap of $2.4 billion compared with the targets.

Decreased spending by Otsuka, now in the final years of delamanid's phase III clinical trial, resulted in a slight reordering of the top funders of TB drug R&D in 2015. The Gates Foundation, which spent $48.1 million on TB drug development in 2015 (21% of the total), is now the largest funder, followed by NIAID with $44.5 million (19%). Now in third place, Otsuka spent $29 million (12%), a little less than half of the $65.1 million it spent in 2011. As previously noted, this decrease reflects not only the progression of delamanid's development but also the significant depreciation of the Japanese yen against the U.S. dollar under the Bank of Japan's quantitative easing program, begun in earnest in 2013.[35]

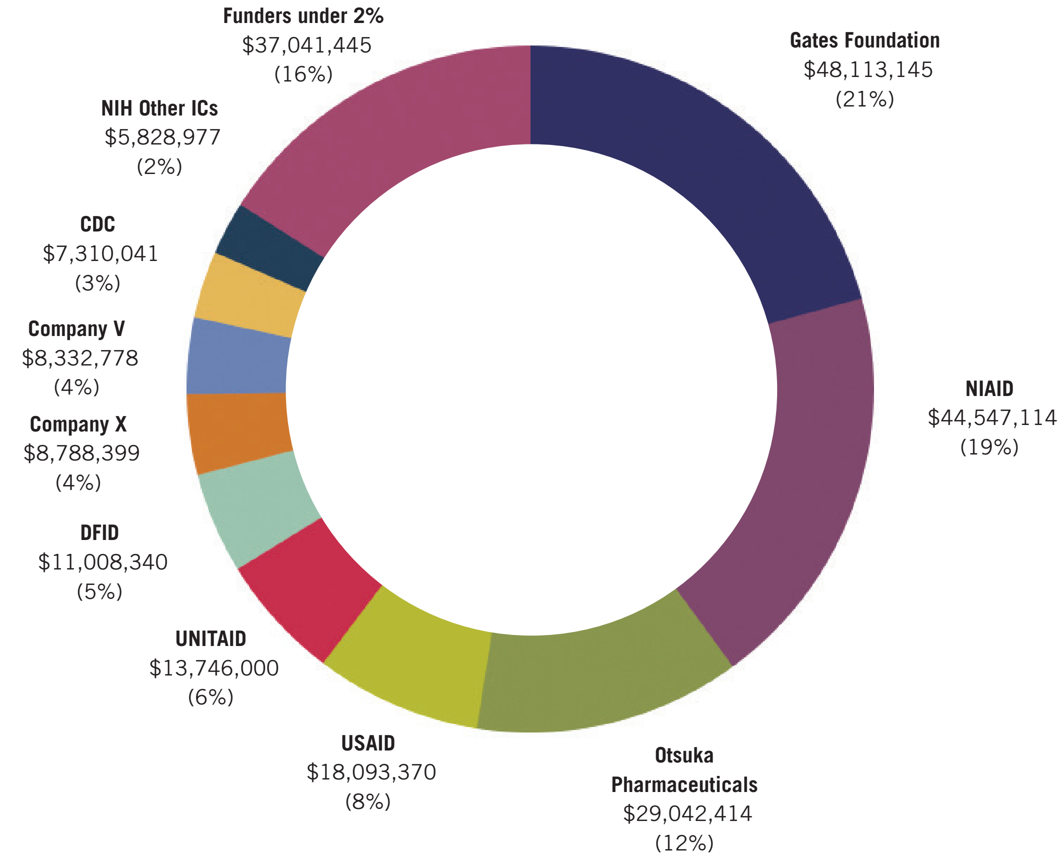
TB drug developers met some—although not all—of the *2011–2015 Global Plan* indicators of success. Most notably, the period saw the first drug approvals of TB drugs from new classes in 40 years when the FDA approved Janssen's bedaquiline in 2012, followed by the approval of Otsuka's delamanid by the European Medicines Agency in 2013.[36,37] Bedaquiline and delamanid each received conditional marketing authorization based on data from phase IIb studies and have yet to complete phase III trials.

Another major success came from research conducted by the CDC's Tuberculosis Trials Consortium (TBTC) that shortened the duration of treatment for latent TB infection from 6–9 months of daily isoniazid to just 12 once-weekly doses of isoniazid in combination with rifapentine (the 3HP regimen). This work was the culmination of 15 years of steady investment by the TBTC and NIAID's AIDS Clinical Trials Group (ACTG). The phase III trial that demonstrated the safety and efficacy of 3HP began in 2001 and published results in 2011.[38] Substudies within the phase III trial subsequently demonstrated the safety of 3HP in children and people with HIV.[39,40] The CDC moved quickly to optimize the regimen's programmatic usefulness in a study comparing treatment completion of 3HP under self-administration versus directly observed therapy.[41] The CDC remains active in TB drug research, spending $7.3 million in 2015. Its current agenda is focused on shortening the duration of DS-TB treatment, and, in 2015, it launched a phase III trial in collaboration with the ACTG that will compare the safety and efficacy of two 4-month rifapentine-based regimens against the 6-month rifampicin-based standard of care.

Shortening curative treatment remains the elusive grand prize of TB drug R&D. The *2011–2015 Global Plan* set a goal of having at least one 4-month regimen for DS-TB approved by regulatory authorities, recommended by the WHO, and available for use by the end of 2016. Instead, three experimental 4-month regimens built around fluoroquinolones all returned disappointing results in phase III trials, setting back this objective at least another five years.[42,43,44]

FIGURE 10

Drugs: $231,852,022



FUNDERS WITH INVESTMENTS UNDER 2%

Macleods Pharmaceuticals	$3,500,000
U.K. Medical Research Council (U.K. MRC)	$3,271,889
European and Developing Countries Clinical Trials Partnership (EDCTP)	$2,847,478
Eli Lilly	$2,750,000
European Commission	$2,720,140
Australian Department of Foreign Affairs and Trade (DFAT)	$2,562,166
Dutch National Postcode Lottery	$1,856,013
French National Agency for AIDS Research (ANRS)	$1,746,424
Global Health Innovative Technology Fund (GHIT)	$1,620,350
National Philanthropic Trust	$1,500,000
Swiss Federal Institute of Technology in Lausanne (EPFL)	$1,227,062
Irish Aid	$1,118,080
Innovative Medicines Initiative (IMI)	$1,080,119
Company R	$880,133
French National Agency for Research (ANR)	$854,868
Korea Drug Development Fund	$712,000
Qurient	$712,000
South African Department of Science and Technology (DST)	$594,074
South African Medical Research Council (SAMRC)	$520,092
Singapore Agency for Science, Technology and Research (A*STAR)	$442,512
Company W	$438,300
Swiss National Science Foundation (SNSF)	$406,548
U.S. Food and Drug Administration (FDA)	$400,000
Institut Pasteur	$355,892
BioDuro	$337,500
Irish Health Research Board	$299,541
Indian Ministry of Health and Family Welfare (MOHFW)	$260,951
Médecins Sans Frontières	$226,344
Foundation Jacqueline Beytout	$208,699
Wellcome Trust	$204,977
South African Department of Health	$191,126
Swedish Research Council	$175,595
Canadian Institutes of Health Research	$167,770
Australian National Health and Medical Research Council (NHMRC)	$160,960
Damien Foundation Belgium	$155,972
Singapore Ministry of Health, National Medical Research Council (Singapore NMRC)	$136,647
Taiwan Centers for Disease Control	$119,085
GlaxoSmithKline (GSK)	$55,631
Korean Ministry of Health and Welfare	$53,400
National Research Council of Thailand	$40,000
Stop TB Partnership	$39,500
Health Research Council of New Zealand	$29,843
Indian Council of Medical Research (ICMR)	$28,248
German Federal Ministry of Education and Research (BMBF)	$11,181
Faber Daeufer	$10,000
National University Health System, Singapore	$7,425
Individual donors to TB Alliance	$4,908

> "Available resources definitely have an impact on the amount of research being conducted . . . Increased funding would allow further academic groups to go into the discovery area and develop new compounds and facilitate more public-private approaches."

Christian Lienhardt, Team Leader, Research for TB Elimination, World Health Organization Global TB Programme

The pursuit of treatment shortening met with greater success in DR-TB drug trials. The *2011–2015 Global Plan*'s goal of seeing a nine-month regimen (including at least one new drug) for multidrug-resistant TB (MDR-TB)—a form of TB that is resistant to the first-line drugs isoniazid and rifampicin—in phase III trials has been met thanks to USAID's support of the STREAM study. STREAM is the largest MDR-TB drug trial in history and is being conducted by the International Union Against Tuberculosis and Lung Disease (IUATLD). Stage 1 of STREAM (which does not include a new drug) will provide the first evidence from randomized controlled trials on the safety and efficacy of a nine-month MDR-TB regimen, modified from a regimen first studied in Bangladesh and subsequently evaluated in several cohort studies in West Africa. This regimen received the WHO's conditional recommendation in 2016, and results from STREAM Stage 1 are impatiently awaited to confirm the findings from the observational cohorts that underpinned the WHO's endorsement.[45] Stage 2 of STREAM introduces new TB drug bedaquiline into the nine-month regimen to see whether its addition can replace the injectable agent (kanamycin) or enable the duration of therapy to be further reduced to just six months. Through its support of STREAM, USAID has become one of the largest funders of TB drug R&D. In 2015, USAID spent $18.1 million on TB drug research, rising to fourth place.

UNITAID has offered substantial support for TB drug development through two large grants: one to the TB Alliance to develop child-friendly formulations of first-line TB drugs, and the second to PIH, MSF, and IRD to study optimal combinations of new and repurposed DR-TB drugs in the endTB project. By supporting these projects, UNITAID addresses important gaps in TB drug development. The lack of pediatric formulations of TB drugs has left doctors and nurses reliant on an inexact alchemy of splitting, mixing, and matching improperly formulated tablets to get the right amount of each drug into children's bodies. In November 2015, the TB Alliance announced the availability of properly dosed pediatric formulations of first-line drugs, a long overdue advancement.[46] The endTB project promises to fill a similarly important gap in knowledge: how to best combine new TB drugs bedaquiline and delamanid with each other and with older, repurposed drugs such as linezolid and clofazimine. UNITAID did not even appear on the list of TB research donors as recently as 2012, but it has climbed through the ranks to become the 10th largest donor overall and the fifth largest donor to TB drug R&D, on which it spent $13.7 million in 2015.

While worthy of celebration, the above successes also stand as examples of a worrying trend: the greatest movements in TB drug development over the last five years came from optimizing and repurposing existing drugs rather than discovering and advancing a wealth of new compounds through the early stages of clinical development. In comparing the *2011–2015 Global Plan*'s drug R&D targets to reality, the health of the TB drug pipeline emerges as the area of biggest discrepancy and concern. In 2010, there were three compounds in phase I trials, a number predicted to increase to 21 by 2015 given full funding. Instead, by January 2016, the pipeline had regressed to two candidates in phase I: Qurient's Q203 and Innovative Medicines for Tuberculosis Foundation's PBTZ 169. Currently, the TB drug pipeline has just six new drugs from five classes in development (bedaquiline, delamanid, pretomanid, sutezolid, Q203, and PBTZ 169), and two of these are already on the market.[47]

Although many compounds wait in the wings of preclinical work, the experience of the last five years demonstrates that inadequate trickles of funding will not nurture the plurality of compounds required to maintain a robust drug pipeline and to develop the novel regimens needed to get ahead of drug resistance and end TB. From the perspective of Christian Lienhardt, team leader of research for TB elimination, WHO Global TB Programme, the major problem is that "products being pushed from preclinical to clinical development remain very limited (Q203 being the only one in phase I), and the development of some (AZD5847, TBA-354) has been stopped or discontinued, or remains stagnant (sutezolid), so the pipeline of new TB drugs remains weak."

TB Drugs R&D Progress Report

2011–2015 *Global Plan* Indicators of Success	Target (2015)	Reality (2015)
Number of new and/or repurposed drugs in phase I trials	21	2
Number of single or combination phase II trials investigating new and/or repurposed drugs	34	17
Number of new regimens for DS-TB in phase III trials	3	8
Number of new regimens for DR-TB in phase III trials	2	5
Duration of treatment of LTBI	2–3 months	3 months

Vaccines

> "The reality is that if we want to end TB, we will need a vaccine. And for that, we need an acceleration in investment in vaccines, and we need to sustain that, between now and 2024."
>
> **—Lucica Ditiu, Executive Director, Stop TB Partnership**

The *2011–2015 Global Plan* called for $445 million in funding for TB vaccine R&D in 2015 and $1.9 billion over the five-year period. In 2015, funders gave $80.7 million to TB vaccine development, resulting in a total of $475 million for vaccine research from 2011 to 2015. These numbers leave an annual gap of $364 million and a five-year gap of $1.4 billion.

The Gates Foundation remained the largest funder of TB vaccine R&D in 2015, with investments of $26.9 million, one-third of the total. GlaxoSmithKline Biologicals, participating in TAG's survey for the first time, emerged as the second-largest supporter of TB vaccine research, with $17.6 million in spending. NIAID followed closely behind with nearly $17 million. Other top funders of TB vaccine R&D each gave under $3 million, although the EC noted that its $1.6 million in spending will increase substantially next year when two large TB vaccine initiatives it is supporting receive their next payments.

Measured against the *2011–2015 Global Plan* indicators of success, TB vaccine developers came up short. The outsized ambition of the *2011–2015 Global Plan*'s vaccine section—which set a goal of seeing four, nine, and 20 vaccine candidates enter phase III, phase IIb, and phase I trials, respectively—is striking. Instead, the TB vaccine field arrived at the end of 2015 with zero candidates having entered phase III, two entering phase IIb, and 14 entering phase I. While the shortfall in funding may be partly to blame for this yawning gap, many of the challenges that upset an easy path toward achieving these targets proved more scientific than financial in nature. In particular, disappointing results from the phase IIb trial of TB vaccine candidate MVA85A, published in February 2013, meant that instead of pursuing an unceasing forward march through ascending clinical trial stages, TB vaccine developers and funders halted for some heavy introspection.

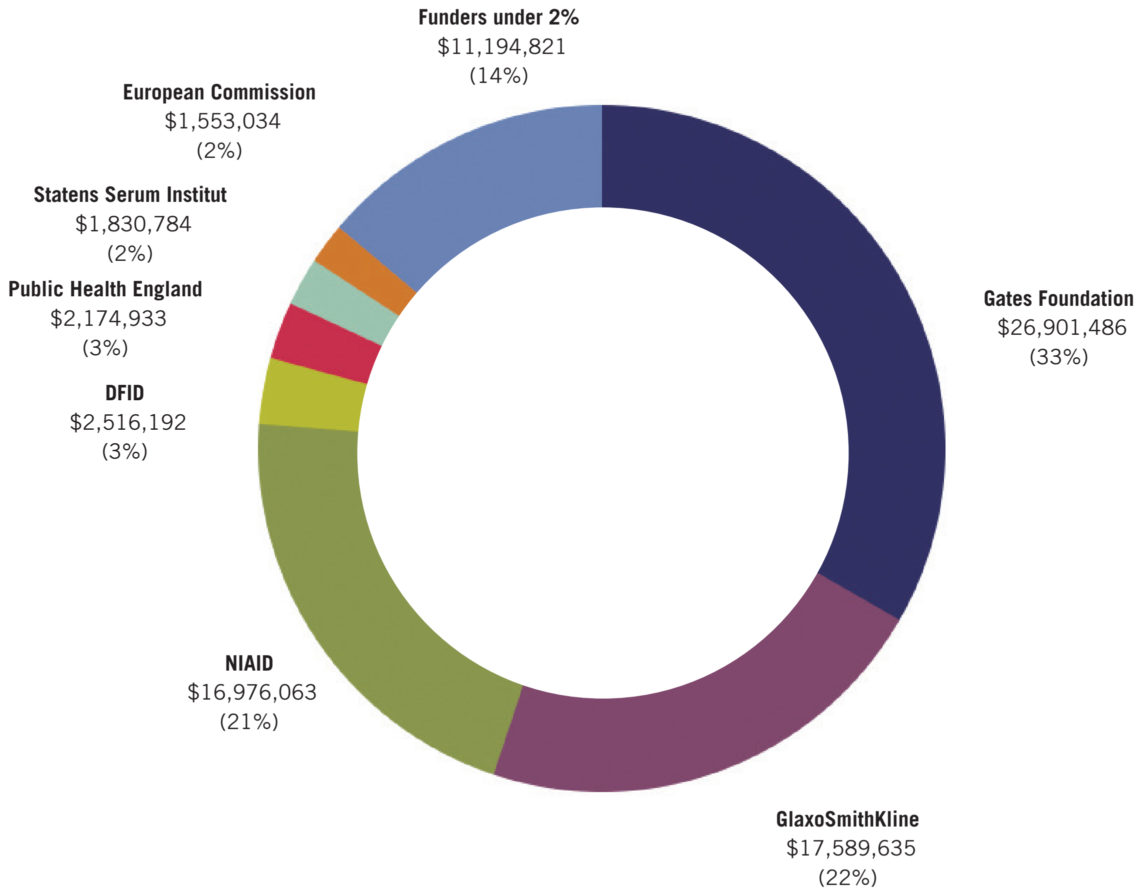
In the words of Gilla Kaplan, "before we move new vaccine candidates into large clinical trials, we need to figure out what criteria can help us identify potential candidates that are likely to have impact." David Lewinsohn expressed a similar opinion, saying that the MVA85A trial "caused everybody to go back and look and say, well, how robust were those upstream indicators?"

At the beginning of the *2011–2015 Global Plan* period, TB vaccine developers expended considerable energy devising "stage gate" criteria for deciding which candidate vaccines to advance to different stages of development; these criteria were published in *Tuberculosis Vaccines: a Strategic Blueprint for the Next Decade (the Blueprint)*.[48] Decision aides like the *Blueprint* are only as good as the information that goes into them, and the utility of some of the chosen criteria came up against formidable research needs on the basic-science end of TB vaccine R&D, including the immunological complexity of TB infection, the need to refine preclinical animal models to more closely resemble human disease, the absence of a human-challenge model of TB infection, and the lack of biomarkers able to act as reliable surrogates for prevention of infection or disease.

In addition to more preclinical and fundamental discovery activities on the leftward side of the pipeline, Lewinsohn sees a continued need in "the downstream space, taking candidates that have good product profiles behind them and then taking them into late-stage trials." The fallout of the MVA85A trial has not

FIGURE 11

Vaccines: $80,736,948



FUNDERS WITH INVESTMENTS UNDER 2%

Norwegian Agency for Development Cooperation (NORAD)	$1,388,031
German Federal Ministry of Education and Research (BMBF)	$1,139,433
Max Planck Institute for Infection Biology	$1,100,000
U.S. National Institutes of Health, Other Institutes and Centers (NIH Other ICs)	$990,390
European and Developing Countries Clinical Trials Partnership (EDCTP)	$921,051
Biofabri	$838,238
Global Health Innovative Technology Fund (GHIT)	$810,175
Japanese Ministry of Health, Labour and Welfare	$631,950
Serum Institute of India	$569,033
Japan BCG Laboratory	$499,350
Institut Pasteur	$397,708
Danish Council for Independent Research	$391,718
U.K. Medical Research Council (U.K. MRC)	$294,133
Irish Health Research Board	$284,716
Canadian Institutes of Health Research	$178,039
Swiss National Science Foundation (SNSF)	$168,043
Japan Agency for Medical Research and Development (AMED)	$129,004
Lundbeck Foundation	$127,901
Indian Council of Medical Research (ICMR)	$125,600
U.S. Food and Drug Administration (FDA)	$63,978
World Health Organization (WHO)	$58,064
Innovation Fund Denmark	$55,727
Norwegian Institute of Public Health	$32,538

been a halt to all clinical trials—although some planned studies were stopped early, significantly revised, or cancelled altogether—but a pause to rethink and redesign clinical trials. In this context, the gulf between the *2011–2015 Global Plan* targets and reality is less a sign of failure than an indication that the TB vaccine field made an important course correction based on emerging evidence from the clinic and the lab.

Although these nascent efforts point in a promising direction, the newly operative TB vaccine R&D strategy includes some signs of retrenchment in ambition that threaten to leave behind some of the populations most vulnerable to TB. Unlike earlier phase IIa and IIb trials, many of which were conducted in either adults with HIV or infants, vaccine developers are now conducting most studies in HIV-negative adolescents and adults. Adolescents and adults account for the majority of TB transmission, so mathematical modeling suggests that a vaccine that interrupts transmission in these groups would have a bigger impact on the global TB epidemic. In addition, the complexities of pediatric- and HIV-associated TB have led many vaccine developers to conclude that developing a vaccine for HIV-negative adolescents and adults first will be easier. Time will tell whether this proves to be a wise strategy, but in the meantime, it raises important questions of equity. For any disease, the allure of a vaccine is its universality—the long-lasting protection it can offer to a broad spectrum of humanity. Vaccines of this type may not be possible to develop for every disease, including perhaps TB, but a TB vaccine that cannot be safely used in the populations most in need of more effective preventive measures risks not confronting the epidemic where its burden falls hardest.

TB Vaccines R&D Progress Report

2011–2015 *Global Plan* Indicators of Success	Target (2015)	Reality (2015)
Number of new vaccine candidates that have entered phase I trials	20	14
Number of vaccine candidates that have entered phase II trials	9	7
Number of vaccine candidates that have entered phase IIb trials	3	2
Number of vaccine candidates that have entered phase III trials	4	0*

* TAG does not count the phase III trial of *Mycobacterium vaccae*, a whole-cell mycobacterial vaccine being developed as an adjunct to TB chemotherapy, since its developer, China's Anhui Longcom, has refused to publicly present details on the progress of this trial at global forums.

Operational Research

"You see the numbers of TB globally declining, but declining very slowly. And we're very focused on new drugs, new drug regimens, new diagnostics, but we're not focused enough on how to implement what we currently have. Because I do believe that if we implemented everything we have optimally, then we would have a much stronger impact on global TB incidence."

—Jonathan Golub, Associate Professor of Medicine, Epidemiology & International Health, Johns Hopkins University Center for Tuberculosis Research

The *2011–2015 Global Plan* called for $86 million in funding for TB operational research in 2015 and $359 million over the five-year period. In 2015, funders gave $61.0 million to TB operational research, resulting in a total of $351 million from 2011 to 2015. These numbers leave an annual gap of $25 million and a five-year gap of $8 million.

For the first time since TAG began tracking TB R&D, the Gates Foundation emerged as the biggest supporter of operational research, giving $17.7 million (29% of the total) in 2015. NIAID, traditionally the largest TB operational research funder, followed in second place with $12.0 million (19%). Other major financial contributors to TB operational research included the U.K. Department for International Development (DFID) and USAID, each with 10 percent of the total. The Indian Ministry of Health and Family Welfare joined the ranks of top TB operational research funders for the first time with $1.1 million in spending, most of it on prevalence surveys and evaluations of TB diagnostic tests.

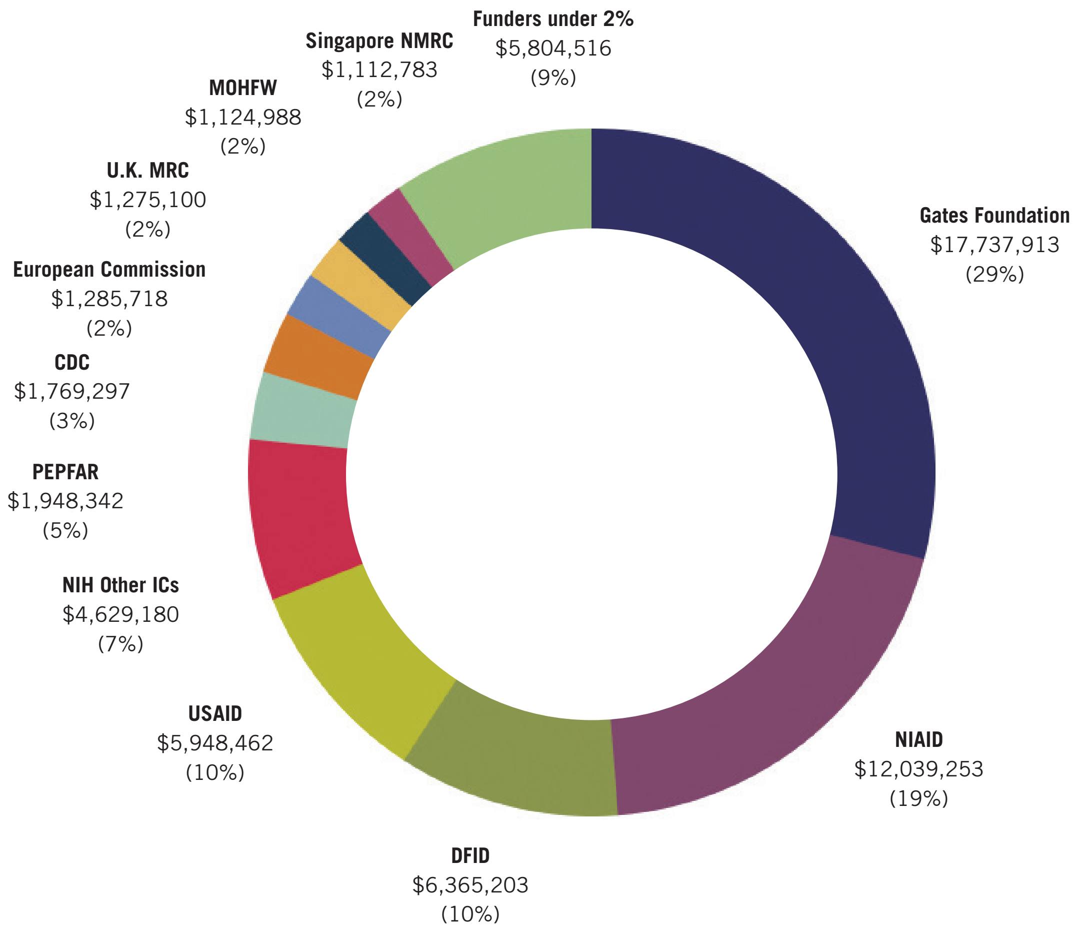
Among all the research areas covered by the *2011–2015 Global Plan*, operational research came the closest to reaching the specified targets, although this does not mean implementers have satisfied most TB operational research needs. If anything, the need for operational research has only grown since the *2011–2015 Global Plan* was written. The introduction of new tools like GeneXpert, delamanid, and bedaquiline has highlighted how operational research should be understood as a final stage of the product development pathway, since lessons generated by operational research can inform rollout as well as future product optimization and development. Invoking GeneXpert as an example, Jonathan Golub, Associate Professor of Medicine, Epidemiology & International Health at The Johns Hopkins University Center for Tuberculosis Research, explained, "operational research needs to be done when a new technology is developed to see how well it can be implemented. And then after seeing what problems are encountered during implementation, we need to go back to the lab folks and say, yes, you've done a great job of diagnosing TB, but we need it to work better in this setting or with this population."

Early assessments of GeneXpert implementation unveiled some critical deficiencies that newer iterations of GeneXpert are designed to address. GeneXpert Omni—which is smaller, sturdier, dustproof, and battery operated—has the potential to jump over many of the hurdles that slowed down GeneXpert's rollout: a dependence on electricity, an annual maintenance requirement, and a susceptibility to dust and other difficult-to-control field conditions. Cepheid's new cartridge—GeneXpert Ultra—is currently undergoing evaluation to back-up Cepheid's claim that it is more sensitive than the original GeneXpert MTB/RIF cartridge and requires less processing time. If each is as good as the developer promises, the combination of GeneXpert Omni and Ultra could be powerful. However, no product is perfect, and even this combination will warrant thoughtful operational research both to identify future research needs and to generate information on how TB programs can integrate new tools into health systems in ways that improve patient outcomes.

Operational research on GeneXpert has taught the TB field that a singular focus on a single new tool is tunnel vision. New and improved products will not have a dramatic impact on the TB epidemic unless integrated into and implemented alongside other components of good TB programs. One of those components is contact tracing, which Golub believes is starting to receive more attention thanks to operational research:

FIGURE 12

Operational Research: $61,040,756



FUNDERS WITH INVESTMENTS UNDER 2%

Taiwan Centers for Disease Control	$902,585
Indian Council of Medical Research (ICMR)	$878,061
Canadian Institutes of Health Research	$644,949
Netherlands Organization for Health Research and Development (ZonMw)	$559,040
World Health Organization (WHO)	$490,158
Norwegian Agency for Development Cooperation (NORAD)	$478,003
Médecins Sans Frontières	$319,073
German Federal Ministry of Education and Research (BMBF)	$305,724
European and Developing Countries Clinical Trials Partnership (EDCTP)	$299,399
Wellcome Trust	$206,088
Swiss National Science Foundation (SNSF)	$174,968
Indian Ministry of Science and Technology, Department of Biotechnology	$134,864
Colombia Department of Science, Technology and Innovation	$108,800
Norwegian Public Health Association	$92,768
French National Agency for AIDS Research (ANRS)	$66,846
LHL International	$53,111
Colombia National Institute of Health	$51,300
South African Department of Health	$16,356
Australian Department of Foreign Affairs and Trade (DFAT)	$15,373
Colombia Ministry of Health	$4,630
Firland Foundation	$2,200
Philippine Tuberculosis Society	$221

“One of the fruits of operational research is that people are starting to pay attention to household contact investigations. And there’s been a lot of studies on different ways to do that, optimize that, and I think that . . . is one of the biggest moves forward because we’ve known in the U.S. that contact investigations are key for diagnosing and preventing TB.”

Among the TB experts interviewed by TAG, many thought that an insufficient amount of operational research might actually be discouraging both private- and public-sector players from getting involved in TB research. “This has a major negative effect if you are a pharmaceutical company and you see the lack of support for the TB community to come together and test, use, and roll out a new tool,” said Lucica Ditiu. “Seeing the limited funding for grants, assistance, advocacy, community engagement, and coordination in pushing something out there, it’s very difficult to maintain your enthusiasm to invest.” The trick may be to avoid turning operational research into a never-ending series of pilot projects that preempt national scale-up. This happened in India, where the Revised National Tuberculosis Control Program has struggled to translate pilot studies of GeneXpert into a nationwide expansion of the test.[49]

Pediatric TB Research

"Like our system for treating TB, children are falling out of the R&D pipeline as if it were a sieve."

—Mercedes Becerra, Professor of Global Health and Social Medicine, Harvard Medical School

Since 2011, pediatric TB research has moved from total neglect to significant but far from sufficient investment. The *2011–2015 Global Plan* did not include specific targets for pediatric research—a reflection of the issue's low stature on the global health agenda. To rectify this exclusion, a group of stakeholders including UN agencies and initiatives (WHO, UNICEF, Stop TB Partnership), TB technical agencies and implementers (CDC, USAID, IUATLD), and civil society groups (TAG) published the *Roadmap for Childhood TB (Roadmap*) in 2013.[50] In effect, this became a complementary *Global Plan* for kids. The year before, the WHO published its first-ever estimates of pediatric TB incidence and mortality, estimating there were 500,000 new cases of TB in children and 72,000 deaths in 2011.[51] Two years later, researchers at Harvard Medical School published a study suggesting that up to a million children develop TB annually, double the number estimated by WHO and three times the number of pediatric TB cases diagnosed and notified to national TB programs.[52] This led the WHO to revise its methodology, and in its 2015 *Global TB Report*, it published new figures estimating that in 2014 one million children fell ill with TB and 140,000 died from the disease.[53] Brought out of the shadows, the problem of TB in children turned out to be much bigger than the authors of the *Roadmap* had anticipated.

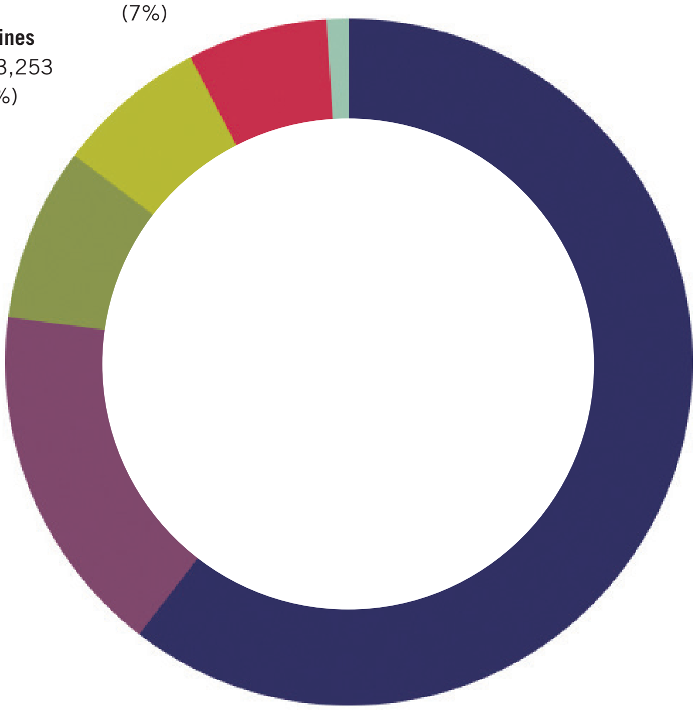
How should an improved understanding of the burden of TB in kids factor into funding for pediatric research? Mercedes Becerra, one of the authors of the Harvard Medical School study, suggested an answer: "So we now realize there's at least one million children out there with TB every year. That is about 10 percent of all TB cases in a year. Should we be using this indicator to compare the distribution of R&D funding? Relative to the burden, it's a disproportionately low investment." The *Roadmap* set a goal of spending $200 million on research related to pediatric TB between 2011 and 2015—an amount equal to just two percent of the overall target of $9.84 billion for TB R&D over these years. During this period, reported funding for pediatric TB research amounted to $106 million, half of the targeted amount, and only three percent of the $3.29 billion spent on TB R&D overall. Children with TB have yet to receive adequate resources for the research needed to improve their preventive, diagnostic, and treatment options.

More alarming, data collected by TAG suggest that spending on pediatric TB research may be experiencing the same plateau effect that governed overall TB R&D funding during the *2011–2015 Global Plan* period. Pediatric TB R&D received $26.7 million in funding in 2015, about even with the $25.7 million spent in 2014 and the $25.3 million spent in 2013. The NIH (NIAID and other NIH institutes and centers) and UNITAID remained the largest pediatric TB R&D funders with respective spending of $7.7 million and $4.2 million. Several pharmaceutical companies are active in pediatric TB research, led by the Indian generics company Macleods Pharmaceuticals, which has taken the lead on developing child-friendly formulations of second-line MDR-TB drugs. Company X and Company V, two pharmaceutical companies that report to TAG anonymously, reported pediatric-related research activities. As in previous years, Otsuka, which is completing its pharmacokinetic (PK) and safety study of delamanid in children, notified TAG that it cannot disaggregate pediatric spending from its overall investment in delamanid. Total funding for pediatric TB research would be higher taking Otsuka's activities into account, although by an unknown amount.

Most funding for pediatrics went to drug development, which comprised 60 percent of the total with $16.1 million, followed by diagnostics with $4.4 million (17%) and basic science with $2.2 million (8%). Pediatric TB drug development continues to focus on PK and safety studies, although the field is poised to take tentative steps beyond these activities in the next five years with planned or ongoing trials that will evaluate preventive therapy for children exposed to MDR-TB and treatment shortening for children with DR-TB and less severe forms of DS-TB.[54]

FIGURE 13

Pediatric TB R&D Funding by Research Category, 2015
Total: $26,700,543



Despite the dominance of funding for drug development within pediatric TB R&D investments, Becerra cautioned that pediatric research needs should not be equated with product development: "We have this long-term neglect of basic research looking at child-specific disease . . . If there isn't enough funding to pursue that area first, then we're going to have very few tools making it out of basic science that are specific to children." In 2015, basic science research on pediatric TB infection and disease amounted to just $2.2 million. Most of this came from the NIH, where NIAID and the Eunice Kennedy Shriver National Institute of Child Health and Human Development funded grants supporting projects to understand mechanisms of TB disease among HIV-infected children, the impact of TB on immune changes during pregnancy, and the host factors underlying protection against TB in adolescents.

One bright spot worth highlighting is the noticeable uptick in funding for studies seeking to improve the diagnosis, treatment, and prevention of childhood TB in the household, the setting in which children are most often exposed to TB. The Indian Council of Medical Research, for example, is supporting a study investigating the prevalence of TB infection and disease among household contacts of MDR-TB patients. Its counterpart in the United Kingdom, the U.K. Medical Research Council, is funding work probing the immunology of children who are exposed to TB at home but remain uninfected. These and similar household studies hold more than just scientific or public health importance; they help demonstrate that there is a market for pediatric TB and a need to invest in this area. "We think that 3.5 million children a year can be identified in the homes of TB patients, and they need treatment for infection. That's a big number . . . A developer could consider the pediatric TB population as a market," said Becerra.

TABLE 3

Pediatric TB R&D Funders by Rank, 2015

2015 RANK	FUNDING ORGANIZATION	FUNDER TYPE	2015 PEDIATRIC TB R&D FUNDING	PERCENTAGE OF TOTAL 2015 PEDIATRIC TB R&D FUNDING
1	U.S. National Institutes of Health, National Institute of Allergy and Infectious Diseases (NIAID)	P	$4,254,143	15.93
2	UNITAID	M	$4,208,000	15.76
3	Macleods Pharmaceuticals	C	$3,500,000	13.11
4	U.S. National Institutes of Health, Other Institutes and Centers (NIH Other ICs)	P	$3,440,487	12.89
5	Company X	C	$3,100,000	11.61
6	U.K. Medical Research Council (U.K. MRC)	P	$2,816,619	10.55
7	Bill & Melinda Gates Foundation	F	$655,905	2.46
8	European and Developing Countries Clinical Trials Partnership (EDCTP)	P	$576,086	2.16
9	Serum Institute of India	C	$569,033	2.13
10	Indian Ministry of Health and Family Welfare (MOHFW)	P	$500,000	1.87
11	Australian National Health and Medical Research Council (NHMRC)	P	$436,905	1.64
12	Company V	C	$417,044	1.56
13	U.S. Agency for International Development (USAID)	P	$400,000	1.50
14	Médecins Sans Frontières	F	$316,297	1.18
15	Norwegian Agency for Development Cooperation (NORAD)	P	$304,907	1.14
16	Total Foundation	F	$279,520	1.05
17	Indian Council of Medical Research (ICMR)	P	$231,965	0.87
18	South African Department of Science and Technology (DST)	P	$147,340	0.55
19	French National Agency for Research (ANR)	P	$100,627	0.38
20	Wellcome Trust	F	$97,965	0.37
21	Canadian Institutes of Health Research	P	$78,114	0.29
22	U.S. Centers for Disease Control and Prevention (CDC)	P	$69,297	0.26
23	Thrasher Research Fund	F	$63,786	0.24
24	World Health Organization (WHO)	M	$57,246	0.21
25	Norwegian Institute of Public Health	P	$32,538	0.12
26	Damien Foundation Belgium	F	$30,188	0.11
27	South African Department of Health	P	$16,336	0.06
28	French National Agency for AIDS Research (ANRS)	P	$194	0.00
	Total		**$26,700,543**	

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

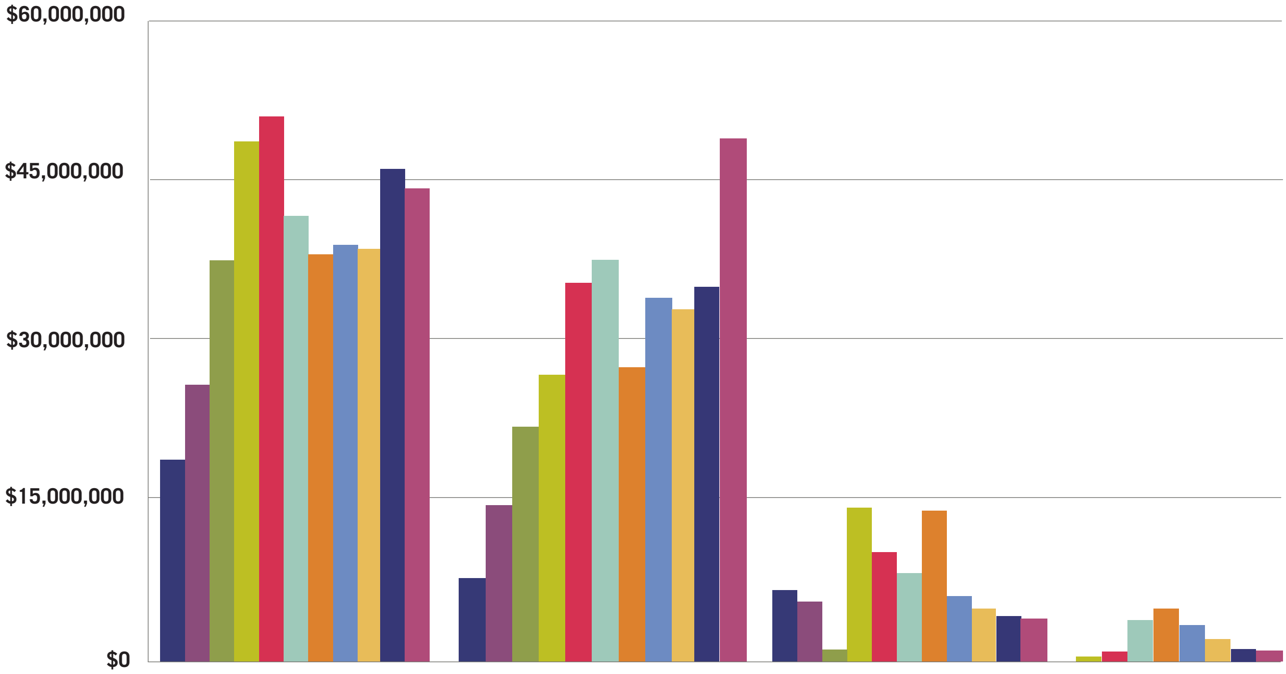
Trends in TB R&D Funding among Product Development Partnerships

The numbers in figure 14 represent the annual costs (external and internal) of research activities reported by the four product development partnerships (PDPs) active in TB research. PDPs are nonprofit organizations designed to leverage public, private, philanthropic, and academic resources to meet innovation needs that, due to a lack of commercial appeal, would be unlikely to attract significant investments from the market. Since PDPs are grant recipients, and not original-source funders, TAG tracks PDP spending separately from the other institutions included in this report.

FIND, which evaluates new diagnostics and coordinates efforts among a large number of independent diagnostic developers, reported spending $2.6 million in 2015. Aeras and the TuBerculosis Vaccine Initiative reported spending of $41.7 million and $962,667, respectively, on TB vaccine development. The TB Alliance, which is involved in TB drug development, reported costs of $49.5 million, a sizeable $14.2 million increase over the $35.3 million it spent in 2014. This increase accords with the TB Alliance's engagement in a number of large and/or complex clinical trials aiming to shorten and simplify the treatment of DS-, DR-, and extremely drug-resistant TB. As in previous years, the Gates Foundation was the largest supporter of the four PDPs. In 2015, Gates reported grants to the TB Alliance, Aeras, and FIND totaling $27.7 million, $13 million, and $669,170, respectively. Other major donors to PDPs include international development agencies in the United States, United Kingdom, and Australia.

FIGURE 14

Total TB R&D Spending by PDPs, 2005-2015



	Aeras	TB Alliance	FIND	TBVI
2005	$18,580,139	$7,874,983	$6,778,239	N/A
2006	$25,923,809	$14,808,362	$5,492,942	N/A
2007	$37,704,051	$22,624,182	$1,145,409	N/A
2008	$48,679,266	$26,885,734	$14,177,202	$339,741
2009	$50,792,515	$35,643,490	$9,975,320	$841,333
2010	$41,572,980	$37,538,794	$8,212,896	$3,700,914
2011	$38,166,117	$27,824,033	$13,938,587	$4,731,422
2012	$38,904,315	$34,388,929	$5,726,157	$3,434,338
2013	$38,515,120	$33,104,121	$4,267,945	$2,169,584
2014	$45,620,984	$35,330,086	$3,788,686	$1,140,577
2015	$41,687,352	$49,534,555	$2,619,871	$962,667

Looking Ahead to 2020: Science, Meet Politics

> "There can be no end to TB without an end to political indifference in this R&D agenda."
>
> **—Lynette Mabote, Team Leader, Regional HIV, TB and Human Rights Programmes, AIDS and Rights Alliance for Southern Africa**

The *2011–2015 Global Plan* will be succeeded by the *Global Plan to End TB, 2016–2020: the Paradigm Shift* (*2016–2020 Global Plan*). For this new plan to be successful in achieving its vision of a paradigm shift—"a time when the usual and accepted way of doing or thinking about something changes completely," a definition borrowed from the Cambridge English Dictionary—the next five years of TB research will need to be better resourced than the last. The unfulfilled R&D goals of the *2011–2015 Global Plan* have carried over into the *2016–2020 Global Plan*, which calls for $9 billion in funding for TB R&D through 2020.[55]

TB researchers managed to take significant steps forward between 2011 and 2015 despite receiving only one-third of the targeted funding. A target of $9 billion for TB R&D in the next five-year period keeps the goalposts in the same position where they stood during the *2011–2015 Global Plan*. The TB field will not achieve this target—which it previously missed by over $6.5 billion—in 2016–2020 without doing something different. The experience of the last five years suggests that, even more than a lack of resources, TB research suffered from a critical anemia of political will. The politics of funding emerged as a dominant theme in the interviews TAG conducted with TB experts, and Lynette Mabote, team leader of regional HIV, TB and human rights programmes at the AIDS and Rights Alliance for Southern Africa, expressed the feeling of many when she stated, "there can be no end to TB without an end to political indifference in this R&D agenda." She went on to describe TB R&D funding as "in dire straits" due to "political apathy threatening fragile progress."

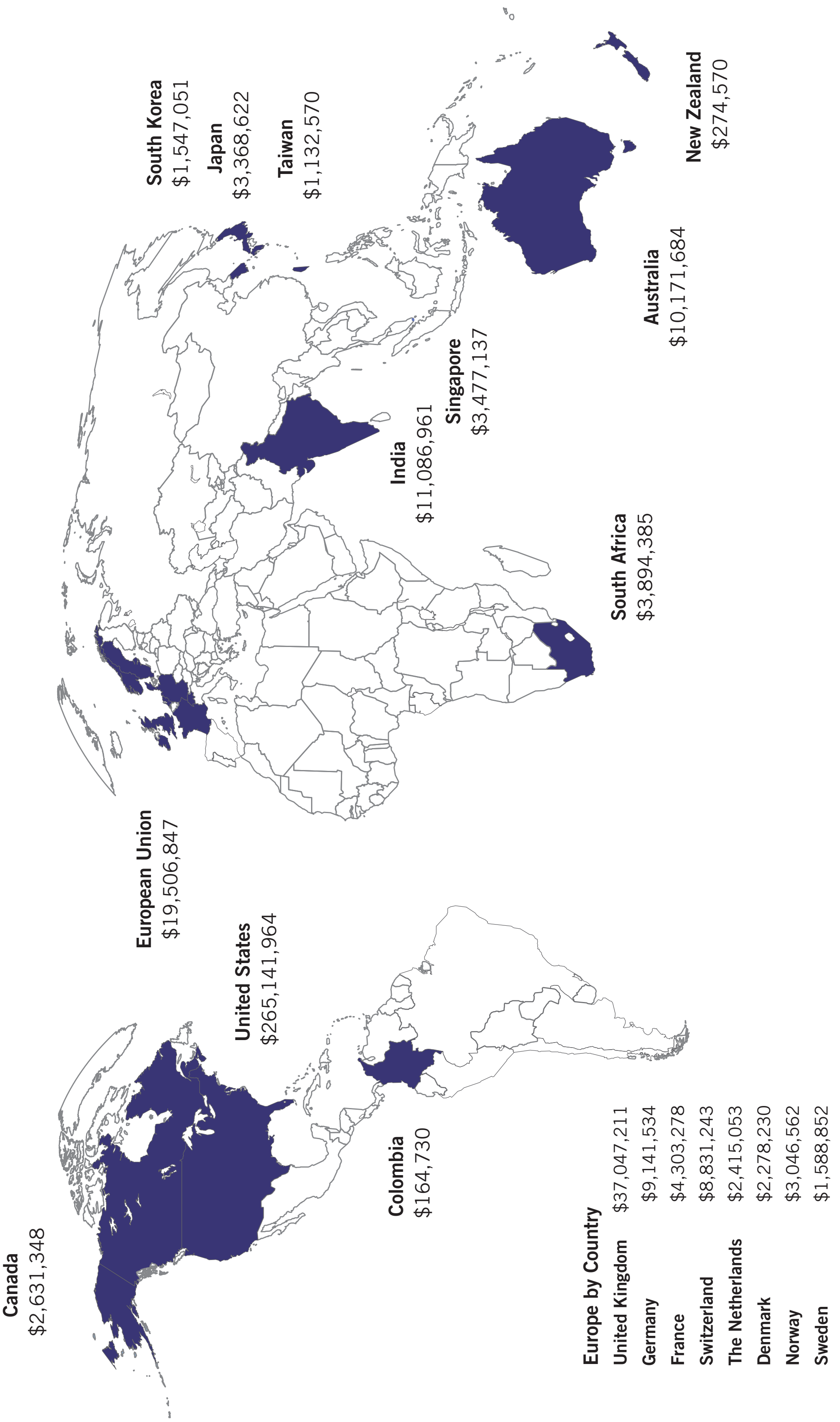
Political commitment does not easily lend itself to target setting. Unlike funding, it cannot be reduced to an aspirational number or annually surveyed. Yet political will is a precondition for any substantial increase in funding, and its presence or absence will determine whether research dollars grow, stagnate, or decline. When the opening chapter of the *2011–2015 Global Plan* proclaimed that "political commitment, backed by the financial commitments of both endemic and donor countries, is central to global efforts to stop TB," it had all of the right pieces, but arranged them in the wrong order. It is political commitment that backs financial commitment and maintains funding over time. The money will follow the politics, an idea the Stop TB Partnership understood when it launched the *2006–2015 Global Plan to Stop TB*, the predecessor to the *2011–2015 Global Plan*, in Davos, Switzerland, at the World Economic Forum at an event headlined by the President of Nigeria, the U.K. Chancellor of the Exchequer, and Bill Gates.

The TB R&D field will need to return to this understanding of politics to ensure that research under the *2016–2020 Global Plan* receives the political backing required to secure $9 billion in investment. Marshaling funding for research into any disease requires savvy political engagement, but this is especially true for TB, where over 60 percent of money for R&D comes from the public sector, a point Stephen Lewis emphasized as follows: "The world never fully appreciates that it's the public sector that carries the weight of R&D for TB. Of the top 10 funders, the public sector provides 50 percent of the total, foundations and multilaterals provide slightly over 20 percent of the total, and commercial pharmaceuticals provide roughly seven percent of the total."

Lewis continued by saying that "there is no question that the brand-name drug manufacturers are delinquent in the extreme," highlighting the paucity of pharmaceutical industry investment in TB research, but he also expressed his frustration with policymakers and donors for letting abstract figures cloud the human futures that depend on TB R&D. "This is life and death for millions of women, men, and children. By comparison, the death toll in Syria, Yemen, South Sudan, Afghanistan, the Democratic Republic of the Congo, Pakistan, Iraq, Lebanon, and Turkey, taken collectively, is a modest fraction of the toll taken by TB. And even HIV/AIDS is now eclipsed. People should be taking to the streets." The *2016–2020 Global Plan* attempts to quantify

FIGURE 15

Country Contributions to TB R&D, 2015



Europe by Country	
United Kingdom	$37,047,211
Germany	$9,141,534
France	$4,303,278
Switzerland	$8,831,243
The Netherlands	$2,415,053
Denmark	$2,278,230
Norway	$3,046,562
Sweden	$1,588,852

"The world never fully understands nor appreciates that it's the public sector that carries the weight of R&D for tuberculosis. Of the top 10 funders, the public sector provides 50 percent of the total, foundations and multilaterals provide slightly over 20 percent of the total, and commercial pharmaceuticals provide roughly seven percent of the total. There is no question that the brand-name drug manufacturers are delinquent in the extreme."

—Stephen Lewis, Co-Director, AIDS-Free World

the lives that will be lost if TB R&D continues on its underfunded trajectory: a five-year delay in satisfying the R&D funding targets could result in an additional 8 million TB cases and 1.4 million TB deaths by 2030.[56]

The sizeable proportion of TB R&D funding that comes from just a few nations reveals the TB field's limited success in engaging policymakers from a wide swathe of countries. The United States, with the world's largest gross domestic product (GDP), ranks above all other countries in terms of TB R&D spending as a percentage of GDP. In 2015, U.S. government agencies gave a combined $265.1 million to TB R&D, 43 percent of total funding and 67 percent of public funding. This reliance on a single country leaves TB R&D in a precarious position, one Valerie Mizrahi described as "sitting with the U.S. taxpayer." Yet the U.S. presidential election campaign—ongoing at the time of this report's publication—suggests that funding from the U.S. government cannot be assumed as a given. Turnover in the U.S. executive and congressional branches could radically alter U.S. support for TB R&D and other global health initiatives. Electoral unpredictability has also thrown up uncertainty for science funding in other leading donor countries. In June 2016, voters in the U.K. approved a referendum to exit the European Union, a move widely interpreted as a blow to research on both sides of the English Channel.[57]

Given the political seizures that threaten to roil public funding in the United States and Europe, TB researchers would be wise to expand their base of support to a wider array of countries. For years, members of the TB R&D community have called on the BRICS nations, which bear the greatest burden of TB, to allocate more domestic funding to TB R&D. David Lewinsohn echoed many when he said, "we have to really focus on India, South Africa, Russia, [China], and Brazil. Both in terms of the size of their economies and their research capacity, BRICS countries could and should be contributing much more to TB research." Despite repeated entreaties, several ministerial declarations, and millions of their citizens' lives cut short by TB, the BRICS countries have not stepped up for TB research in a major way. Among them, India gives the most to TB research in absolute terms, with $11.1 million in 2015. However, when assessing TB R&D funding as a percentage of GDP, South Africa ranks above India, although its 2015 spending on TB research totaled just $3.9 million. (Like the Japanese yen, the value of the South African rand experienced significant depreciation against the U.S. dollar in 2015, which may explain South Africa's dip in funding from $4.7 million in 2014 to $3.9 million in 2015.)[58]

While the *2011–2015 Global Plan* called on the BRICS and other endemic countries to mobilize up to half of the required resources for TB research, it did not provide a detailed plan for making this a reality. The WHO's *Global Action Framework for TB Research* (*Global Action Framework*), published in 2015, has finally provided a systematic approach for accomplishing this long-sought goal. The *Global Action Framework* calls on countries to create national strategic plans for TB research by taking a census of existing efforts, building consensus around R&D priorities, and "activating domestic research funding mechanisms" to complement international support.[59] Crucially, the WHO expects that every country can pursue the principles in the framework, and its Global TB Programme has already begun to work with several governments that have elected to become "pathfinder countries" and create the first set of national strategic plans for TB research. If implemented widely, the *Global Action Framework* could become a vehicle for expanding effective political engagement in TB R&D in the countries where it has previously been minimal or absent.

TABLE 4

Country Funding for R&D and TB R&D as a Percentage of GDP

COUNTRY	TB R&D FUNDING 2015	CHANGE IN TB R&D FUNDING OVER 2014	GDP 2015 (USD BILLIONS)	R&D EXPENDITURE AS PERCENTAGE OF GDP RANK ORDER	TB R&D EXPENDITURE AS PERCENTAGE OF GDP RANK ORDER
United States	$265,141,964	↑	$17,947	8	1
Switzerland	$8,831,243	↑	$665	6	2
United Kingdom	$37,047,211	↓	$2,849	15	3
South Africa	$3,894,385	↓	$313	19	4
Singapore	$3,477,137	↓	$293	12	5
Norway	$3,046,562	↓	$388	14	6
Denmark	$2,278,230	↓	$295	4	7
Australia	$10,171,684	↑	$1,340	9	8
India	$11,086,961	↑	$2,074	18	9
Sweden	$1,588,852	↓	$493	3	10
The Netherlands	$2,415,053	↓	$753	13	11
Germany	$9,141,534	↓	$3,356	7	12
Taiwan*	$1,132,570	↑	$523	5	13
France	$4,303,278	↓	$2,422	10	14
Canada	$2,631,348	↓	$1,551	16	15
New Zealand	$274,570	↓	$174	17	16
European Union	$19,506,847	↓	$16,229	11	17
South Korea	$1,547,051	↑	$1,378	1	18
Japan	$3,368,622	↑	$4,123	2	19
Colombia	$164,730	↓	$292	20	20

* Data on GDP taken from the National Statistics Bureau of the Republic of China (Taiwan); all other data on GDP and R&D expenditure come from the World Bank.

> “The level of underfunding is so pervasive that it seems like we’ve almost gotten used to it, and we have been sitting there thinking that this is okay, and we should be happy with the amount that we’ve got. But it’s not okay . . . I am completely of the view that without new tools, we are not going to achieve anywhere close to the targets we’re aiming for.”
>
> **—Valerie Mizrahi, Director, Institute of Infectious Disease and Molecular Medicine, University of Cape Town**

What would stronger support for TB R&D from endemic countries look like? Lynette Mabote provided a detailed vision for how this could take hold in the Southern African Development Community (SADC), a group of 15 nations in Southern Africa. Lynette’s assessment is worth quoting from at length, as the situation she describes looks similar in other regions with heavy TB burdens but low national spending on TB research. Lynette characterized support for TB R&D within SADC over the last five years as “nonexistent” and largely viewed as “insignificant in SADC’s development agenda.” For example, an April 2015 review of SADC’s Regional Indicative Strategic Development Plan found an overreliance on donor funding for TB treatment as well as for R&D. “Only two countries in the SADC region (Malawi and South Africa) spend above one percent of their GDP on R&D, a target endorsed by the African Union in 2006. R&D is dominated by academics from major universities and thus is not thought of as a matter of national policy,” said Lynette. TAG’s data on TB R&D funding from South Africa confirm this diagnosis. South African universities conduct some of the world’s most innovative TB research, but in 2015 they received more funding from the NIH and the Gates Foundation than from the South African Medical Research Council or other departments of the South African government.

The primary challenge to increasing political support for TB research in SADC countries, according to Lynette, “has been the articulation of clear indicators which monitor financing toward TB R&D. For example, the 2007–2015 Strategic Framework for the Control of Tuberculosis in the SADC region had no clear indicators to monitor funding for TB R&D.” Future plans for tackling TB in the SADC region should borrow indicators from the WHO *Global Action Framework*, including regular award of national research operating funds, national funding for TB research capacity, and annual national competitions for health research operating funds. Efforts to implement the *Global Action Framework* in SADC and other regions should begin now; there is no time to waste. The stagnation in global funding for TB R&D over the past five years “highlights the need for regions, including those within the African continent, to realign their priorities and to ‘rethink’ the R&D agenda,” said Lynette. She cautioned, however, that political engagement on TB R&D must “move away from scholarly ‘think tanks’ into actionable strategies which support R&D resource mobilization.”

The call to move the rethink of TB R&D outside of think tanks points to the necessity of engaging TB-affected communities in the research process. Communities where TB R&D is conducted have the right to participate in research as more than just trial participants. “Community engagement in TB research is key in raising community research priorities in TB research,” said Dorothy Namutamba. “Communities need to be well informed so that they appreciate the importance of participating in research, and with this engagement, the absorption of the key outcomes of TB research will be made easier.” Namutamba pointed out that building research literacy in TB-affected communities can strengthen resource mobilization: “Communities play a critical role in advocacy for increased TB research, urging all governments and funding agencies to invest in TB research. [But first] they need to have a clear understanding of the importance of TB R&D.” The idea is simple but powerful: communities with fluency in the science of TB will be better positioned to advocate in support of it before their governments.

Political developments over the past year suggest that grassroots appeals to mobilize new funding and rethink the TB R&D agenda are finding more receptive audiences in UN conference rooms than in national parliaments. In particular, two UN-led processes that culminated in September 2016 have created unprecedented opportunities for the TB research movement to engage political leaders through international frameworks. The first is the final report of the UN Secretary-General’s High-Level Panel on Access to Medicines, published on September 14, 2016. The report issued a formidable set of recommendations—many long advocated for by civil society—to promote innovation and access to health technologies in ways that uphold human rights and address the market failures that have resulted in meager funding for diseases like TB.[60]

Among its recommendations, the report calls on governments "to increase their current levels of investment in health technologies innovation to address unmet needs," "test and implement new and additional models for financing and rewarding public health R&D," and come together to negotiate "a binding R&D Convention that delinks the costs of R&D from end prices to promote access to good health for all."[61]

The second development followed a week later with the first-ever UN High-Level Meeting on Antimicrobial Resistance (AMR). The threat of DR-TB underlined many of the resulting discussions about the narrow window of opportunity for governments to curb the spread of drug-resistant infections. By the end of the meeting, UN member states adopted a political declaration outlining a broad intention to tackle antimicrobial resistance through joint action, including the need to resolve "the lack of investment in research and development . . . for new antimicrobial and alternative medicines, rapid diagnostic tests, vaccines and other important technologies."[62] Together, this AMR declaration and the report of the UN Secretary-General's High-Level Panel on Access to Medicines have momentarily captured the attention of governments and created new channels for engaging political leaders in the fight against TB. It will be up to members of the TB community—activists and scientists—to add the teeth of targets, clear implementation plans, and accountability mechanisms to these documents to ensure that they make a meaningful difference in the lives of people affected by TB.

Conclusion

The $3.29 billion spent on TB R&D between 2011 and 2015 amounted to just one-third of the $9.84 billion called for by the *2011–2015 Global Plan*. Most concerning, annual funding for TB R&D posted declines in three separate years—2012, 2014, and 2015—and in this last year, funding fell by $53.4 million, sending many categories of research back to the level of funding they received in 2011. Reversing this decline will require a forthright engagement of political leaders, many of whom do not see TB as an urgent problem whose solution will depend on science. Efforts to capture and keep political will and then translate it into a significant and sustained increase in financial support for TB R&D must unfold at both the high level and the grassroots level, where the mobilization of communities—including the research community—in support of R&D will be essential. That TB researchers managed to make many advances over the past five years despite receiving only a fraction of required funding should not be taken as cause to allow this situation to repeat itself under the *2016–2020 Global Plan*. The next phase of R&D may require even more costly and complex endeavors to build on existing tools, and flat or diminished funding will not be sufficient to support the science the world needs to eliminate TB. In our *2014 Report on Tuberculosis Research Funding Trends*, we called for a TB research movement with "muscle, money, and political commitment."[63] The same ingredients remain in urgent demand as the world moves into the first years of what is being hailed as the TB elimination era.

Endnotes

1. Stop TB Partnership. The Global Plan to Stop TB: 2011–2015. Geneva: World Health Organization; 2010. Available from: http://www.who.int/tb/publications/tb-global-plan/en/. (Accessed 2016 September 10)

2. World Health Organization. Global tuberculosis report 2015. Geneva: World Health Organization; 2015. Available from: http://www.who.int/tb/publications/global_report/en. (Accessed 2016 September 10)

3. World Health Organization. Drug-resistant TB: surveillance & response. Geneva: World Health Organization; 2014. Available from: http://www.who.int/tb/publications/mdr_surveillance/en/. (Accessed 2016 September 22)

4. Huidrom R, Kose MA, Ohnsorge F. A ride in rough waters. Finance & Development. 2016;53(3):34–37. Available from: http://www.imf.org/external/pubs/ft/fandd/2016/09/huidrom.htm.

5. Global Knowledge Partnership on Migration and Development. Migration and remittances factbook 2016. Washington, D.C.: World Bank; 2015. Available from: http://www.knomad.org/. (Accessed 2016 September 19)

6. Dandekar V. Pfizer draws curtain on anti-infective research; refocuses on next-generation vaccines. PharmAsia News [Internet]. 2013 May 13 (cited 2016 September 19). Available from: https://www.pharma-medtechbi.com/publications/pharmasia-news/2013/5/13/.

7. Mullin E. Global tuberculosis R&D takes hit with AstraZeneca site closure. FierceBiotech [Internet]. 2014 February 24 (cited 2016 September 19). Available from: http://www.fiercebiotech.com/research/global-tuberculosis-r-d-takes-hit-astrazeneca-site-closure.

8. Copley C. Novartis hands over experimental TB drugs in antibiotic pullback. Reuters [Internet]. 2014 August 20 (cited 2016 September 19). Available from: http://www.reuters.com/article/us-novartis-tuberculosis-idUSKBN0GK19J20140820.

9. World Health Organization. Global tuberculosis report 2015.

10. Jouvenceau, Anne (INSERM, Paris, France). E-mail with: Mike Frick (Treatment Action Group, New York, NY). 2016 August 17.

11. Scano, Fabio (Office of the World Health Organization Representative in the People's Republic of China, Beijing, China). E-mail with: Mike Frick (Treatment Action Group, New York, NY). 2016 August 19.

12. Afanasyev, Nikita (World Health Organization, Moscow, Russia). E-mail with: Mike Frick (Treatment Action Group, New York, NY). 2016 August 19.

13. Lang, Hannu (European Commission, Brussels, Belgium). E-mail with: Mike Frick (Treatment Action Group, New York, NY). 2016 September 2.

14. Boon, Cheryl (Global Affairs Canada, Ottawa, Canada). E-mail with: Mike Frick (Treatment Action Group, New York, NY). 2016 August 29.

15. de Kort, Marcel (Dutch Directorate-General for International Cooperation, The Hague, The Netherlands). E-mail with: Mike Frick (Treatment Action Group, New York, NY). 2016 June 21.

16. Lessem E. The tuberculosis treatment pipeline: activity, but no answers. In: Clayden P, Collins S, Frick M, et al.; i-base/Treatment Action Group. 2016 pipeline report. New York: Treatment Action Group; 2016. Available from: http://www.pipelinereport.org. (Accessed 2016 September 10)

17. See, for example, The Economist. Japan adjusts its quantitative-easing programme [Internet]. 2015 December 18 (cited 2016 September 10). Available from: http://www.economist.com/news/finance-economics/21684516-central-bank-joins-effort-get-japanese-companies-spend-their-cash.

18. See, for example, historical exchange rates published by the OANDA Corporation: OANDA Corporation. Available from: https://www.oanda.com/solutions-for-business/historical-rates/main.html. (Accessed 2016 September 10)

19. Stop TB Partnership. Global Plan.

20. Frick M. TB R&D's shift to the left. TAGline Spring 2015 [Internet]. 2015 April 9. Available from: http://www.treatmentactiongroup.org/tagline/2015/spring/tb-rd%E2%80%99s-shift-left. (Accessed 2016 September 10)

21. Frick M. The tuberculosis prevention pipeline. In: Clayden P, Collins S, Frick M, et al.; i-base/Treatment Action Group. 2016 pipeline report. New York: Treatment Action Group; 2016. Available from: http://www.pipelinereport.org. (Accessed 2016 September 10)

22.. Hanekom WA. Experimental medicine. Presentation at: TuBerculosis Vaccine Initiative annual meeting; 2016 February 1–5; Les Diablerets, Switzerland. Available from: http://www.tbvi.eu/wp-content/uploads/2016/02/Hanekom.pdf. (Accessed 2016 September 26)

23. See, for example, Prideaux B, Via L, Zimmerman M, et al. The association between sterilizing activity and drug distribution into tuberculosis lesions. Nat Med. 2015;21(10):1223–7. doi: 10.1038/nm.3937.

24. See, for example, Kester J, Fortune S. Persisters and beyond: mechanisms of phenotypic drug resistance and drug tolerance in bacteria. Crit Rev Biochem Mol Biol. 2014;49(2):91–101. doi: 10.3109/10409238.2013.869543.

25. Stop TB Partnership. 2011–2015 Global Plan.

26. World Health Organization. WHO endorses new rapid tuberculosis test [Internet]. 2010 December 8 (cited 2016 September 22). Available from: http://www.who.int/tb/features_archive/new_rapid_test/en/.

27. World Health Organization. The use of lateral flow urine lipoarabinomannan assay (LF-LAM) for the diagnosis and screening of active tuberculosis in people living with HIV: policy update. Geneva: World Health Organization; 2015. Available from: http://www.who.int/tb/publications/use-of-lf-lam-tb-hiv/en/. (Accessed 2016 September 19)

28. Lessem E. The tuberculosis diagnostics pipeline. In: Clayden P, Collins S, Frick M, et al.; i-base/Treatment Action Group. 2016 pipeline report. New York: Treatment Action Group; 2016. Available from: http://www.pipelinereport.org. (Accessed 2016 September 10)

29. Peter JG, Zijenah LS, Chanda D, et al. Effect on mortality of point-of-care, urine-based lipoarabinomannan testing to guide tuberculosis treatment initiation in HIV-positive hospital inpatients: a pragmatic, parallel-group, multicountry, open-label, randomized controlled trial. Lancet. 2016;387(10024):1187–97. doi: 10.1016/S0140-6736(15)01092-2.

30. World Health Organization. Global tuberculosis report 2013. Geneva: World Health Organization; 2015. Available from: http://www.who.int/mediacentre/news/releases/2013/tuberculosis-report-2013/en/. (Accessed 2016 September 10)

31. Lessem E. The tuberculosis diagnostics pipeline.

32. World Health Organization. WHO warns against the use of inaccurate blood tests for active tuberculosis [Internet]. 2011 July 20 (cited 2016 September 10). Available from: http://www.who.int/mediacentre/news/releases/2011/tb_20110720/en/.

33. Ibid.

34. World Health Organization. Use of tuberculosis interferon-gamma release assays (IGRAs) in low- and middle-income countries: policy statement. Geneva: World Health Organization; 2011. Available from: http://www.who.int/tb/features_archive/policy_statement_igra_oct2011.pdf. (Accessed 2016 September 20)

35. See, for example, The Economist. Japan adjusts its quantitative-easing programme.

36. U.S. Food & Drug Administration. FDA approves first drug to treat multi-drug resistant tuberculosis in forty years [Internet]. 2012 December 31 (cited 2016 September 19). Available from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm333695.htm.

37. European Medicines Agency. Deltyba (delamanid): summary of opinion [Internet]. 21 November 2013 (cited 2016 September 19). Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002552/smops/Positive/human_smop_000572.jsp&mid=WC0b01ac058001d127.

38. Sterling T, Villarino E, Borisov A, et al. Three months of rifapentine and isoniazid for latent tuberculosis infection. N Engl J Med. 2011;365(23):2155–66. doi: 10.1056/NEJMoa1104875.

39. Sterling TR, Scott NA, Miro JM, et al. Three months of weekly rifapentine plus isoniazid for treatment of M. tuberculosis infection in HIV co-infected persons. AIDS. 2016:19(30):1607–15. doi: 10.1097/QAD.0000000000001098.

40. Villarino ME, Scott NA, Weis SE, et al. Treatment for preventing tuberculosis in children and adolescents: a randomized clinical trial of a 3-month, 12-dose regimen of a combination of rifapentine and isoniazid. JAMA Pediatr. 2015;169(3):247–55. doi: 10.1001/jamapediatrics.2014.3158.

41. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (U.S.) 2000. Identifier NCT01582711, Study 33: adherence to latent tuberculosis infection treatment 3HP SAT versus 3HP DOT; 2015 July 30 (cited 2016 September 19). Available from: https://clinicaltrials.gov/ct2/show/NCT01582711.

42. Gillespie S, Crook A, McHugh T, et al. Four-month moxifloxacin-based regimens for drug-sensitive tuberculosis. N Engl J Med. 2014;371(17):1577–87. doi: 10.1056/NEJMoa1407426.

43. Merle C, Fielding K, Sow O, et al. A four-month gatifloxacin-containing regimen for treating tuberculosis. N Engl J Med. 2014;371(17): 1588–98. doi: 10/1056/NEJMoa1315817.

44. Jindani A, Harrison T, Nunn A, et al. High-dose rifapentine with moxifloxacin for pulmonary tuberculosis. N Engl J Med. 2014;371(17):1599–1608. doi: 10.1056/NEJMoa1314210.

45. World Health Organization. Rapid diagnostic test and shorter, cheaper treatment signal new hope for multidrug-resistant tuberculosis patients [Internet]. 2016 May 12 (cited 2016 September 10). Available from: http://www.who.int/mediacentre/news/releases/2016/multidrug-resistant-tuberculosis/en.

46. TB Alliance. TB Alliance and partners announce world's first availability of appropriate, child-friendly TB medicines in correct doses [Internet]. 2015 November 24 (cited 2016 September 10). Available from: http://www.tballiance.org/news/tb-alliance-announces-worlds-first-appropriate-child-friendly-tb-medicines.

47. Lessem E. The tuberculosis treatment pipeline.

48. Brennan MK, Thole J. Tuberculosis vaccines: a strategic blueprint for the next decade. Tuberculosis (Edinb). 2012;92(S1):S6–13. doi: 10.1016/S1472-9792(12)70005-7.

49. Asia Pacific Network of Positive People, Delhi Network of Positive People, Coalition of People Living with HIV in India, et al. Open letter to J.P. Nadda, Minister of Health and Family Welfare re: TB case detection—urgent need to scale up rapid TB test machines and cartridges [Internet]. 2015 September 15 (cited 2016 September 19). Available from: https://brokentbpromises.wordpress.com/featured-two/.

50. World Health Organization, Stop TB Partnership, Treatment Action Group, International Union Against Tuberculosis and Lung Disease, U.S. Agency for International Development, U.S. Centers for Disease Control and Prevention, and UNICEF. Roadmap for childhood tuberculosis. Geneva: World Health Organization; 2013. Available from: http://apps.who.int/iris/bitstream/10665/89506/1/9789241506137_eng.pdf. (Accessed 2016 September 19)

51. World Health Organization. Global tuberculosis report 2012. Geneva: World Health Organization; 2012. Available from: http://apps.who.int/iris/bitstream/10665/75938/1/9789241564502_eng.pdf. (Accessed 2016 September 10).

52. Jenkins H, Tolman A, Yuen C, et al. Incidence of multidrug-resistant tuberculosis disease in children: systematic review and global estimates. Lancet. 2014;383(9928):1572–79. doi: 10.1016/S0140-6736(14)60195-1.

53. World Health Organization. Global tuberculosis report 2015.

54. McKenna L. The pediatric tuberculosis treatment pipeline: beyond pharmacokinetics and safety data. In: Clayden P, Collins S, Frick M, et al.; i-base/Treatment Action Group. 2016 pipeline report. New York: Treatment Action Group; 2016. Available from: http://www.pipelinereport.org. (Accessed 2016 September 10)

55. Stop TB Partnership. The Global Plan to End TB, 2016–2020: the Paradigm Shift. Geneva: UNOPS; 2015. Available from: http://www.stoptb.org/global/plan/plan2/. (Accessed 2016 September 10)

56. Ibid.

57. See, for example, Cressey D. Brexit watch: scientists grapple with the fallout. Nature. 2016 July 8. Available from: http://www.nature.com/news/brexit-watch-scientists-grapple-with-the-fallout-1.20226. (Accessed 19 September 2016)

58. Bhoola F. Analysis: why the rand is falling. Mail & Guardian [Internet]. 2016 January 18 (cited 2016 September 26). Available from: http://mg.co.za/article/2016-01-18-how-currency-markets-work-and-why-the-rand-is-falling.

59. World Health Organization. A global action framework for TB research in support of the third pillar of WHO's end TB strategy. Geneva: World Health Organization; 2015. Available from: http://www.who.int/tb/publications/global-framework-research/en/. (Accessed 2016 September 26)

60. United Nations Secretary-General's High-Level Panel on Access to Medicines. Report of the United Nation's Secretary-General's High-Level Panel on Access to Medicines: promoting innovation and access to health technologies. New York: United Nations Development Programme; 2016. Available from: http://www.unsgaccessmeds.org/. (Accessed 2016 September 20)

61. Ibid.

62. United Nations high-level meeting on antimicrobial resistance. Draft political declaration of the high-level meeting of the General Assembly on antimicrobial resistance [UN Doc AMR-16-16108]. New York: United Nations General Assembly; 2016. Available from: http://www.un.org/pga/71/even-latest/high-level-meeting-on-antimicrobial-resistance/. (Accessed 2016 September 26)

63. Treatment Action Group. 2014 report on tuberculosis research funding trends: 2005–2013. New York: Treatment Action Group; 2014. Available from: http://www.treatmentactiongroup.org/tbrd2014. (Accessed 2016 September 19)

Appendix 1

Top Reporting TB R&D Funders, 2015

2015 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
1	NIAID	P	$178,686,059
2	Bill & Melinda Gates Foundation	F	$110,985,743
3	NIH Other Ics	P	$34,920,532
4	U.S. Agency for International Development (USAID)	P	$34,053,650
5	Ostuka Pharmaceuticals	C	$29,042,414
6	U.K. Department for International Development (DFID)	P	$23,034,975
7	GlaxoSmithKline (GSK)	C	$17,645,266
8	U.S. Centers for Disease Control and Prevention (CDC)	P	$14,072,846
9	European Commission	P	$13,775,984
10	UNITAID	M	$13,746,000
11	U.K. Medical Research Council (U.K. MRC)	P	$10,692,435
12	Indian Council of Medical Research (ICMR)	P	$8,951,412
13	Company X	C	$8,788,399
14	Company V	C	$8,332,778
15	Company Y	C	$6,850,000
16	Wellcome Trust	F	$6,653,184
17	German Federal Ministry of Education and Research (BMBF)	P	$6,501,534
18	Australian Department of Foreign Affairs and Trade (DFAT)	P	$5,139,706
19	Swiss National Science Foundation (SNSF)	P	$4,874,818
20	Qiagen	C	$4,870,000
21	Australian National Health and Medical Research Council (NHMRC)	P	$4,734,126
22	European and Developing Countries Clinical Trials Partnership (EDCTP)	P	$4,650,743
23	Macleods Pharmaceuticals	C	$3,500,000
24	Public Health England	P	$3,260,041
25	Eli Lilly	C	$2,750,000
26	Max Planck Institute for Infection Biology	P	$2,640,000
27	Canadian Institutes of Health Research	P	$2,631,348
28	Norwegian Agency for Development Cooperation (NORAD)	P	$2,613,222
29	Institut Pasteur	F	$2,441,449
30	Global Health Innovative Technology Fund (GHIT)	M	$2,430,526
31	French National Agency for Research (ANR)	P	$2,362,871

BASIC SCIENCE	INFRASTRUCTURE/ UNSPECIFIED	DIAGNOSTICS	DRUGS	VACCINES	OPERATIONAL RESEARCH
$80,881,310	$10,403,610	$13,838,709	$44,547,114	$16,976,063	$12,039,253
$4,023,233	$3,145,874	$11,064,092	$48,113,145	$26,901,486	$17,737,913
$14,498,371	$6,324,841	$2,648,773	$5,828,977	$990,390	$4,629,180
$0	$10,011,818	$0	$18,093,370	$0	$5,948,462
$0	$0	$0	$29,042,414	$0	$0
$0	$0	$3,145,240	$11,008,340	$2,516,192	$6,365,203
$0	$0	$0	$55,631	$17,589,635	$0
$0	$0	$4,993,508	$7,310,041	$0	$1,769,297
$3,209,556	$2,443,362	$2,564,173	$2,720,140	$1,553,034	$1,285,719
$0	$0	$0	$13,746,000	$0	$0
$3,856,053	$406,455	$1,588,805	$3,271,889	$294,133	$1,275,100
$275,294	$7,469,804	$174,406	$28,248	$125,600	$878,061
$0	$0	$0	$8,788,399	$0	$0
$0	$0	$0	$8,332,778	$0	$0
$0	$0	$6,850,000	$0	$0	$0
$5,796,315	$202,458	$243,346	$204,977	$0	$206,088
$1,670,180	$2,496,593	$878,425	$11,181	$1,139,433	$305,724
$0	$0	$2,562,166	$2,562,166	$0	$15,373
$4,105,273	$19,986	$0	$406,548	$168,043	$174,968
$0	$0	$4,870,000	$0	$0	$0
$3,188,625	$285,969	$1,098,572	$160,960	$0	$0
$0	$0	$582,815	$2,847,478	$921,051	$299,399
$0	$0	$0	$3,500,000	$0	$0
$1,085,108	$0	$0	$0	$2,174,933	$0
$0	$0	$0	$2,750,000	$0	$0
$1,540,000	$0	$0	$0	$1,100,000	$0
$1,571,528	$0	$69,062	$167,770	$178,039	$644,949
$387,213	$0	$359,975	$0	$1,388,031	$478,003
$1,468,894	$0	$218,955	$355,892	$397,708	$0
$0	$0	$0	$1,620,350	$810,175	$0
$1,441,141	$0	$66,861	$854,868	$0	$0

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

Appendix 1

Top Reporting TB R&D Funders, 2015 (continued)

2015 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
32	Swiss Federal Institute of Technology in Lausanne (EPFL)	P	$2,301,582
33	U.S. President's Emergency Plan for AIDS Relief (PEPFAR)	P	$1,948,342
34	French National Agency for AIDS Research (ANRS)	P	$1,940,408
35	Dutch National Postcode Lottery	P	$1,856,013
36	Statens Serum Institut	P	$1,830,784
37	Singapore Ministry of Health, National Medical Research Council (Singapore NMRC)	P	$1,815,489
38	Japanese Ministry of Health, Labour and Welfare	P	$1,722,841
39	Swiss Initiative in Systems Biology (SystemsX.ch)	P	$1,654,844
40	Singapore Agency for Science, Technology and Research (A*STAR)	P	$1,645,314
41	Swedish Research Council	P	$1,588,852
42	National Philanthropic Trust	F	$1,500,000
43	Indian Ministry of Health and Family Welfare (MOHFW)	P	$1,493,809
44	South African Medical Research Council (SAMRC)	P	$1,345,066
45	Japan International Cooperation Agency (JICA)	P	$1,222,657
46	South African Department of Health	P	$1,159,795
47	Irish Aid	P	$1,118,080
48	Taiwan Centers for Disease Control	P	$1,102,570
49	Innovative Medicines Initiative (IMI)	P	$1,080,119
50	U.S. National Science Foundation	P	$996,557
51	Company R	C	$880,133
52	Biofabri	C	$838,238
53	Médecins Sans Frontières	F	$801,991
54	National Research Foundation, South Africa	P	$731,142
55	Korea Drug Development Fund	P	$712,000
56	Qurient	C	$712,000
57	Indian Ministry of Science and Technology, Department of Biotechnology	P	$641,740
58	South African Department of Science and Technology (DST)	P	$637,937
59	World Health Organization (WHO)	M	$618,189
60	Irish Health Research Board	P	$584,257
61	Serum Institute of India	C	$569,033
62	Netherlands Organization for Health Research and Development (ZonMw)	P	$559,040

BASIC SCIENCE	INFRASTRUCTURE/ UNSPECIFIED	DIAGNOSTICS	DRUGS	VACCINES	OPERATIONAL RESEARCH
$1,074,520	$0	$0	$1,227,062	$0	$0
$0	$0	$0	$0	$0	$1,948,342
$126,943	$0	$194	$1,746,424	$0	$66,846
$0	$0	$0	$1,856,013	$0	$0
$0	$0	$0	$0	$1,830,784	$0
$566,059	$0	$0	$136,647	$0	$1,112,783
$463,925	$196,080	$430,886	$0	$631,950	$0
$1,654,844	$0	$0	$0	$0	$0
$831,566	$0	$371,235	$442,512	$0	$0
$1,413,257	$0	$0	$175,595	$0	$0
$0	$0	$0	$1,500,000	$0	$0
$0	$63,110	$44,761	$260,951	$0	$1,124,988
$824,974	$0	$0	$520,092	$0	$0
$0	$0	$1,222,657	$0	$0	$0
$571,741	$364,237	$16,336	$191,126	$0	$16,356
$0	$0	$0	$1,118,080	$0	$0
$0	$0	$80,900	$119,085	$0	$902,585
$0	$0	$0	$1,080,119	$0	$0
$350,921	$0	$645,636	$0	$0	$0
$0	$0	$0	$880,133	$0	$0
$0	$0	$0	$0	$838,238	$0
$0	$0	$256,574	$226,344	$0	$319,073
$682,074	$49,068	$0	$0	$0	$0
$0	$0	$0	$712,000	$0	$0
$0	$0	$0	$712,000	$0	$0
$451,510	$0	$55,366	$0	$0	$134,864
$0	$0	$43,863	$594,074	$0	$0
$0	$0	$69,967	$0	$58,064	$490,158
$0	$0	$0	$299,541	$284,716	$0
$0	$0	$0	$0	$569,033	$0
$0	$0	$0	$0	$0	$559,040

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

Appendix 1

Top Reporting TB R&D Funders, 2015 (continued)

2015 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
63	Japan BCG Laboratory	C	$499,350
64	U.S. Food and Drug Administration (FDA)	P	$463,978
65	Korean Ministry of Health and Welfare	P	$439,972
66	Company W	C	$438,300
67	Japan Agency for Medical Research and Development (AMED)	P	$423,124
68	Science Foundation Ireland	P	$417,774
69	Danish Council for Independent Research	P	$391,718
70	BioDuro	C	$337,500
71	Australian Research Council	P	$297,852
72	Fondation Total	F	$279,520
73	Health Research Council of New Zealand	P	$274,570
74	Damien Foundation Belgium	F	$239,828
75	Korean Ministry of Science, ICT and Future Planning	P	$225,170
76	Foundation Jacqueline Beytout	F	$208,699
77	Cepheid	C	$200,000
78	QuantaMatrix	C	$178,000
79	Korea Centers for Disease Control and Prevention	P	$169,909
80	Swiss Lung Foundation	F	$157,452
81	Research Council of Norway	P	$139,788
82	Lundbeck Foundation	F	$127,901
83	SK Telecom C	C	$125,490
84	LG Life Sciences	C	$115,700
85	Southeastern Norway Regional Health Authority	P	$115,134
86	Colombia Department of Science, Technology and Innovation	P	$108,800
87	Howard Hughes Medical Iinstitute	F	$100,000

BASIC SCIENCE	INFRASTRUCTURE/ UNSPECIFIED	DIAGNOSTICS	DRUGS	VACCINES	OPERATIONAL RESEARCH
$0	$0	$0	$0	$499,350	$0
$0	$0	$0	$400,000	$63,978	$0
$0	$0	$386,572	$53,400	$0	$0
$0	$0	$0	$438,300	$0	$0
$294,120	$0	$0	$0	$129,004	$0
$0	$0	$417,774	$0	$0	$0
$0	$0	$0	$0	$391,718	$0
$0	$0	$0	$337,500	$0	$0
$297,852	$0	$0	$0	$0	$0
$0	$279,520	$0	$0	$0	$0
$244,727	$0	$0	$29,843	$0	$0
$0	$0	$83,856	$155,972	$0	$0
$225,170	$0	$0	$0	$0	$0
$0	$0	$0	$208,699	$0	$0
$0	$0	$200,000	$0	$0	$0
$0	$0	$178,000	$0	$0	$0
$80,909	$0	$89,000	$0	$0	$0
$0	$157,452	$0	$0	$0	$0
$139,788	$0	$0	$0	$0	$0
$0	$0	$0	$0	$127,901	$0
$0	$0	$125,490	$0	$0	$0
$0	$0	$115,700	$0	$0	$0
$115,134	$0	$0	$0	$0	$0
$0	$0	$0	$0	$0	$108,800
$100,000	$0	$0	$0	$0	$0

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

Appendix 1

Top Reporting TB R&D Funders, 2015 (continued)

2015 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
88	Norwegian Public Health Association	P	$92,768
89	European Molecular Biology Organization	F	$73,067
90	Somalogic	C	$71,741
91	Thrasher Research Fund	F	$63,786
92	U.K. National Institue for Health Research (NIHR)	P	$59,760
93	Innovation Fund Denmark	P	$55,727
94	LHL International	P	$53,111
95	Colombia National Institute of Health	P	$51,300
96	YD Diagnostics	C	$50,000
97	International Union of Immunological Societies	F	$48,918
98	National Research Council of Thailand	P	$40,000
99	Stop TB Partnership	M	$39,500
100	Norwegian Institute of Public Health	P	$32,538
101	Global BioDiagnostics	C	$31,774
102	Taiwan Ministry of Science and Technology	P	$30,000
103	Else Kröner-Fresenius Foundation	F	$25,000
104	National Health Laboratory Service Research Trust, South Africa	P	$20,445
105	National University Health System, Singapore	P	$16,334
106	Faber Daeufer	C	$10,000
107	Foundation CHU Sainte-Justine	F	$6,455
108	Individual donors to TB Alliance	F	$4,908
109	Colombia Ministry of Health	P	$4,630
110	Firland Foundation	F	$2,200
111	Philippine Tuberculosis Society	F	$221
			$620,600,596

BASIC SCIENCE	INFRASTRUCTURE/ UNSPECIFIED	DIAGNOSTICS	DRUGS	VACCINES	OPERATIONAL RESEARCH
$0	$0	$0	$0	$0	$92,768
$73,067	$0	$0	$0	$0	$0
$71,741	$0	$0	$0	$0	$0
$0	$0	$63,786	$0	$0	$0
$59,760	$0	$0	$0	$0	$0
$0	$0	$0	$0	$55,727	$0
$0	$0	$0	$0	$0	$53,111
$0	$0	$0	$0	$0	$51,300
$0	$0	$50,000	$0	$0	$0
$0	$48,918	$0	$0	$0	$0
$0	$0	$0	$40,000	$0	$0
$0	$0	$0	$39,500	$0	$0
$0	$0	$0	$0	$32,538	$0
$0	$0	$31,774	$0	$0	$0
$30,000	$0	$0	$0	$0	$0
$25,000	$0	$0	$0	$0	$0
$20,445	$0	$0	$0	$0	$0
$0	$0	$8,910	$7,425	$0	$0
$0	$0	$0	$10,000	$0	$0
$6,455	$0	$0	$0	$0	$0
$0	$0	$0	$4,908	$0	$0
$0	$0	$0	$0	$0	$4,630
$0	$0	$0	$0	$0	$2,200
$0	$0	$0	$0	$0	$221
$139,794,597	**$44,369,155**	**$62,807,118**	**$231,852,022**	**$80,736,948**	**$61,040,756**

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

Appendix 2

TB Experts Interviewed by TAG

1	Mercedes Becerra	Professor, global health and social medicine, Harvard Medical School
2	Lucica Ditiu	Executive director, Stop TB Partnership
3	Jonathan Golub	Associate professor, medicine, epidemiology and international health, The Johns Hopkins University Center for Tuberculosis Research
4	Gilla Kaplan	Director, tuberculosis program, Bill & Melinda Gates Foundation
5	David Lewinsohn	Professor, pulmonary and critical care medicine, Oregon Health & Science University; chair, Stop TB Partnership working group on new TB vaccines
6	Stephen Lewis	Co-director, AIDS-Free World
7	Christian Lienhardt	Team leader, research for TB elimination, World Health Organization Global TB Programme
8	Lynette Mabote	Team leader, regional HIV, TB and human rights programmes, AIDS and Rights Alliance for Southern Africa
9	Valerie Mizrahi	Director, Institute of Infectious Disease and Molecular Medicine, University of Cape Town
10	Dorothy Namutamba	Programmes manager, International Community of Women Living with HIV Eastern Africa; co-chair, Community Research Advisors Group
11	Jérôme St-Denis	Senior advocacy and resource mobilization officer, FIND

Treatment Action Group
90 Broad St, Suite 2503
New York, NY 10004 USA
Tel 1.212.253.7922
Fax 1.212.253.7923

tag@treatmentactiongroup.org

www.treatmentactiongroup.org

Treatment Action Group

ISBN 978-0-9905242-8-1