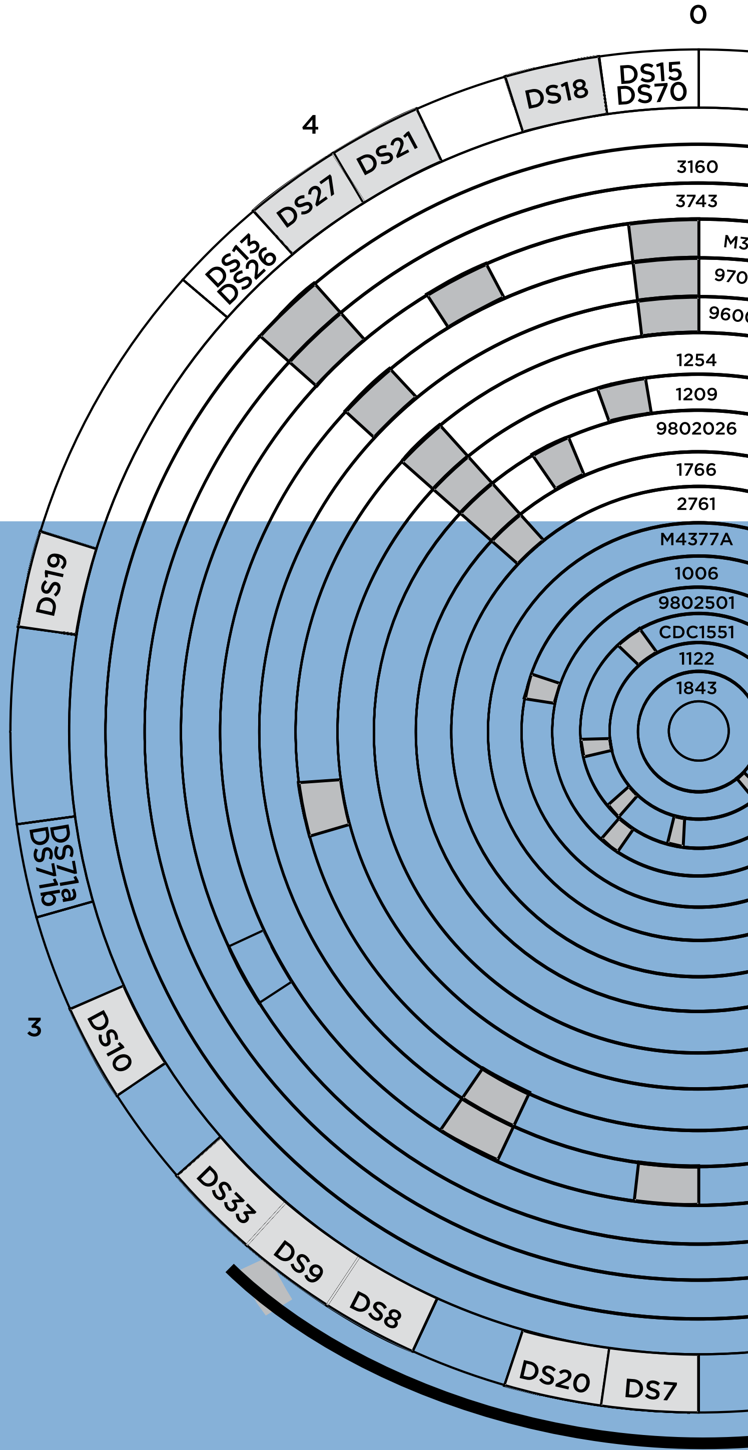
TAG
Treatment Action Group

Stop TB Partnership

TUBERCULOSIS RESEARCH AND DEVELOPMENT:

2014 Report on Tuberculosis Research Funding Trends, 2005–2013

2ND EDITION



MAY 2015

TREATMENT ACTION GROUP

BY MIKE FRICK

ACKNOWLEDGMENTS

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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 strengthen global and U.S.-focused advocacy to increase funding and ensure ambitious research, programs, and policies for people with TB and HIV.

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BY MIKE FRICK

EDITED BY MARK HARRINGTON AND ANDREA BENZACAR

DEDICATION

This report is dedicated to Gary, a man in Los Angeles with XDR-TB, to his sister, Stephanie, and to his physician, Dr. Caitlin Reed.

This is a story of two siblings and a doctor trying to get the best drugs to fight drug-resistant TB.

After spending four years in Russia, Gary moved back to the United States to begin a new chapter in his life, but several years later found himself facing an old foe: tuberculosis. Previously treated for "chronic pneumonia" in Russia, Gary started to experience cough, weight loss, and fever. After several rounds of short-course treatment with levofloxacin, Gary was finally diagnosed with extensively drug-resistant tuberculosis (XDR-TB) in Los Angeles. Perhaps as a result of receiving substandard treatment for his initial case of TB, Gary's resurgent disease proved resistant to almost every available drug; his best chance at cure lay with new TB drugs bedaquiline and delamanid as well as with experimental compounds such as PA-824. His physician, Dr. Caitlin Reed, advocated for Gary to receive the few drugs to which his TB remained susceptible. Fortunately, they were able to get bedaquiline, now on the market in the United States. But broken and nonexistent compassionate use mechanisms prevented him from getting other drugs. In particular, Otsuka's unwillingness to release delamanid under compassionate use left Gary to endure the heavy side effects of a potentially ineffective, disabling regimen, including possibly irreversible nerve damage and hearing loss. Gary remains in treatment under Dr. Reed's care; Otsuka remains obdurate in its refusal to give Gary delamanid.

Like Dr. Reed, Gary's sister Stephanie has advocated tirelessly for her brother to receive optimal treatment. Stephanie, along with Gary's other sister, shoulders the daily responsibilities of Gary's care. The advocacy and care demonstrated by Dr. Reed and Stephanie make them remarkable. Both have demonstrated a deep dedication to advocating for Gary's health while retaining a sensitive awareness that many patients lack advocates capable of negotiating the daunting complexities of obtaining medicines under compassionate use. The vast majority of patients with drug-resistant TB receive no treatment at all. Gary's case illustrates that even those who do must fight to get effective, tolerable treatment. People with TB need new tools to fight the disease, especially its drug-resistant forms, but they also need compassionate systems of treatment and care that can connect them to the most recent medical advances—whether they have tireless, committed advocates or not.

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Executive Summary

Reader beware: funding data presented in this report may be less encouraging than they appear. A quick glance at Treatment Action Group's ninth annual *Report on Tuberculosis Research Funding Trends* would suggest good news: funding for tuberculosis research and development (TB R&D) increased by US$37.9 million over 2012 to reach a total of $676.7 million in 2013. The foundation of the TB research enterprise, however, is shakier than at any other time since Treatment Action Group (TAG) began tracking funding levels in 2005. With an increase of $37.9 million, reported TB R&D funding has bounced back to the level observed in 2011, the year before TAG reported the first-ever decline in TB research spending in 2012. Yet this return to 2011 levels is driven by increased spending by a single philanthropic donor—the Bill & Melinda Gates Foundation (Gates Foundation)—as well as a sizeable increase in the number of funding institutions reporting to TAG.

If one looks at the data closely, the structural weaknesses of the TB R&D field become apparent. In the private sector, pharmaceutical companies are running for the exits, disbanding TB research programs as part of an industrywide pivot away from anti-infectives research toward efforts to develop new biologicals, including vaccines and drugs for chronic illnesses. Each year brings news of another major pharmaceutical company leaving TB R&D. Following Pfizer's exit in 2012, AstraZeneca and Novartis announced the closures of their TB drug discovery programs in 2013 and 2014, respectively. As a result, TB R&D spending from private-sector companies dropped 11.8% from 2012–2013. Since 2011, private-sector contributions to TB R&D have fallen by one-third. Combined, the private sector now spends less than $100 million on TB R&D annually. Total spending of just $99.6 million by this sector in 2013 falls below the $99.9 million industry spent on TB research in 2009 at the peak of the economic crisis. Political leaders may have declared the worst of the decade's opening economic malaise over, but TB research has not left the recession behind.

As more and more private-sector companies pull out of TB R&D, the onus of responsibility falls increasingly on public institutions and country governments. Public institutions contributed 60 percent of total TB R&D spending in 2013, or just under $400 million. Sixty-two percent of public spending comes from a single country—the United States—where perennial budgetary battles in the U.S. Congress create uncertainty and, in some instances, capricious cuts to longstanding research endeavors. Federally mandated, across-the-board budget cuts under sequestration in 2013 led to lower TB R&D spending by the U.S. National Institute of Allergy and Infectious Diseases (NIAID) and the U.S. Centers for Disease Control and Prevention (CDC)—the first- and ninth-largest funders of TB R&D globally.

Significant funding shortfalls persist in every category of TB research tracked by TAG. In the *2011–2015 Global Plan to Stop TB* (*2011–2015 Global Plan*), the Stop TB Partnership laid out a roadmap for TB research across five areas—basic science, diagnostics, drugs, vaccines, and operational research—and estimated required spending for each. Now at the midpoint of the period covered by the *2011–2015 Global Plan*, it is apparent that the world is far off track for meeting the minimum financial conditions for success. Of the $9.8 billion in funding called for between 2011 and 2015, the world invested just $1.99 billion by the end of 2013.

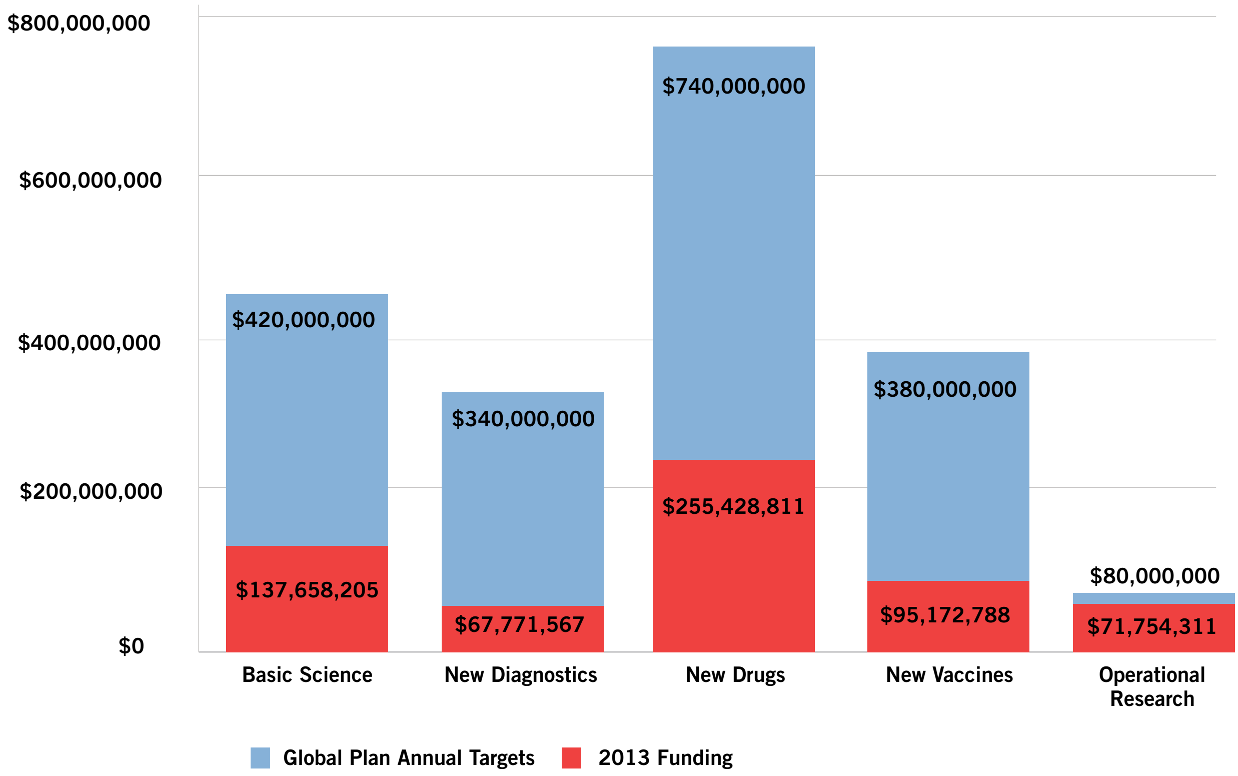
An editorial opening the *2011–2015 Global Plan* called for a "quantum leap in TB research." The exponential increase in TB research envisioned by the authors of the *2011–2015 Global Plan* has not materialized. While we have progressed far slower than the speed of light, the word "quantum" still holds relevance for our current moment. The Latin root of quantum means "how much?" With the next iteration of the *Global Plan* already under development, one of the most pressing questions remains: how much money will be required to develop and roll out the new diagnostics, drugs, and vaccines needed to achieve "a world free of TB" by 2035, a vision endorsed by the 67th World Health Assembly in May 2014.

For the 8.6 million people who developed active TB disease in 2012, the question becomes: "How long?" The world waited over 40 years between the introduction of rifampicin and the approval of the next new drug from a new class of drugs (bedaquiline) in December 2012. Over 120 years elapsed between the advent of smear microscopy and the introduction of GeneXpert for the diagnosis of TB. And the world is still waiting for a vaccine that can replace or improve the bacille Calmette-Guérin (BCG) vaccine introduced in 1921. TB-affected communities and patients cannot afford to wait several decades more to see the next generation of tools to fight TB.

1. Introduction

FIGURE 1

Annual Global Plan Research Funding Targets versus 2013 Funding



This report marks the ninth year TAG has collected data on global investments in TB R&D. The *2014 Report on Tuberculosis Research Funding Trends* presents nine years of data and takes an in-depth look at funding for TB research in 2013. Since our first report in 2006, TAG's resource-tracking efforts have sought to hold governments, the private sector, and other TB research funders accountable for achieving the funding targets established by the Stop TB Partnership in its series of *Global Plans to Stop TB*. For the ninth straight year, we report that funding fell short in every category of TB research.

In 2006, the Stop TB Partnership released the *Global Plan to Stop TB 2006–2015*, a 10-year strategy outlining the implementation and research required to achieve two goals: first, halving TB prevalence and deaths compared with 1990 levels by 2015; and, second, eliminating TB as a public health threat by 2050. The Stop TB Partnership updated this strategy in 2010 by publishing the *Global Plan to Stop TB 2011–2015*. This current roadmap calls for annual R&D spending of $2 billion, or $9.8 billion over five years, based on estimates of minimum required funding in five areas of research: basic science, diagnostics, drugs, vaccines, and operational research. Now halfway through the second *Global Plan*, and anticipating the development of the third, the scale of the world's failure to match any of the funding targets called for by the Stop TB Partnership and its members has become clear.

The slow march of TB research over the 2006–2013 period has been mirrored in faltering progress against the global TB epidemic. The World Health Organization (WHO) estimated that in 2012 there were 8.6 million new cases of TB disease and 1.3 million TB deaths.[1] When placed within the uncertainty bounds of confidence intervals, these numbers remain indistinguishable from those reported in 2006, the first year TAG collected TB R&D funding data, when 8.8 million people developed active TB disease and 1.6 million died.[2] Globally, new TB infections are decreasing at a rate of two percent per year, a pace that, if maintained, will make TB elimination a dream deferred to well into the next century.[3]

TABLE 1.1

TB R&D Funders by Rank, 2013

2013 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
1	U.S. National Institutes of Health (NIH), NIAID‡	P	$158,797,248
2	Bill & Melinda Gates Foundation‡	F	$147,923,878
3	Otsuka Pharmaceuticals‡	C	$58,717,259
4	NIH Other Institutes and Centers‡	P	$36,656,765
5	U.K. Department for International Development‡	P	$24,640,072
6	U.S. Agency for International Development (USAID)‡	P	$20,429,363
7	European and Developing Countries Clinical Trials Partnership‡	P	$18,980,589
8	European Commission‡	P	$16,858,354
9	U.S. Centers for Disease Control and Prevention (CDC)‡	P	$16,078,985
10	Wellcome Trust‡	F	$14,458,418
11	Company X‡	C	$13,071,337
12	U.K. Medical Research Council (MRC)‡	P	$11,956,068
13	NIH National Heart, Lung and Blood Institute (NHLBI)‡	P	$11,075,642
14	Dutch Directorate-General for International Cooperation (DGIS)‡	P	$9,721,685
15	Department of Foreign Affairs and Trade (DFAT) (AusAID)*	P	$7,197,108
16	Indian Council of Medical Research	P	$7,023,773
17	German Federal Ministry of Education and Research (BMBF)	P	$6,968,480
18	French National Institute of Health and Medical Research (INSERM)	P	$5,964,809
19	Company Y‡	C	$5,000,000
20	Australian National Health and Medical Research Council	P	$4,935,036
21	Emergent BioSolutions	C	$4,882,000
22	Canadian Institutes of Health Research‡	P	$4,490,049
23	Company V	C	$4,278,035
24	Qiagen*	C	$4,100,000
25	UNITAID*	M	$3,412,000
26	Global Health Innovative Technology Fund (GHIT)*	M	$3,349,544
27	Norwegian Agency for Development Cooperation	P	$3,176,614
28	Institut Pasteur Paris‡	F	$3,133,454
29	Eli Lilly and Company‡	C	$3,100,000
30	Company S	C	$3,063,516
31	Irish Aid	P	$2,646,350
32	Carlos III Health Institute	P	$2,427,077
33	Japanese Ministry of Health, Labour and Welfare	P	$2,408,021
34	South African Medical Research Council*	P	$2,248,534
35	U.S. President's Emergency Plan for AIDS Relief (PEPFAR)	P	$2,028,593
36	Alere	C	$2,000,000
37	Swedish Research Council	P	$1,806,504
38	Department of Defense, Medical Research and Development Program*	P	$1,641,914
39	Fondation Mérieux	F	$1,593,370
40	Korea International Cooperation Agency	P	$1,564,244

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 2006

TABLE 1.2

TB R&D Funders by Rank, 2013 (continued)

2013 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
41	French National Agency for AIDS Research (ANRS)	P	$1,330,238
42	Taiwan Centers for Disease Control*	P	$1,269,563
43	Department of Foreign Affairs, Trade and Development Canada	P	$1,241,067
44	U.S. Food and Drug Administration‡	P	$1,200,001
45	French National Agency for Research (ANR)	P	$1,199,084
46	Médecins Sans Frontières*	F	$976,833
47	Japan International Cooperation Agency	P	$970,361
48	Grand Challenges Canada*	P	$912,475
49	International Centre for Genetic Engineering and Biotechnology	P	$893,746
50	Brazil National TB Program	P	$864,596
51	Health Research Council of New Zealand	P	$853,766
52	Bloomberg Foundation	F	$765,000
53	German Research Foundation	P	$752,237
54	U.K. Department of Health	P	$735,371
55	Australian Research Council	P	$659,845
56	National Science Foundation*	P	$598,710
57	World Health Organization (WHO)	M	$576,514
58	WHO TDR (Special Programme for Research and Training in Tropical Diseases)	M	$545,000
59	Japan BCG Laboratory	C	$437,875
60	Indian Ministry of Health and Family Welfare	P	$418,069
61	Danish Council for Independent Research	P	$414,698
62	Génome Québec*	P	$414,457
63	République Gabonaise*	P	$320,598
64	South African Department of Science and Technology	P	$316,776
65	OPEC Fund for International Development	M	$300,956
66	InnovationsFonden*	P	$251,805
67	Indian Ministry of Science and Technology, Department of Biotechnology	P	$235,326
68	Korea Centers for Disease Control and Prevention	P	$232,200
69	Korea Health Industry Development Institute*	P	$227,341
70	World Bank*	M	$199,996
71	Research Council of Norway	P	$181,049
72	BioDuro	C	$180,000
73	Quantimetrix Corp.*	C	$172,000
74	Statens Serum Institut	P	$170,060
75	Firland Foundation*	F	$163,598
76	South-Eastern Norway Regional Health Authority	P	$149,119
77	Seegene Corp.*	C	$147,273

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 2006

TABLE 1.3

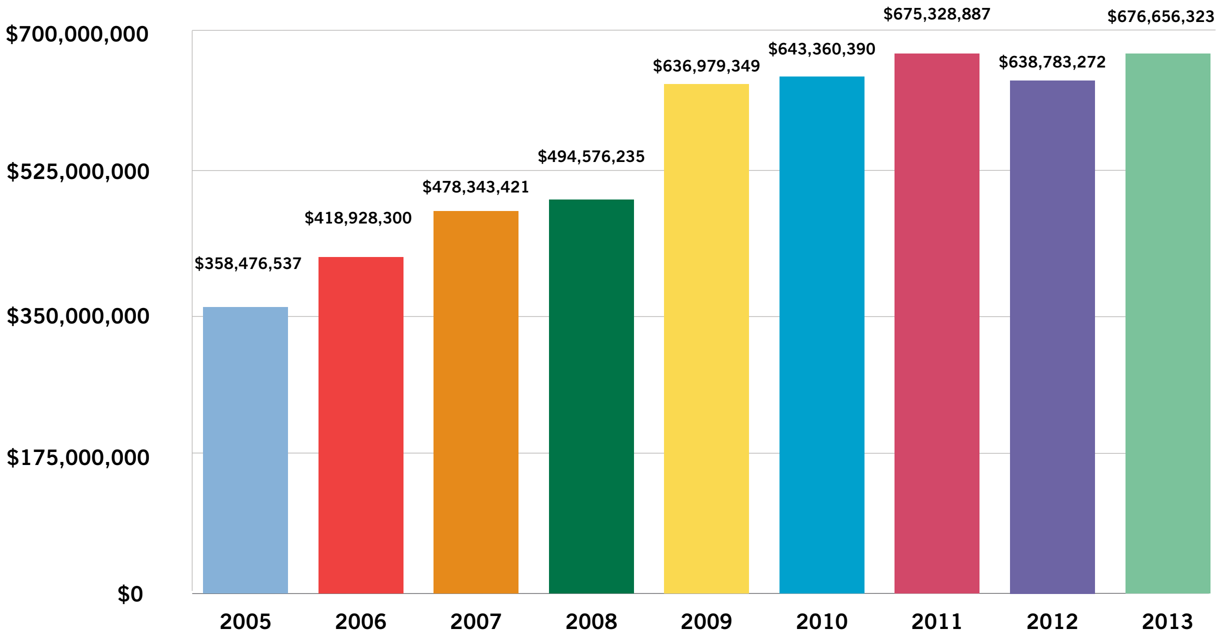
TB R&D Funders by Rank, 2103 (continued)

2013 RANK	FUNDING ORGANIZATION	FUNDER TYPE	TOTAL
78	South African National Research Foundation*	P	$143,548
79	Danish International Development Agency‡	P	$115,168
80	Japan Health Sciences Foundation	F	$100,800
81	Howard Hughes Medical Institute*	F	$100,000
82	World Diabetes Foundation	F	$88,646
83	Economic & Social Research Council	P	$81,401
84	Financial Management Corps†‡	C	$71,380
85	Biofabri	C	$65,036
86	Institut Mérieux*	C	$65,036
87	Nipro Corporation*	C	$50,000
88	Hain Lifescience*	C	$49,978
89	Oppenheimer Memorial Trust*	F	$48,523
90	State Trustees of Victoria*	P	$45,664
91	Claude Leon Foundation*	F	$42,963
92	Company T	C	$42,606
93	École Polytechnique Fédérale de Lausanne	P	$42,304
94	U.K. Defence Science and Technology Laboratory	P	$38,873
95	Australia-China Council*	P	$36,531
96	FIT Biotech	C	$32,518
97	Japan Science and Technology Agency	P	$30,240
98	Taiwan Ministry of Science and Technology*	P	$30,000
99	Gulbenkian Foundation	F	$29,266
100	ZonMw‡	P	$28,951
101	National Research Foundation of Korea	P	$27,167
102	Biometrix Technology, Inc.*	C	$25,800
103	Fondation Recherche Médicale*	F	$23,708
104	Individual donors to iM4TB	F	$21,152
105	Japan Society for the Promotion of Science	P	$16,128
106	University College London Hospitals Charitable Foundation*	F	$16,014
107	KNCV Tuberculosis Foundation	F	$14,192
108	Technology Strategy Board	P	$12,136
109	European Centre for Disease Prevention and Control	P	$11,719
110	Faber Daeufer	C	$9,000
111	WHO-Stop TB Partnership	M	$7,000
112	British Society for Antimicrobial Chemotherapy*	F	$5,067
113	Thrasher Research Fund	F	$4,209
114	Individual donors to TB Alliance	F	$1,310

P = Public-Sector R&D Agency; C = Corporation/Private Sector; M = Multilateral; F = Foundation/Philanthropy;
* New donor; † As reported by the Korean Institute of Tuberculosis, ‡ Organization has reported to TAG each year since 2006

FIGURE 2

Total TB R&D Funding, 2005-2013



The pace of research is falling far behind the spread of many forms of drug-resistant TB (DR-TB), which is more difficult to diagnose and treat than drug-sensitive TB (DS-TB). The WHO estimated that in 2012 450,000 people developed multidrug-resistant TB (MDR-TB), of whom only 94,000 were notified to national TB programs and 77,000 started treatment.[4] Patients with MDR-TB must endure two years of treatment with highly toxic drugs of marginal efficacy that carry side effects including hearing loss, psychosis, skin discoloration, and cardiac disturbances. Most people with DR-TB wait months for an accurate diagnosis due to the lack of a point-of-care diagnostic test capable of identifying TB and its patterns of drug resistance quickly and at all levels of health systems. For these patients, the development of new diagnostics, drugs, and vaccines would help to end a treatment odyssey where the best available options are also options of last resort. Those people with extensively drug-resistant TB (an estimated 9.6% of MDR-TB cases) have even fewer options.

On a macro level, population-based modeling confirms that new strategies and tools will be needed to reduce TB deaths by 95 percent and cut the number of new TB cases by 90 percent by 2035—the targets of the post-2015 global TB strategy approved by the 67th World Health Assembly (WHA) in May 2014.[5] Maintaining the current two percent annual rate of decline in TB incidence would leave the world with an epidemic in 2050 that looks virtually unchanged from the epidemic today, with a TB incidence rate 1,000 times greater than the elimination threshold.[6] Different modeling groups have evaluated how the introduction of new vaccines, optimized drug regimens, rapid diagnostics, and mass treatment of latent TB infection would accelerate the epidemic's end.[7,8] In acknowledgment of this, the third pillar of the WHA resolution—"intensified research and innovation"—calls for the discovery, development, and rapid uptake of new tools by 2025. In frank language, the resolution states that "achievements with existing tools," even when paired with universal health coverage (a best-case scenario), "would be remarkable but not sufficient to maintain the rate of progress required to achieve the 2035 [TB elimination] targets."[9]

2. Methodology

TAG collected original-source funding data through an electronic survey that asked funders to report disbursements in TB R&D made in 2013 and classify spending by one of six research categories (see below). We sent surveys to 195 organizations, including known TB R&D funders and potential but unconfirmed funders of TB research. Ninety-six organizations returned the survey; of these, 73 provided funding data, and 23 indicated that they did not support TB research in 2013. In addition, we collected data for five institutions using publicly available, online databases of grants and awards. In total, we uncovered TB R&D investments from 114 unique institutions.

The reach and yield of this year's survey represent a much-expanded operation over previous years. By comparison, in 2012 TAG surveyed 135 institutions, received 67 surveys in response and uncovered funding data from 85 organizations. Casting a wider net allowed us to include 32 institutions in the report for the first time. We refer to these organizations as "new funders." Some of these groups are indeed new, such as the Global Health Innovative Technology Fund established in Japan in 2013, or are funding TB R&D for the first time, such as UNITAID. Others are newly reporting to TAG, but not new to TB research. Among these, we are pleased to include new funders from underrepresented geographic areas—for example, government ministries of health and technology in Taiwan—as well as organizations within our own backyard (e.g., the U.S. Department of Defense and the U.S. National Science Foundation).

Since the number of organizations included in this year's report increased by nearly one-third over last year, the results section analyzes the global total both including and excluding the 32 new funders to see how funding levels would differ if the survey more closely resembled last year's in scope. Unless otherwise noted, all calculations include the full data set from all 114 donors identified by TAG.

Data reported in non-U.S. currencies were converted into U.S. dollars using the July 1, 2013, currency exchange rates provided by the OANDA Corporation. All dollar figures in the report are presented in U.S. dollars. To avoid double-counting, TAG did not include spending by product development partnerships (PDPs) such as Aeras or the TB Alliance in total figures, as these organizations function as funding recipients rather than original-source donors. All figures represent 2013 disbursements, or the actual transfer of funds made in 2013, rather than awards, commitments, or budgetary promises of future funding.

Research areas tracked by TAG:

- **Basic science**: undirected, investigator-initiated research to uncover fundamental knowledge about Mycobacterium tuberculosis (MTB) and closely related mycobacterial organisms.
- **Diagnostics:** preclinical or clinical trials of diagnostic technologies and algorithms.
- **Drugs:** preclinical or clinical research on treatments and treatment strategies for TB disease and infection.
- **Vaccines:** preclinical and clinical research on TB vaccines, including both preventive and immunotherapeutic vaccines.
- **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.
- **Infrastructure/unspecified:** TB research that the donor is unable to further classify.

2.1 Limitations

The accuracy of the data presented in this report depends on the number of eligible organizations that complete and return the electronic survey as well as the relative size of reported versus unreported investments. More funders than ever returned the survey this year, producing the most comprehensive picture to date on global TB R&D funding.

In 2012, the top 30 funders accounted for 96 percent of total TB R&D spending. This year, TAG collected data from all but two of the previous year's top 30 donors—the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) and the Max Planck Institute for Infection Biology (MPIIB). In 2012, the Global Fund reported spending $6.0 million on TB-related operational research, enough to rank 19th overall, while the MPIIB reported spending $2.9 million, ranking 29th. If funding at each of these institutions held steady in 2013, their inclusion would increase this year's total by 1.3%.

Of particular note for this year's findings, more private-sector companies than ever returned surveys to TAG. In several cases, companies requested that their TB R&D spending be reported anonymously in order to protect strategic or proprietary information. In these situations, TAG assigned the company a pseudonym such as "Company X." We are grateful to all the companies that entrusted their data to us and encourage more private-sector parties to report transparently.

2.2 Corrections

TABLE 2

Total TB R&D Funding Corrected to Include the EDCTP, 2005–2013

Year	Original Total TB R&D Funding	EDCTP TB R&D Funding	Total TB R&D Funding Corrected to Include the EDCTP	Percent Change
2005	$357,426,170	$1,050,367	$358,476,537	0.29
2006	$417,824,708	$1,103,592	$418,928,300	0.26
2007	$473,920,682	$4,422,739	$478,343,421	0.93
2008	$491,476,917	$3,099,318	$494,576,235	0.63
2009	$619,209,536	$17,769,813	$636,979,349	2.87
2010	$630,446,462	$12,913,928	$643,360,390	2.05
2011	$657,815,332	$17,513,555	$675,328,887	2.66
2012	$627,389,725	$11,393,547	$638,783,272	1.82
2013	$676,656,323	$18,980,589	$676,656,323	0

Following the publication of the *2013 Report on Tuberculosis Research Funding Trends*, the European and Developing Countries Clinical Trials Partnership (EDCTP) reached out to TAG to suggest changes in the categorization of its spending. Traditionally, TAG listed the EDCTP in figure 13 alongside PDPs and other international programs that conduct TB research but are not original-source donors. This treatment of EDCTP data began in the 2011 report and was designed to avoid double-counting funding reported by the EDCTP with funding reported by the European Commission Directorate-General for Research and Innovation under its Seventh Framework Programme supporting health and biomedical research. As a result, EDCTP disbursements were not included in the total figures reported by TAG in previous years' reports.

The EDCTP generously provided detailed data on its TB research spending dating back to 2005, allowing TAG to distinguish EDCTP numbers from those reported by the European Commission. Consequently, we have made the decision to list the EDCTP as a stand-alone entity separate from the European Commission. The numbers in this year's report reflect corrected totals and subtotals inclusive of EDCTP funding from 2005 to 2012. Table 2 shows EDCTP investments by year alongside the original and corrected figures.

TAG makes every effort to capture comprehensive data on TB R&D funding and encourages donors not included here to share their data and support the accuracy of this report. Please contact TAG at tbrdtracking@treatmentactiongroup.org if you have information or corrections to share. All corrections will enter next year's report, although TAG may issue more substantial corrections online in between report years.

2.3 Acknowledgments

Resource tracking is a collaborative enterprise, and TAG could not do it without the consistent support of funding institutions across the world. The funding officers that complete our survey each year make this report possible and deserve special thanks. Table 1 acknowledges those organizations that have reported to TAG each year since 2006 with a double dagger (‡) appearing next to their names.

3. Results

In 2013, TAG uncovered TB research investments of $676.7 million, an increase of 5.9% ($37.9 million) over the $638.8 million reportedly spent in 2012. Although higher than 2012 funding levels, this represents just 33.8% of the $2 billion annual target in the *2011–2015 Global Plan*. At $676.7 million, funding in 2013 returns to the level observed in 2011, when the global community reported spending $675.3 million on TB R&D. This level is consistent with the overall trend observed since 2009 of relatively flat funding. However, as pointed out by numerous observers, flat funding in nominal terms (as reported here) often masks real declines, since inflation does not stand still for flat budgets.[10]

TAG encourages readers to exercise caution in interpreting the 2012–2013 increase given the large number of new funders that returned the 2013 survey. Among funders that have consistently reported to TAG, one donor (the Gates Foundation) spent $36.3 million more in 2013 than in 2012, a figure that could account for nearly all of the $37.9 million increase. Removing the 32 new funders from the analysis leaves total TB R&D spending in 2013 at $648.4 million, a smaller increase of $10 million compared to 2012. The fact that the value of combined spending by new donors ($28.3 million) approaches the reported increase over 2012 ($37.9 million) suggests that the story is less about a true increase and more closely resembles flat or decreased funding. The sizeable increase from the Gates Foundation and the substantial investments from new funders likely mask declines among groups previously reporting to TAG.

3.1 Trends in TB R&D Funding by Funder Category

FIGURE 3

Total TB R&D Funding by Funder Category, 2013
Total: $676,656,323

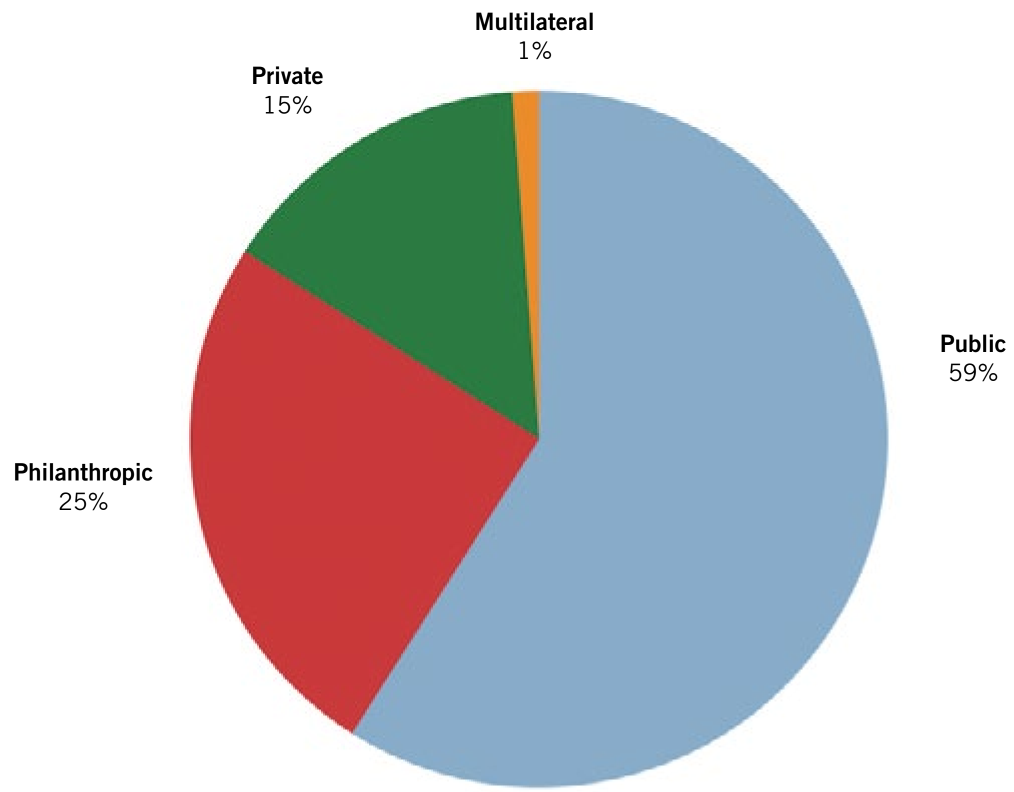
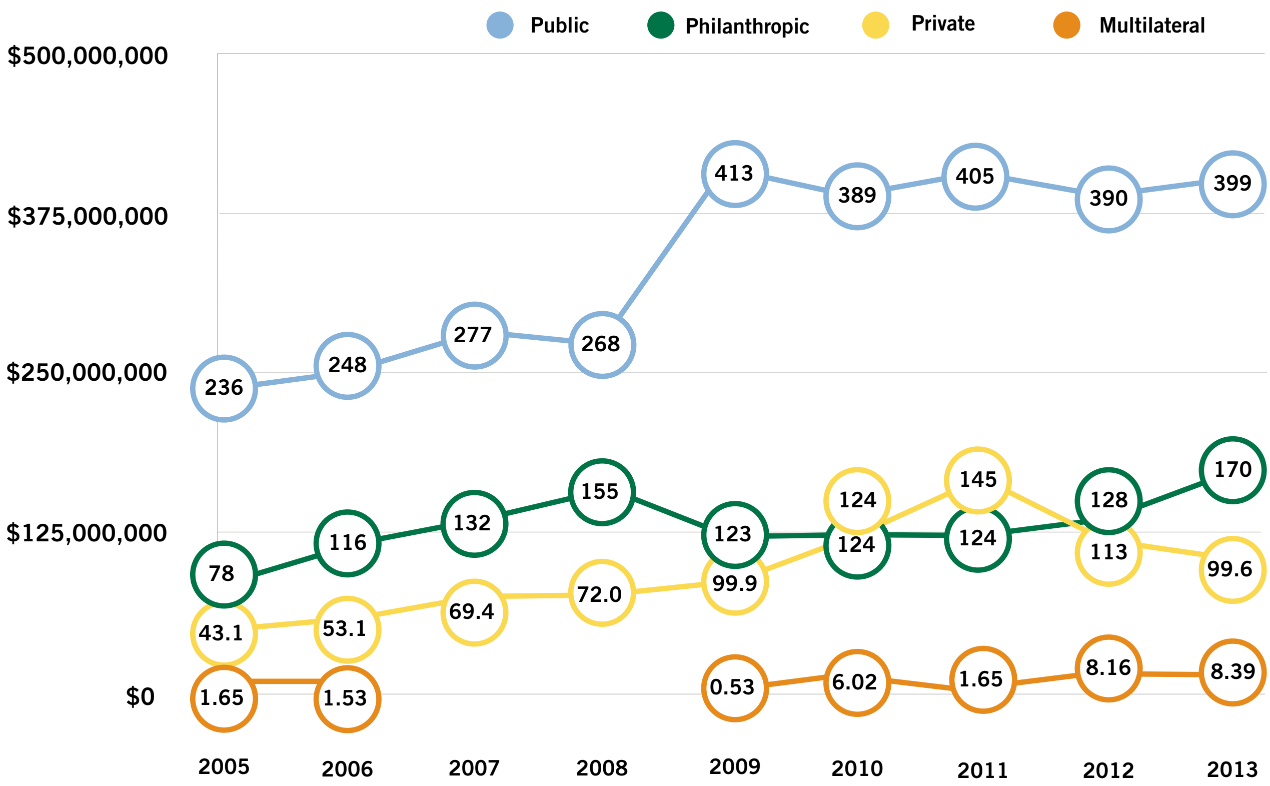


FIGURE 4

Total TB R&D Funding by Funder Category, 2005-2013 (in USD millions)



TB research has always relied heavily on a small number of funders from the public and philanthropic sectors, but this dependence further consolidated in 2013 following the exit of several major pharmaceutical companies from the field. In 2013, the 10 largest funders gave 76% of the total. Eighty-eight percent of funding came from the top 20 donors and 94% from the top 30. Two institutions—NIAID and the Gates Foundation—gave 45% of all money spent on TB research globally in 2013.

As in previous years, public institutions accounted for the vast majority of TB research funding with 60% of the $676.7 million total, or just under $400 million. Most of this support stems from public institutions in a single country—the United States—where federal agencies collectively account for 62.3% ($248.5 million) of all public money spent on TB research worldwide in 2013. The next-largest share of public support comes from the United Kingdom with 9.4% ($37.5 million) followed by the European Union with 8.9% ($35.9 million). European Union member states give additional support to TB R&D outside of consolidated E.U. channels. Not counting contributions to E.U. funding mechanisms, governments in the Netherlands, France, and Germany gave $9.8 million, $8.5 million, and $7.7 million to TB research in 2013, respectively. Sweden, Norway, and Denmark lag far behind their continental neighbors with under $5 million each. Outside of the Western hemisphere, the government of India contributed more than any other country, with 2013 TB R&D spending of $8.6 million.

The pharmaceutical industry's long goodbye to TB research continued, as evidenced by an 11.8% decline from the $112.9 million spent in 2012 to the $99.6 million spent in 2013. This reduces private-sector investments below the $99.9 million spent by industry in 2009 at the peak of the global economic crisis. It also marks a 31.3% decline in private-sector spending since the apex of $144.9 million spent by this sector in 2011. The public sector now gives four times more money to TB R&D than private industry does, and philanthropic institutions give nearly twice as much.

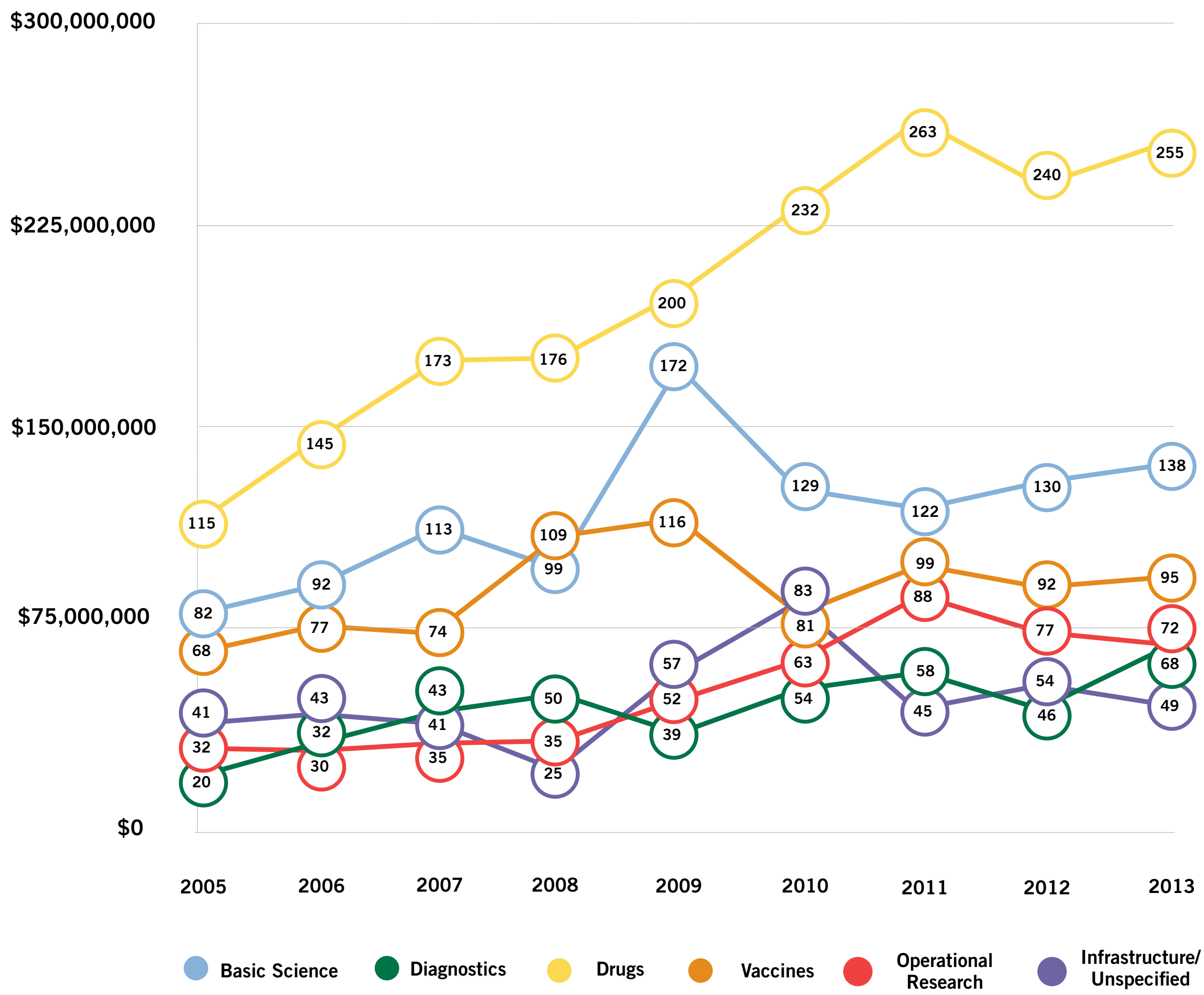
This year's decline in private-sector spending reflects two forces: flight and erosion. Several pharmaceutical companies have exited TB research entirely—a trend started by Pfizer in 2012 and continued by AstraZeneca in 2013 and Novartis in 2014. This leaves the TB research field with just three major pharmaceutical companies with active research programs: Otsuka, Company V, and Company X. The abandonment of TB research reflects a larger structural shift within the pharmaceutical industry away from anti-infectives work.[11] Some companies are concentrating on developing therapies for noncommunicable diseases, while others see money to be made in developing new biologicals and vaccines.[12] The spring of 2014 saw a flurry of merger and acquisition activity in the pharmaceutical sector, indicating the extent to which companies are rethinking portfolios, concentrating on core business and, in some cases, trying to take over the R&D pipelines of smaller firms located in more lucrative tax environments.[13,14,15]

Exits from the TB research field do not account for the full decrease in private-sector spending. Many of the most active pharmaceutical players in TB drug research invested less in 2013 than in previous years. As the third largest funder of TB research overall, Otsuka spent $58.7 million in 2013, accounting for nearly 60 percent of industry funding for TB R&D. Investments made by Company X have decreased by more than half over the same period, falling from $31.2 million in 2011 to $13.1 million in 2013.

Partially as a result of decreased industry spending, philanthropic institutions increased their share of total TB R&D funding from 20 percent in 2012 to 25 percent in 2013. Like the public and private sectors, one institution accounts for over half of all philanthropic spending on TB research: the Gates Foundation gave $147.9 million to TB R&D in 2013. The next-largest philanthropic donor is the Wellcome Trust, which ranks 10th among all funders and gave $14.5 million in 2013.

FIGURE 5

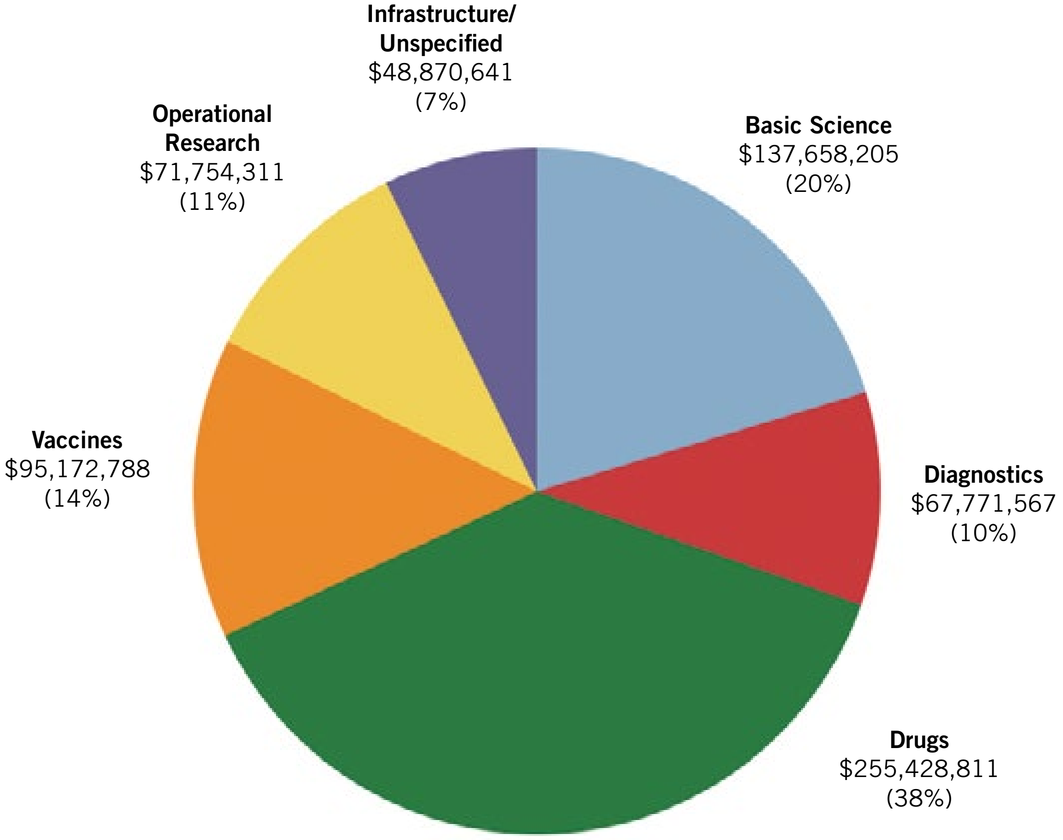
Total TB R&D Funding by Research Category, 2013 (in USD millions)



3.2 Trends in TB R&D Funding by Research Category

FIGURE 6

Total TB R&D Funding by Research Category, 2005–2013
Total: $676,656,323

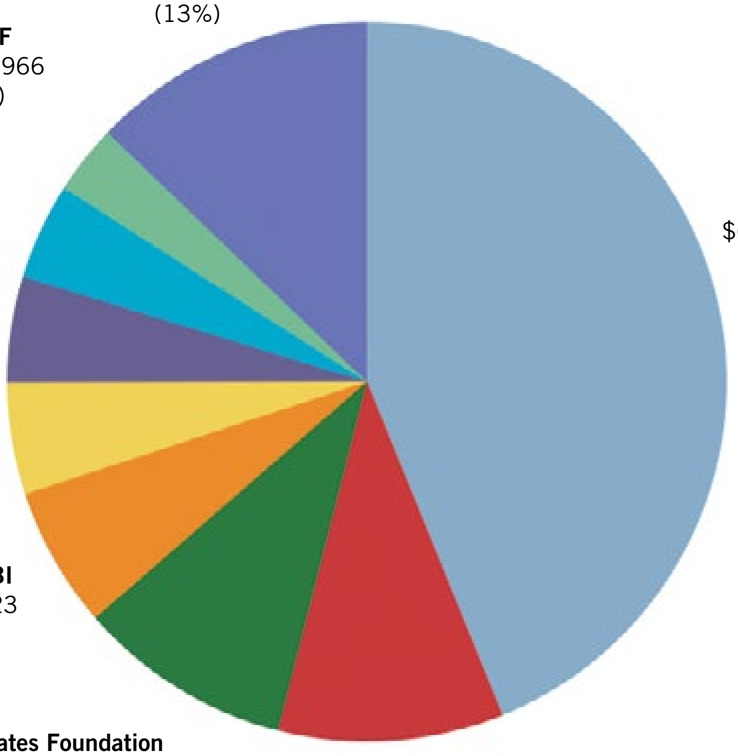


As in previous years, drug R&D commanded the largest share of funding in 2013, with 37.7% of the total. Basic science remained the second-largest category, with 20.3% of the total, followed by vaccine research (14.1%), operational research (10.6%), diagnostics research (10.0%), and infrastructure/unspecified projects (7.2%). These proportions are virtually unchanged from 2012. Compared with 2012, funding increased modestly in each category of TB research with the exception of operational research, where spending declined by $5.7 million. Funding fell short of the *2011–2015 Global Plan* spending targets in every category of TB R&D. Operational research spending came the closest to meeting the targeted amount, shy by just 10.3%. Spending on TB drugs equaled one-third of the targeted $740 million, while in every other area 2013 funding totaled less than a third of the goal.

Basic Science

FIGURE 7

Basic Science: $137,658,205



FUNDERS WITH INVESTMENTS UNDER 2%

Wellcome Trust	$2,713,150
Australian National Health and Medical Research Council	$2,533,294
Institut Pasteur Paris	$1,995,812
Canadian Institutes of Health Research	$1,399,813
Carlos III Health Institute	$1,269,860
Swedish Research Council	$875,316
German Research Foundation	$752,237
French National Agency for Research (ANR)	$705,388
Health Research Council of New Zealand	$700,635
International Centre for Genetic Engineering and Biotechnology	$554,469
Norwegian Agency for Development Cooperation	$484,224
Japan BCG Laboratory	$437,875
Génome Québec	$414,457
Japanese Ministry of Health, Labour and Welfare	$332,186
Grand Challenges Canada	$322,050
République Gabonaise	$320,598
OPEC Fund for International Development	$300,956
Research Council of Norway	$181,049
French National Agency for AIDS Research (ANRS)	$168,577
National Science Foundation	$150,203
South-Eastern Norway Regional Health Authority	$149,119
South African National Research Foundation	$143,548
Department of Defense, Medical Research and Development Program	$122,049
Australian Research Council	$118,726
Japan Health Sciences Foundation	$100,800
Howard Hughes Medical Institute	$100,000
South African Medical Research Council	$75,461
Oppenheimer Memorial Trust	$48,523
Claude Leon Foundation	$42,963
Japan Science and Technology Agency	$30,240
Fondation Recherche Médicale	$23,708
Firland Foundation	$20,000
South African Department of Science and Technology	$18,175
Japan Society for the Promotion of Science	$16,128
Indian Ministry of Science and Technology, Department of Biotechnology	$11,581
Indian Council of Medical Research	$8,380
Company S	$4,959
European Centre for Disease Prevention and Control	$1,194

The *2011–2015 Global Plan* calls for annual investments of $420 million in basic science. In 2013, donors gave $137.7 million to basic-science research, leaving a gap of $282.3 million.

The U.S. National Institutes of Health (NIH) provided $83.03 million in funding for TB-related basic-science research, or 60.3% of total spending in this area. Within the NIH, NIAID alone gave $60.4 million, the National Heart, Lung and Blood Institute (NHLBI) $8.7 million, and other NIH institutes and centers $13.9 million—a figure nearly matched by the Gates Foundation, which gave $13.3 million. Other top funders of basic science all come from Europe, led by the European Commission and the U.K. Medical Research Council, with funding of $6.9 million and $6.6 million, respectively.

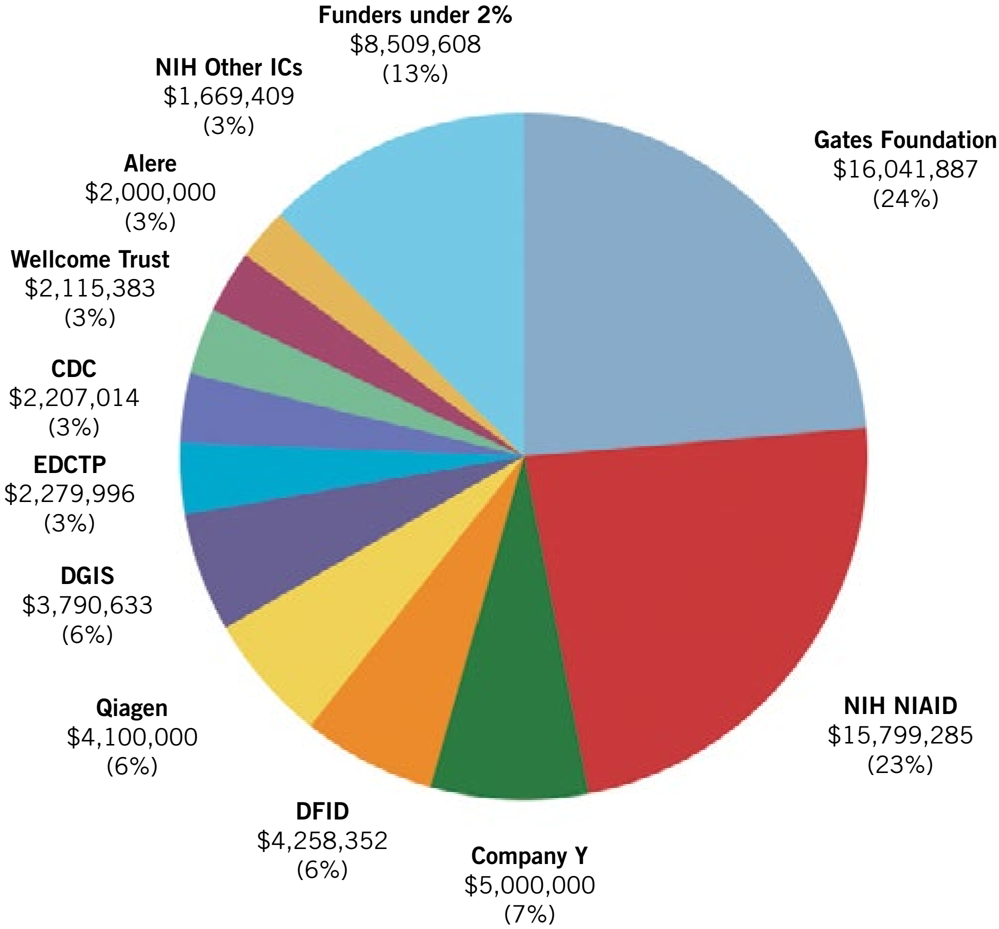
Basic science forms the bedrock of efforts to develop new diagnostics, drugs, and vaccines to fight TB. The biology underlying the continuum between MTB infection and TB disease remains imperfectly understood, as do the many factors that govern the interaction between MTB and the human immune system. The lack of biomarkers that correlate with immunity against TB or successful therapeutic intervention holds back progress in diagnostic, drug, and vaccine research. Identification of these biomarkers—the genes, biological processes, or clinical phenotypes that act as precursors or signals of a particular disease state or response to immunization or treatment—would greatly speed progress in TB drug and vaccine development.

Funding gaps in basic science may discourage young investigators from entering the field and building careers in TB R&D. In a climate of shrinking funding for biomedical research, many early-career scientists are more sensitive than ever to the relative fortunes of different fields.[16] Many funders of basic science pursue undirected grant making, meaning that they fund the best science without issuing calls for TB-specific proposals. This characterizes funding from groups as diverse as the Wellcome Trust, a private philanthropy in the United Kingdom, to the European Commission's Seventh Framework Programme, to the U.S. National Science Foundation. While undirected grant programs may sustain the research of scientists committed to tackling TB, these mechanisms may be less effective at sparking new interest in TB research among a wider pool of scientific talent.

Diagnostics

FIGURE 8

Diagnostics: $67,771,567



FUNDERS WITH INVESTMENTS UNDER 2%

U.S. Agency for International Development (USAID)	$1,200,000
Japan International Cooperation Agency	$970,361
Department of Defense, Medical Research and Development Program	$749,998
NIH National Heart, Lung and Blood Institute (NHLBI)	$558,675
World Health Organization	$472,408
Japanese Ministry of Health, Labour and Welfare	$457,652
National Science Foundation	$433,577
Grand Challenges Canada	$429,400
Médecins Sans Frontières	$373,304
French National Agency for AIDS Research (ANRS)	$343,495
Swedish Research Council	$297,980
Korea Health Industry Development Institute	$227,341
Canadian Institutes of Health Research	$205,604
Institut Pasteur Paris	$182,631
Quantimetrix Corp.	$170,000
Australian National Health and Medical Research Council (NHMRC)	$170,240
Health Research Council of New Zealand	$153,131
Seegene Corp.	$147,273
Norwegian Agency for Development Cooperation	$145,662
German Federal Ministry of Education and Research (BMBF)	$134,228
Taiwan Centers for Disease Control	$112,487
Korea Centers for Disease Control and Prevention	$86,000
Nipro Corporation	$50,000
Hain Lifescience	$49,978
Firland Foundation	$47,600
State Trustees of Victoria	$45,664
Australian Research Council	$43,381
Company T	$42,606
Carlos III Health Institute	$38,025
Australia-China Council	$36,531
Fondation Mérieux	$32,518
ZonMw	$28,951
Biometrix Technology, Inc.	$25,800
University College London Hospitals Charitable Foundation	$16,014
South African Medical Research Council	$15,238
Technology Strategy Board	$12,136
Thrasher Research Fund	$1,719

The *2011–2015 Global Plan* calls for annual investments of $340 million in research to develop new TB diagnostics. In 2013, donors gave $67.8 million to diagnostics research, leaving a gap of $272.2 million.

The Gates Foundation and NIAID are the first- and second-largest funders of diagnostics research, with 2013 investments of $16.0 and $15.8 million. Two industry groups rank among the top five diagnostics funders in 2013: Company Y, with spending of $5.0 million, and Qiagen with $4.1 million. A third private-sector company, Alere, ranks 10th, with 2013 investments of $2 million.

The need for diagnostics research remains great, even in the wake of the introduction of GeneXpert, a platform that can diagnose TB and resistance to rifampicin in less than two hours. For all its improvements over smear microscopy, GeneXpert is not a true point-of-care test, as operational research over the past year has made clear. The machine depends on a stable supply of electricity, requires annual maintenance, and has not had a measurable effect on reducing TB mortality.[17]

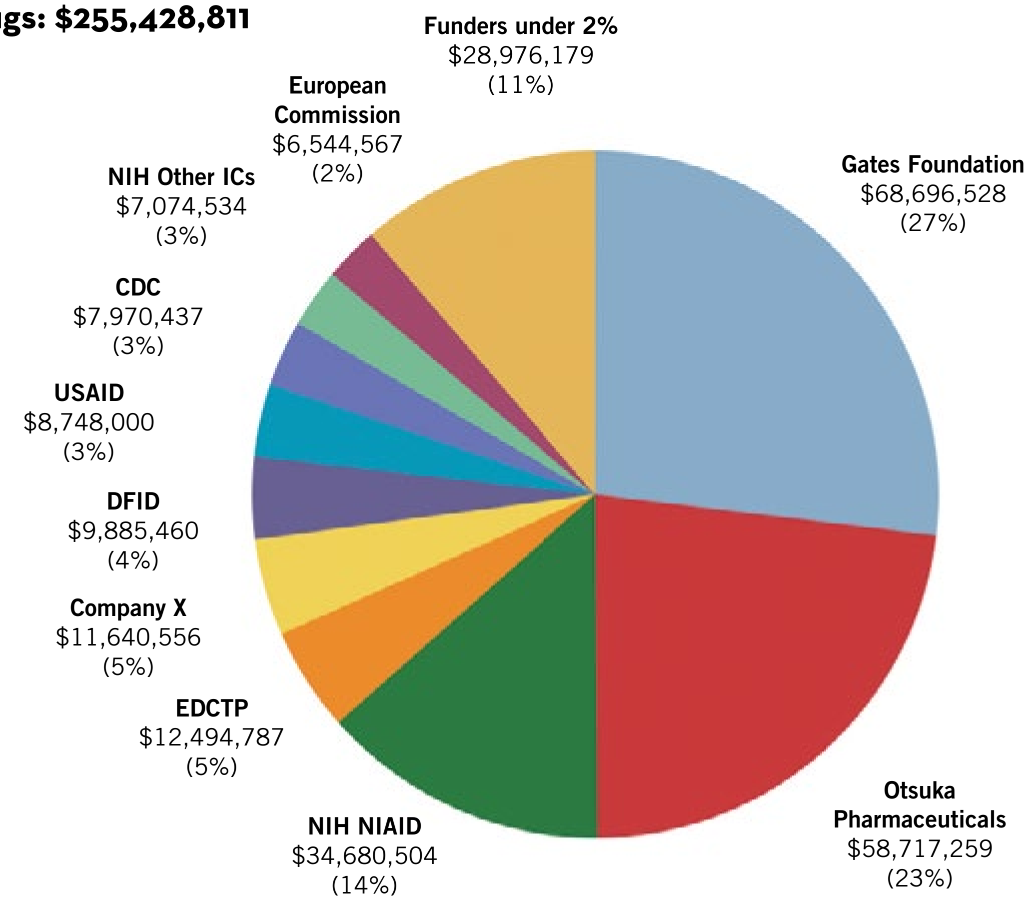
The experience of GeneXpert provides a cautionary lesson for other diagnostic developers that tests must be designed with patients and health systems in mind. TAG and others have called for a patient-centered approach to TB diagnostics R&D in which diagnostics under development embody five principles: cure, access to care, systems of care, patient empowerment, and sustainability.[18] In short, diagnostics are useful only insofar as they account for the strengths and weaknesses of health systems and produce results that link patients to appropriate, effective treatment without undue delay or confusion.

The development of rapid and decentralized drug susceptibility tests for fluoroquinolones and other second-line TB drugs would represent a major advance over the current standard, mycobacterial culture, which takes weeks to return results. Bolstering funding for diagnostics research will only increase in importance as TB drug developers advance regimens that, if successful, would introduce fluoroquinolones and potentially other second-line drugs into first-line therapy. The advent of rapid, molecular diagnostics would also reduce the hazardous guesswork behind MDR-TB treatment, which in places without high-level laboratory capacity leaves many patients on regimens to which their TB is resistant while awaiting culture results.[19] New research demonstrating how quickly effective treatment renders MDR-TB non-infectious conveys the importance of fully funding efforts to develop patient- and provider-friendly drug susceptibility tests.[20]

Drugs

FIGURE 9

Drugs: $255,428,811



FUNDERS WITH INVESTMENTS UNDER 2%

Company V	$4,278,035
UNITAID	$3,412,000
Eli Lilly and Company	$3,100,000
Irish Aid	$2,646,350
Department of Foreign Affairs and Trade (DFAT) (AusAID)	$2,320,500
U.K. Medical Research Council (MRC)	$1,696,073
Wellcome Trust	$1,634,746
Company S	$1,295,000
U.S. Food and Drug Administration	$1,200,001
Canadian Institutes of Health Research	$943,609
French National Agency for AIDS Research (ANRS)	$687,375
Carlos III Health Institute	$635,324
Institut Pasteur Paris	$619,230
WHO Special Programme for Research and Training in Tropical Diseases	$545,000
Australian National Health and Medical Research Council (NHMRC)	$511,073
Swedish Research Council	$499,117
Australian Research Council	$497,738
Taiwan Centers for Disease Control	$390,709
Department of Defense, Medical Research and Development Program	$384,867
French National Agency for Research (ANR)	$322,656
NIH National Heart, Lung and Blood Institute (NHLBI)	$201,716
BioDuro	$180,000
Global Health Innovative Technology Fund	$149,335
Danish International Development Agency	$115,168
Grand Challenges Canada	$107,350
Médecins Sans Frontières	$104,057
Indian Ministry of Science and Technology, Department of Biotechnology	$100,560
International Centre for Genetic Engineering and Biotechnology	$60,410
Indian Council of Medical Research	$51,846
German Federal Ministry of Education and Research (BMBF)	$47,689
École Polytechnique Fédérale de Lausanne	$42,304
U.K. Defence Science and Technology Laboratory	$38,873
Firland Foundation	$36,000
National Research Foundation of Korea	$27,167
U.K. Department of Health	$21,344
Individual donors to iM4TB	$21,152
South African Medical Research Council	$15,238
KNCV Tuberculosis Foundation	$14,192
Faber Daeufer	$9,000
WHO-Stop TB Partnership	$7,000
British Society for Antimicrobial Chemotherapy	$5,067
Individual donors to TB Alliance	$1,310

The *2011–2015 Global Plan* calls for annual investments of $740 million in research to develop new TB drugs or repurpose existing ones. In 2013, donors gave $255.4 million to drug research, leaving a gap of $484.6 million.

The fact that the world's largest charity—the Gates Foundation—is now the largest contributor to TB drug development symbolizes the increasing dependence of TB drug R&D on philanthropic and public dollars. The Gates Foundation gave $68.7 million to TB drug R&D in 2013, or 27 percent of total spending. Ostuka, long the biggest funder of TB drug research, fell to the number two position in 2013, with investments of $58.7 million (23% of the total). NIAID remained the third-largest donor, with funding of $34.7 million (13.6%).

Aside from Otsuka, Company X is the only private-sector player to count among the top 10 funders of TB drug R&D. Other top funders are either public research networks—including the EDCTP and the CDC's Tuberculosis Trials Consortium—or international development agencies including the U.K. Department for International Development (DFID) and the U.S. Agency for International Development (USAID).

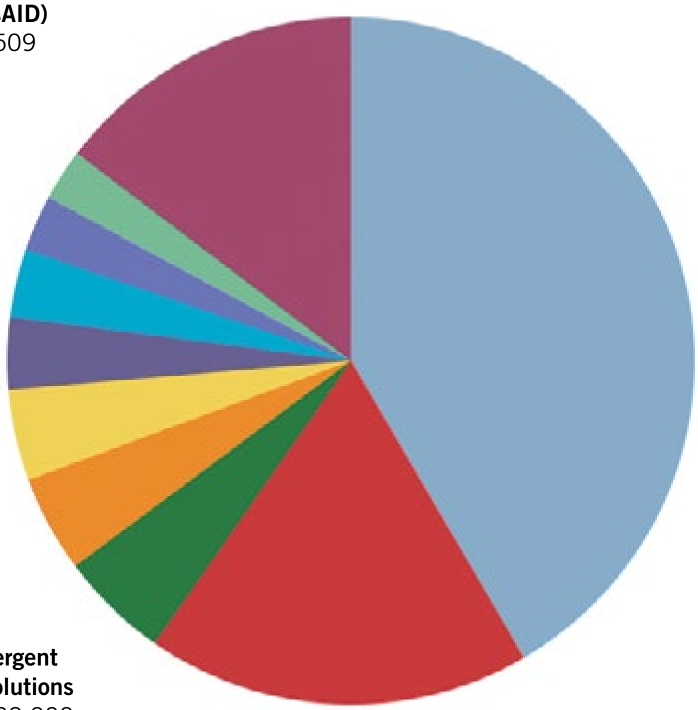
The consequences of private-sector withdrawal from TB drug research go beyond just disappearing research dollars. When companies like Pfizer and AstraZeneca pull out, their TB drug compounds are left to languish in early stages of the pipeline. Intellectual property protections often make these compounds inaccessible to the public research consortia that could take them forward in trials of new TB drug regimens. When Pfizer discontinued TB research in 2012, it sold its TB drug candidate, sutezolid, to Sequella, an undercapitalized private biotech company.[21] The public sector is picking up the tab on sutezolid's development even as Sequella refuses to allow many public research networks to study the drug in combination with others.[22] In 2013, Sequella reported receiving most its funding from NIAID. The public sector is also paying for the development of AstraZeneca's AZD5847, which took three years to complete a single two-week early bactericidal activity study.[23] AstraZeneca pledged to see AZD5847 through to phase II results, but the real money behind this effort comes from NIAID.

Public institutions may be well placed to take new drugs and drug regimens forward into phase III trials, as USAID is doing through its support of the STREAM trial, the largest MDR-TB drug trial in history. The pharmaceutical sector's absence is felt most acutely in phase I and early discovery. Phase I of the TB drug pipeline sits empty,[24] guaranteeing that the recent approvals of bedaquiline and delamanid will offer a temporary reprieve from the usual drought between new TB drugs.

Vaccines

FIGURE 10

Vaccines: $95,172,788



FUNDERS WITH INVESTMENTS UNDER 2%

Company S	$1,763,557
Wellcome Trust	$1,682,743
Norwegian Agency for Development Cooperation	$1,624,258
European Commission	$1,513,270
Company X	$1,430,781
Japanese Ministry of Health, Labour and Welfare	$1,108,800
National Heart, Lung and Blood Institute (NHLBI)	$1,035,023
Canadian Institutes of Health Research	$927,878
U.K. Department of Health	$441,870
Danish Council for Independent Research	$414,698
Department of Defense, Medical Research and Development Program	$385,000
Carlos III Health Institute	$365,420
Institut Pasteur Paris	$335,781
Innovations Fonden	$251,805
French National Agency for Research (ANR)	$171,040
Statens Serum Institut	$170,060
Swedish Research Council	$134,091
Biofabri	$65,036
Institut Mérieux	$65,036
FIT Biotech	$32,518
Taiwan Ministry of Science and Technology	$30,000
Gulbenkian Foundation	$29,266
Thrasher Research Fund	$2,490

The *2011–2015 Global Plan* calls for annual investments of $380 million in research to develop new TB vaccines. In 2013, donors gave $95.2 million to vaccine research, leaving a gap of $284.8 million.

In 2013, the Gates Foundation gave $39.6 million to TB vaccine R&D, or 41.6% of the total. The bulk of this support, $31.2 million, went to Aeras, a PDP leading preclinical and clinical trials of new TB vaccines. The Gates Foundation is rethinking its approach toward TB vaccine R&D and will announce its new strategy soon.[25] NIAID remained the second-largest supporter of TB vaccine research, with grants and contracts totaling $17.2 million, or 18.1% of overall spending. Most of this money supports academic research programs at universities in the United States and abroad.

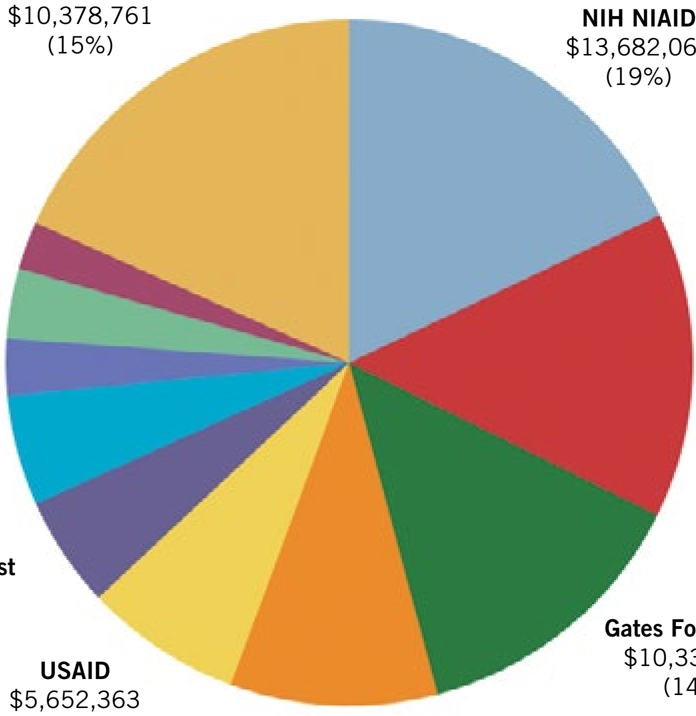
Emergent BioSolutions, the third-largest funder of TB vaccine research in 2013, with $4.9 million, will not appear in future reports. Emergent BioSolutions supported the clinical development of TB vaccine candidate MVA85A, but announced its withdrawal from the field in the wake of disappointing results of a phase IIb trial that failed to find that MVA85A paired with BCG conferred significantly increased protection against TB disease compared to BCG vaccination alone (at least in infants).[26] The dollar amount reported by Emergent BioSolutions in 2013 reflects costs associated with winding down its TB vaccine program.[27] This withdrawal is troubling giving the low level of pharmaceutical industry activity in TB vaccine research. The only other major private-sector players investing in new TB vaccines are Company S, with $1.8 million, and Company X, with $1.4 million in 2013.

The consistently weak financing of TB vaccine R&D could already be having an effect on the scientific approaches developers pursue. Aeras has announced a shift toward trials designed to examine protection against MTB infection rather than TB disease—the endpoint of most trials so far.[28] Prevention-of-infection trials promise to be smaller and less costly since rates of MTB infection are at least an order of magnitude higher than those of TB disease in any given population. Focusing on infection will therefore allow trials to enroll more quickly and follow patients for less time, saving money over the traditional approach.[29] Still, the biology of MTB infection remains incompletely understood, and diagnostics used to identify infection are imperfect. These limitations illustrate the extent to which TB vaccine research would benefit from an infusion of resources in basic science– and diagnostic research programs.

Operational Research

FIGURE 11

Operational Research: $71,754,311



FUNDERS WITH INVESTMENTS UNDER 2%

Department of Foreign Affairs, Trade and Development Canada	$1,241,067
U.K. Medical Research Council (MRC)	$1,183,962
Canadian Institutes of Health Research	$1,013,145
South African Medical Research Council	$901,992
Brazil National TB Program	$864,596
Taiwan Centers for Disease Control	$766,366
Bloomberg Foundation	$765,000
Norwegian Agency for Development Cooperation	$615,235
Médecins Sans Frontières	$499,473
Japanese Ministry of Health, Labour and Welfare	$484,183
Indian Ministry of Health and Family Welfare	$343,852
South African Department of Science and Technology	$298,601
Department of Foreign Affairs and Trade (DFAT) (AusAID)	$272,931
World Bank Total	$199,996
Indian Ministry of Science and Technology, Department of Biotechnology	$123,185
Carlos III Health Institute	$118,448
World Health Organization	$104,106
Korea Centers for Disease Control and Prevention	$103,200
World Diabetes Foundation	$88,646
Economic & Social Research Council	$81,401
Financial Management Corps†	$71,380
Firland Foundation	$59,998
Indian Council of Medical Research	$53,930
Grand Challenges Canada	$53,675
U.K. Department of Health	$44,938
National Science Foundation	$14,931
European Centre for Disease Prevention and Control	$10,525

† As reported by the Korean Institute of Tuberculosis

The *2011–2015 Global Plan* calls for annual investments of $80 million in operational research on the implementation and rollout of new tools. In 2013, donors gave $71.8 million to operational research, leaving a gap of $8.2 million.

While 90 percent of the operational research goal is funded, the goal itself is too small to address the considerable challenges hobbling the introduction of new tools into national TB programs. Total spending of just $71.8 million in this category is disappointing given that for the first time in decades the TB community has new drugs (bedaquiline, delamanid) and diagnostics (GeneXpert) to introduce to patients. The decrease in operational research funding between 2012 and 2013 also says much about how ill prepared TB programs and health systems are to implement and expand the use of new technologies.

Prohibitive pricing and slow moves toward the registration of new tools by developers also factor into the torpid state of operational research spending. The high price of bedaquiline, set through a three-rung price tier according to country Gross National Income—whereby a six-month course of bedaquiline costs $30,000, $3,000, and $900 for high-, middle-, and low-income countries, respectively—limits the ability of cash-strapped TB programs to offer this drug to patients with MDR-TB.[30] Problems also surround the other new TB drug, delamanid. Otsuka, delamanid's developer, has failed to register the drug outside of Europe and Japan. Meanwhile, high-burden countries and other places with the greatest operational research needs cannot get this important new MDR-TB treatment.

NIAID and other NIH institutes and centers remain the first- and second-largest funders of operational research, followed by the Gates Foundation. In 2013, NIAID spent $13.7 million, other NIH institutes and centers $10.9 million, and the Gates Foundation $10.3 million. The international development agencies DFID and USAID also contribute significantly to operational research with respective spending of $7.5 million and $5.7 million. Perhaps most telling, the list of operational research funders includes virtually no private-sector companies. Diagnostic, drug, and vaccine developers from industry have left the difficult work of preparing health systems for the introduction of their technologies to public and philanthropic groups.

This is problematic given the notable absence of government institutions from low- and middle-income countries on the list of top operational research funders. Most operational research spending comes from developed countries, despite the fact that countries with the largest TB burdens tend to be middle-income, including the BRICS nations: Brazil, Russia, India, China, and South Africa. The South African Medical Research Council is the first BRICS country institution to appear on the list, with 2013 operational research spending of $901,992, followed by Brazil's National TB Program with spending of $864,596.

FIGURE 12

Pediatric TB R&D Funding by Research Category, 2013
Total: $25,318,577

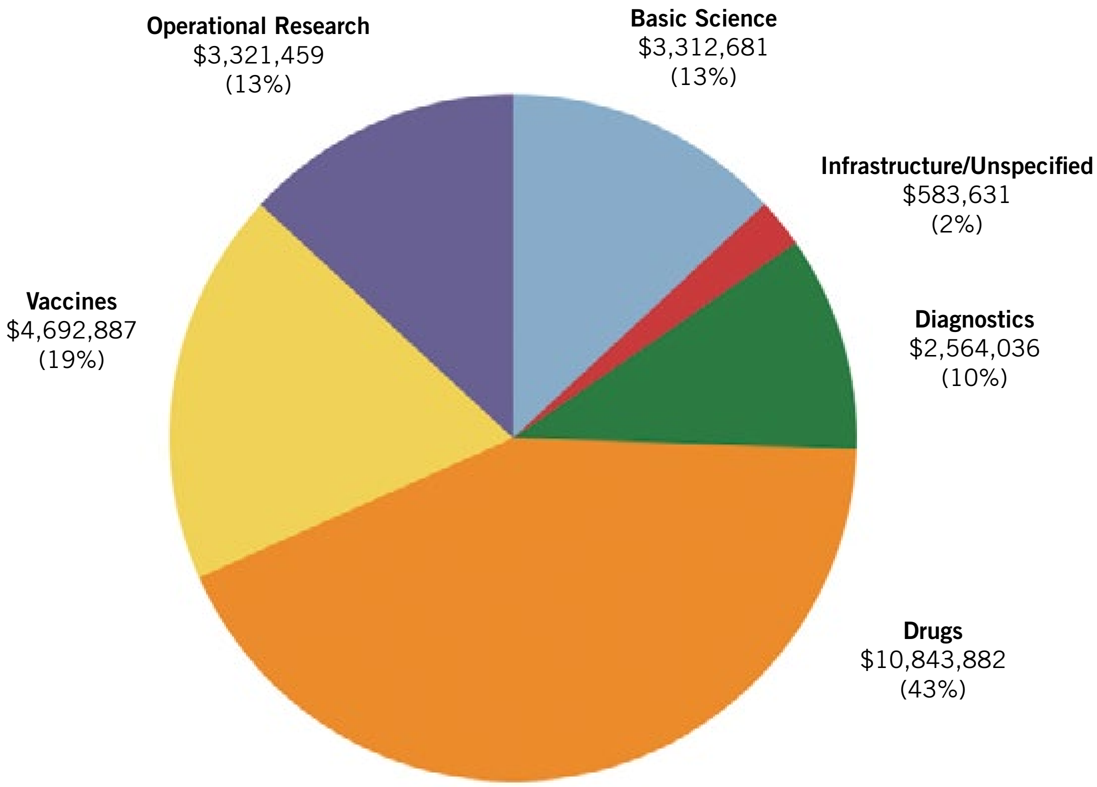


TABLE 3

Pediatric TB R&D Funders by Rank, 2013

2013 RANK	FUNDING ORGANIZATION	FUNDER TYPE	2013 PEDIATRIC TB R&D FUNDING	PERCENT OF TOTAL 2013 PEDIATRIC TB R&D FUNDING	TOTAL 2013 TB R&D FUNDING
1	NIH Other ICs	P	$4,741,873	18.73	$36,656,765
2	USAID	P	$4,338,420	17.14	$20,429,363
3	UNITAID	M	$3,412,000	13.48	$3,412,000
4	European and Developing Countries Clinical Trials Partnership (EDCTP)	P	$2,473,301	9.77	$18,980,589
5	Gates Foundation	F	$2,176,559	8.60	$147,923,878
6	U.K. Medical Research Council (MRC)	P	$2,069,201	8.17	$11,956,068
7	Company X	C	$1,935,487	7.64	$13,071,337
8	Wellcome Trust	F	$1,295,508	5.12	$14,458,418
9	NIH NIAID	P	$1,106,235	4.37	$158,797,248
10	Company V	C	$520,284	2.05	$4,278,035
11	Canadian Institutes of Health Research	P	$393,675	1.55	$4,490,049
12	Médecins Sans Frontières	F	$374,604	1.48	$976,833
13	Australian National Health and Medical Research Council (NHMRC)	P	$151,481	0.60	$4,935,036
14	French National Agency for AIDS Research (ANRS)	P	$114,498	0.45	$1,330,238
15	Grand Challenges Canada	P	$100,000	0.39	$912,475
16	Taiwan Centers for Disease Control	P	$61,927	0.24	$1,269,563
17	Firland Foundation	F	$40,000	0.16	$163,598
18	Indian Council of Medical Research	P	$9,315	0.04	$7,023,773
19	Thrasher Research Fund	F	$4,209	0.02	$4,209
	Total		**$25,318,577**		

Pediatric TB is a neglected field most often described by metaphors that invoke invisibility and disappearance. Children with TB have been described as invisible—excluded from surveillance surveys in many countries or erased from the official record when these data are not disaggregated by age. The particular presentation of TB in children, marked by a lower bacterial load (paucibacillary burden) than adults, entrenches this invisibility by making it difficult to diagnose pediatric TB using commonly available sputum-based tests.[31] Yet children with TB are also sentinels, or windows onto underlying TB incidence, since children are more likely than adults to reflect recent transmission.[32] Just as recognizing children as sentinels has helped to break the invisibility that cloaks their illness, tracking investments in pediatric TB R&D might bring their needs greater clarity and urgency in research.

In 2012, TAG produced the first estimates of global spending on pediatric TB R&D covering the years 2010–2012. During this period, spending ranged from $6.9 million in 2010 to $11.6 million in 2011. In 2013, donors spent $25.3 million on pediatric TB R&D, more than double the $10.3 million reported in 2012. The *Roadmap for Childhood Tuberculosis* estimates that the world must spend $200 million on pediatric TB R&D between 2011 and 2015 to develop new tools to prevent, diagnose, and treat TB in children.[33] Despite a large reported increase from 2012 to 2013, the world has spent just one-fourth of the targeted $200 million on pediatric TB R&D by the midpoint of the 2011–2015 period.

As in previous years, the largest share of pediatric TB R&D spending went to drug development: $10.8 million, or 43% of the total. Vaccines remained the second-largest category, with $4.7 million (19%), followed by operational research and basic science, with $3.3 million (13%) each, and diagnostics, with $2.6 million (10%). Overall, the Eunice Kennedy Shriver National Institute of Child Health and Development (NICHD) at the NIH was the largest funder of pediatric TB R&D in 2013, with $4.7 million—almost one-fifth of the total. The NICHD is supporting several studies evaluating the pharmacokinetic properties and optimal dosing of first- and second-line TB drugs in children with HIV and in pregnant women. UNITAID, which gave $3.4 million to pediatric TB research in 2013 (enough to rank third), is supporting the TB Alliance in efforts to develop fixed-dose combinations of pediatric formulations of first-line drugs—the lack of which has necessitated a grim alchemy of splitting, mixing, and matching existing fixed-dose combination and single-drug tablets to get the right amount of each drug into children's bodies.

While it is encouraging to see activity across all research categories, these projects are proceeding without the guidance of a common research agenda. For TB drug R&D in particular, there is great need for a pediatric TB research agenda that analyzes ongoing and upcoming studies in adults; determines what pediatric data remain missing; and identifies adult studies where adolescents can be included. Without such an agenda, pediatric TB research will proceed in its current piecemeal fashion, with studies in children lagging far behind those in adults. Delineating a clear research agenda would also help to encourage more funders to support pediatric TB R&D and make it easier for already-involved funders to track investments in pediatric TB research against agreed-upon goals.

Pediatric TB R&D investments are difficult to estimate since many funders do not themselves track pediatric-specific spending, and the numbers in this report should be interpreted with this limitation in mind. Among industry groups, Company X and Company V are the only funders that reported data on pediatric-specific projects in 2013, with investments of $1.9 million and $520,284, respectively, in drug development. Otsuka does not track pediatric research within its larger $58.7 million TB drug R&D program, although the company is enrolling a cohort of 6–11-year-olds in a safety study of delamanid.[34] Like surveillance surveys without disaggregation by age, funding streams without mechanisms to track pediatric spending render children invisible in TB research.

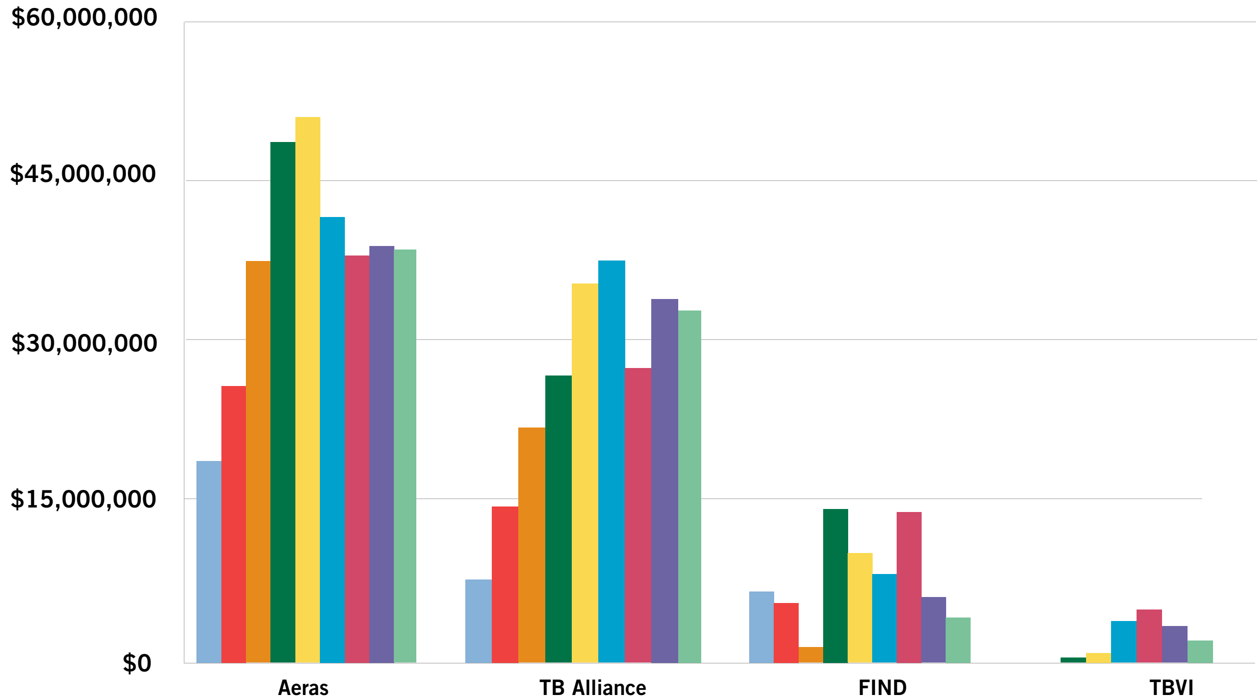
Recognizing this limitation, TAG identified pediatric TB research by conducting a keyword search of the titles and abstracts of projects reported by the 114 funders in this year's report. Search terms included "pediatric," "child," "adolescent," and "infant." We cross-checked these items against pediatric projects noted in the qualitative portion of the survey filled out by funders. This methodology likely misses research endeavors that do not explicitly include children but inform the development of pediatric products. Consequently, the numbers reported here likely underestimate funding for pediatric TB R&D. Future reports will make an effort to capture any data missed in earlier years and update annual totals.

The uncertainty surrounding figures for pediatric TB R&D funding is echoed in the shifting estimates of the size of the TB epidemic in children. In March 2014, researchers at Harvard Medical School published modeling work suggesting that every year at least 1 million children acquire TB, double the number estimated by the WHO and three times the number of pediatric TB cases diagnosed and notified to national TB programs in 2011.[35] Pediatric TB illustrates the adage that when one learns to look for a problem, what once seemed invisible suddenly appears everywhere. As researchers train their vision on pediatric TB, the size of the epidemic appears to grow larger, and the need to increase funding for pediatric TB research becomes more urgent.

3.3 Trends in TB R&D Funding among Product Development Partnerships

FIGURE 13

Total TB R&D Spending by PDPs, 2005–2013



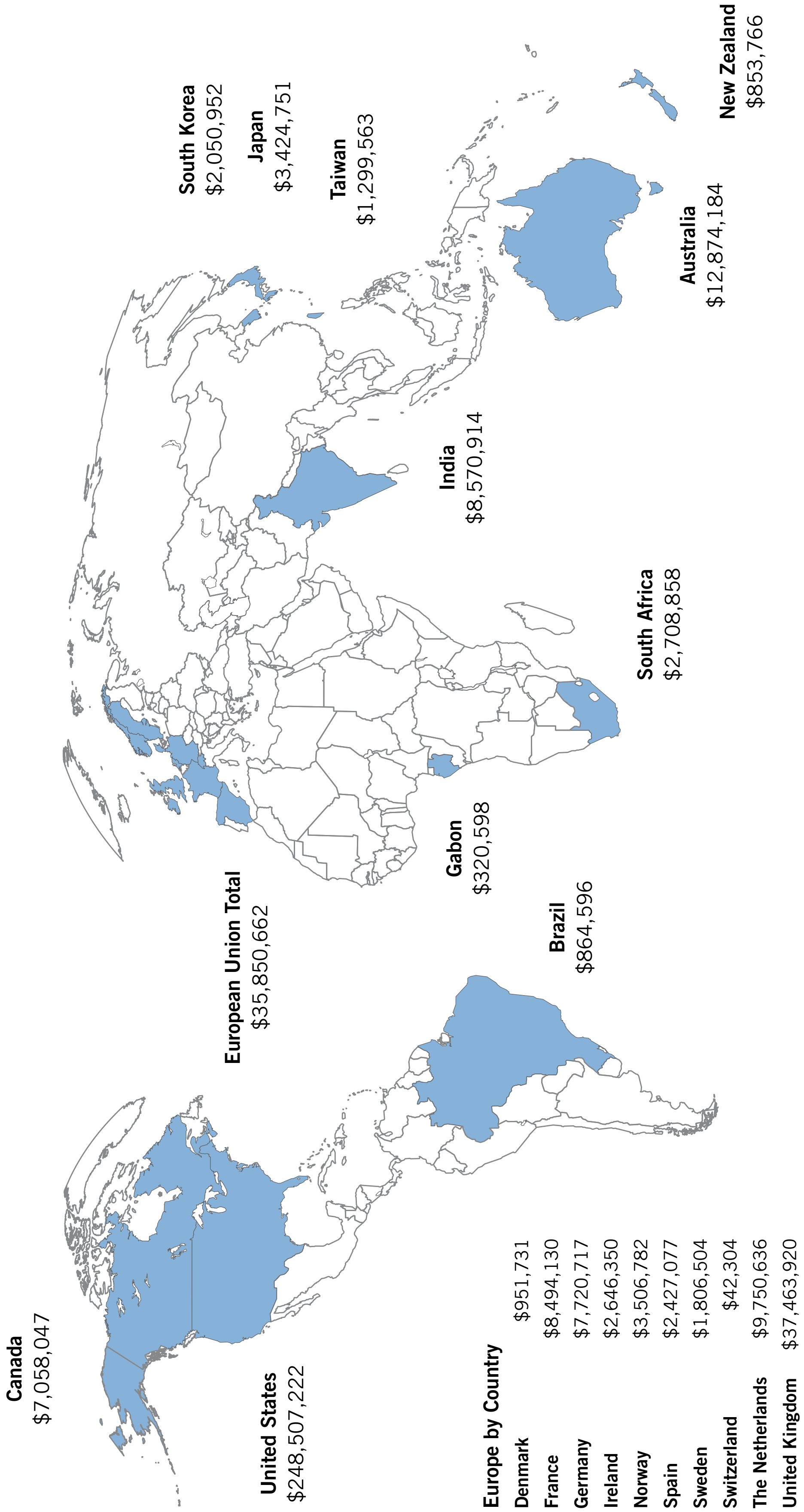
	Aeras	TB Alliance	FIND	TBVI
2005	$18,580,139	$7,874,983	$6,778,239	N/A
2006	$25,923,809	$14,808,362	$5,492,942	N/A
2007	$37,704,051	$22,624,182	$1,145,409	N/A
2008	$48,679,266	$26,885,734	$14,177,202	$339,741
2009	$50,792,515	$35,643,490	$9,975,320	$841,333
2010	$41,572,980	$37,538,794	$8,212,896	$3,700,914
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

Each category of TB product development tracked by TAG contains at least one large PDP. Built on a non-profit business model, PDPs combine resources from public, private, philanthropic, and academic groups to address diseases that, despite exacting a high toll on human health, attract little commercial attention. In diagnostics, the Foundation for Innovative New Diagnostics (FIND) carried out much of the work behind GeneXpert. The Global Alliance for TB Drug Development (TB Alliance) conducts trials of drug regimens for both DS- and DR-TB using combinations of existing drugs paired with its own new drug candidate PA-824. And Aeras and the TuBerculosis Vaccine Initiative (TBVI) together support nearly the entire pipeline of new TB vaccines designed to either replace or boost BCG.

Since PDPs operate as funding recipients and are not original-source donors, TAG tracks their spending separately from other institutions. In 2013, Aeras reported costs of $38.5 million on a range of preclinical and clinical activities, an amount in line with the $38.9 million it reported in 2012. This is much larger than the $2.2 million in costs reported by the TBVI, its European counterpart. Generally speaking, the TBVI focuses on discovery and phase I and IIa studies, while Aeras also conducts larger phase IIb efficacy trials.

FIGURE 14

Country Contributions to TB R&D, 2013



Europe by Country

Denmark	$951,731
France	$8,494,130
Germany	$7,720,717
Ireland	$2,646,350
Norway	$3,506,782
Spain	$2,427,077
Sweden	$1,806,504
Switzerland	$42,304
The Netherlands	$9,750,636
United Kingdom	$37,463,920

The TB Alliance reported R&D expenses of $33.1 million in 2013—a $1.3 million decline over 2012. With support from the Gates Foundation, the TB Alliance recently announced plans to conduct a phase III trial evaluating a three-drug regimen that, if successful, could shorten the duration of DS-TB treatment from six months to four months. The regimen combines the drugs moxifloxacin, pyrazinamide, and PA-824.[36] In 2013, the TB Alliance concluded a long-running phase III trial evaluating whether moxifloxacin, substituted for either isoniazid or ethambutol (standard components of first-line therapy) could shorten DS-TB treatment. Results from the trial failed to demonstrate that the experimental regimen with moxifloxacin was no worse than (noninferior to) the current six-month standard of care.[37] Future trials and sustained investments supporting the TB Alliance's program will be required to achieve the long-sought goal of shorter TB therapies.

Overall, the Gates Foundation is the biggest supporter of PDPs working on TB. In 2013, the TB Alliance, Aeras, FIND, and the TBVI reported receiving $32.9 million, $30.0 million, $9.1 million, and $1.2 million from the Gates Foundation, respectively. These PDPs also drew substantial support from international development agencies including USAID, DFID, Irish Aid, the Norwegian Agency for International Development, and the Australian Department of Foreign Affairs and Trade.

3.4 Trends in TB R&D Funding among the Top 30 Funders

In 2013, the 30 largest funders gave 94% of the $676.7 million spent on TB R&D. Within this group, the distribution of funding is heavily weighted toward the top: 88% of funding comes from the top 20 funders, 76% from the top 10, 63% from the top five and 45% from the two largest contributors, NIAID and the Gates Foundation. The 84 donors that fall outside of the top 30 make up less than 7% of total spending. This incredible degree of concentration reveals the extent to which TB research relies on just a handful of institutions, most of them public and philanthropic organizations in the United States and Europe.

Private-Sector Funders in the Top 30

The composition of the top 30 funders to TB R&D remains largely unchanged from previous years, albeit with fewer industry players. Perhaps most noteworthy, Company X, a company involved in TB drug development, fell out of the top 10 donor list, dropping from sixth place in 2012 to 11th in 2013. Two of its private-sector peers, AstraZeneca and Novartis, left the TB field altogether. In 2012, AstraZeneca ranked 14th overall, with spending of $10.3 million.

Despite decreasing its funding for TB R&D by $1.3 million from 2012 to 2013, Otsuka retained its position as the third-largest funder in 2013, with investments of $58.7 million in drug development. Most of this money supported the phase III trial of delamanid, which received conditional regulatory approval from the European Medicines Agency (EMA) in 2014. Otsuka has also begun a pediatric investigational program for delamanid and, as a condition of EMA approval, will need to conduct a phase IV study to determine an optimal dosing schedule for the drug.[38]

While Otsuka's substantial investments in TB drug R&D set an example unmatched by any of its industry peers, this healthy level of funding has not always produced high-quality research—especially when compared with drug development efforts in HIV and hepatitis C (HCV). A tally of the clinical trials behind newly approved drugs for HIV, HCV, and TB shows 61 trials for dolutegravir (HIV), 67 trials for sofosbuvir (HCV), and six trials for delamanid (TB).[39] More problematic, delamanid's phase II program included a two-month study, a six-month study, and an open-label study—data from which did not always include the same patients and so thoroughly confused the EMA that its Committee for Medicinal Products for Human Use initially rejected delamanid's application before it eventually voted to approve it.[40,41] The volume and quality of TB research coming from the private sector leaves a lot to be desired.

New Funders in the Top 30

The top 30 also contains some funders new to TB research. The Global Health Innovative Technologies Fund (GHIT), a public–private partnership established in Japan in 2013, gave $3.3 million to TB drug and vaccine discovery, enough to rank 26th overall. GHIT includes resources of over $100 million pooled from five Japanese pharmaceutical companies (Astellas, Daiichi Sankyo, Eisai, Shionogi, and Takeda), two Japanese government agencies (the Japanese Ministry of Foreign Affairs and the Ministry of Health, Labour and

Welfare), the Gates Foundation, and the United Nations Development Programme.[42] GHIT's selling point is its drug discovery screening program, in which the participating Japanese pharmaceutical firms have opened their compound libraries for screening to identify potential new treatments for TB and other neglected diseases.

The Australian Department of Foreign Affairs and Trade (DFAT) (AusAID), ranked 15th, is another new entry to the top 30, with investments of $7.2 million. Most of this money, issued through the Australian government's medical research strategy, supported the TB Alliance and Aeras. Formerly an independent agency, AusAID's dissolution into DFAT in 2013 upset Australian health advocates, who saw this as symptomatic of the new government's lack of political commitment to foreign aid.[43] Since then, funding for global health R&D at DFAT has crested and crashed on the learning curve of a more conservative government. DFAT awarded the above-mentioned funding to PDPs in June 2013, but in January 2014 issued an abrupt warning that the agency would not provide further funding through the medical research strategy. Five months later, in June 2014, the Australian Minister for Foreign Affairs reversed course by announcing a new aid policy with commitments to provide $120 million for medical research over four years with $10 million per year earmarked for PDPs working on diseases including TB and malaria.[44]

TABLE 4

2005–2013 NIH Funding for Selected Infectious Diseases (in USD millions)

Research Area	2005	2006	2007	2008	2009*	2010*	2011	2012	2013
Tuberculosis	$158	$150	$188	$142	$216	$224	$209	$218	$207
HIV/AIDS	$2,921	$2,902	$2,906	$2,928	$3,338	$3,407	$3,059	$3,074	$2,898
Malaria	$104	$98	$112	$142	$121	$148	$145	$152	$147
Smallpox	$187	$149	$142	$94	$98	$97	$41	$40	$30
Anthrax	$183	$150	$160	$134	$115	$130	$87	$84	$70

*Includes American Recovery and Reinvestment Act stimulus funds
Source: NIH Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC). Available from: http://report.nih.gov/categorical_spending.aspx.

U.S. Public Agencies in the Top 30

NIAID, the NHLBI, and other NIH institutes and centers (ICs) maintain their positions as leading funders of TB R&D at slightly reduced or stable levels. The consistency of NIH funding in 2013 is notable given the impact of sequestration, which imposed a mandatory 10 percent cut to the overall budgets of U.S. federal agencies. Within the NIH, institutional commitment to TB research appears strong. Speaking at a symposium convened by the WHO HIV/TB Working Group at the 20th International AIDS Conference in July 2014, NIAID director Dr. Anthony Fauci pointed out that when the NIH budget doubled between 1998 and 2003, TB emerged as a big winner. Over the past decade, even as inflation reduced the purchasing power of the NIH budget (which has stayed relatively flat since 2003), the NIH maintained funding for TB at the same effective level; not every disease category has held up as much.[45]

Still, NIH funding does not always align with the size of a disease's global footprint. As table 4 shows, smallpox and anthrax continue to receive tens of millions of dollars in funding despite being eradicated, in the case of the former, and responsible for fewer than five cases per year in the United States, in the case of the latter.[46] The NIH and other U.S. agencies devote some of their spending to research on diseases—emergent, established, or even eradicated—that may pose bioterrorist threats. To this end, TAG for the first time captured TB R&D funding information from the U.S. Department of Defense through its Congressionally Directed Medical Research Program (CDMRP) and found TB drug development grants totaling $1.6 million. TB does not fall under the CDMRP priority research areas—malaria, HIV, dengue, leishmaniasis, and hemorrhagic fever, among others—so any TB spending reflects investigator-driven proposals received by the Department of

Defense under its undirected funding streams. The Department of Defense is a significant funder of medical research,[47,48] and a more explicit focus on TB within the agency's numerous research wings would unlock a welcome pool of new resources.

Outside of the NIH, sequestration also shrank TB R&D spending by the CDC from $18.5 million in 2012 to $16.1 million in 2013. This decrease hit the CDC's TB drug research program hardest—from funding of $9.2 million in 2012 to $7.9 million in 2013. Effects of the sequester included a 13 percent cut to the CDC's Tuberculosis Trial's Consortium (TBTC),[49] a research network that has conducted groundbreaking trials of shorter treatments for active and latent TB on a shoestring budget. The TBTC is poised to begin a phase III trial that, if successful, could shorten treatment for drug-sensitive TB from six months to four months. It remains unclear whether the TBTC will be able to mount other trials alongside this phase III program in the absence of restored funding levels.

USAID is also funding a treatment-shortening trial to reduce the length of MDR-TB treatment from two years to nine months or fewer. Much to the frustration of U.S. advocates, USAID seems to lack the high-level political commitment to TB research seen within the NIH. USAID Director Raj Shah proposed a $45 million cut to USAID's TB program in his fiscal year 2015 (FY2015) budget (19% lower than FY2014-enacted levels), a recommendation taken up by President Obama's FY2015 budget request. Director Shah argued that the United States would make up this amount in TB spending through its commitments to the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund.[50] Data reported to TAG do not bear out this theory, at least in terms of TB R&D spending. PEPFAR funding for TB operational research fell from $6.6 million in 2012 to $2.0 million in 2013. A report issued in July 2014 also indicates that TB allocations within PEPFAR and the Global Fund fall short of rhetorical commitments.[51] Thankfully, the U.S. Congress proposed flat funding or smaller cuts than USAID's own director, but future years may see lower TB R&D spending from USAID if the agency's senior leadership remains uncommitted to TB elimination.

The top 30 donors also include many national research agencies outside of the United States, including the U.K. Medical Research Council (MRC) ($11.9 million, 12th place), the Indian Council of Medical Research ($7.0 million, 16th), the German Federal Ministry of Education and Research ($6.9 million, 17th), the Australian National Health and Medical Research Council (NHMRC) ($4.9 million, 20th), and the Canadian Institutes of Health Research ($4.5 million, 22nd). These institutions give most of their support to investigator-driven basic-science research housed within universities and national academic institutions.

European Public Agencies in the Top 30

The biggest addition to this year's top 30 list is the EDCTP, which TAG is listing as a separate donor for the first time. Ranked seventh overall, the EDCTP gave $19.0 million to TB R&D in 2013, mostly to support trials of new diagnostics, drugs, and vaccines. Established as an independent arm of the European Commission by a delegation agreement in 2003, the EDCTP has funded over 100 clinical trials in 30 African nations with the goal of building the international research capacity and scientific partnership required to address HIV, TB, and malaria. The first wave of the EDCTP (EDCTP 1) will soon yield to EDCTP2, which so far has received funding commitments of $1.7 billion from European member states and the European Commission.[52] The EDCTP2 program will expand the EDCTP1's original focus on phase II and III trials to include phase I and IV studies, allowing the network to address innovation needs for new medical products at both early and late stages of the pipeline. EDCTP2 will also tackle neglected tropical diseases while continuing EDCTP1's work on HIV, TB, and malaria.[53]

Separate from its contributions to the EDCTP, the European Union funds TB research through a financial instrument called Framework Programme 7 (FP7) housed under the European Commission Directorate-General for Research and Innovation. TB funding appears in several of the FP7 "challenges," including those known as "Health," "People," and "Ideas," each of which contains a different focus and the last of which is administered by the European Research Council. FP7 will conclude in 2013 and will be replaced by Horizon 2020—a financing mechanism of $100 billion to spur research and innovation within Europe between 2014 and 2020. (EDCTP2 is included under Horizon 2020 and will make disbursements stretching until 2023.) In 2013, the European Commission gave $16.9 million to TB R&D, a 38.2% reduction from the $27.3 million it gave in 2012. Conversations with European Commission scientific program officers indicate that this decline reflects the conclusion of many FP7 grants and should not be taken as an indication of decreasing European Commission support for TB research, which has remained high throughout the FP7 period and will extend into Horizon 2020.[54]

4. Conclusion

TABLE 5

Summary of Changes in TB R&D Investment, 2005-2013 in USD

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	$676,656,323	$37,873,051	5.93	$318,179,786	88.76

The Stop TB Partnership has begun the planning process for the next *Global Plan to Stop TB*, which will establish research and implementation goals for 2016–2020. As this process gets under way, those involved should take note of the spectacular failure of the global community to achieve any of the R&D funding targets put forward by the first two *Global Plan*s. According to the first and second *Global Plan*s, research spending from 2006 to 2015 should have totaled $18.8 billion. Instead, the world has spent just $5.02 billion on TB R&D over this period. Halfway through the *2011–2015 Global Plan*, the world has given $1.99 billion—barely one-fifth of the targeted amount $9.8 billion. These nominal investments appear even more anemic when one considers the rising costs of biomedical research and the inability of public research budgets in most countries to keep pace with inflation.

In the *20011–2015 Global Plan*, the Stop TB Partnership heralded the creation of a "research movement" with three goals: increase resources for TB research; coordinate priorities among research institutions; and implement "a coherent and comprehensive global TB research roadmap to TB elimination."[55] We are still waiting for that movement to make itself felt, and the small band of TB R&D funders—never more than 120 by TAG's count, never giving more than $700 million in a particular year—now appears in disarray. Some quarters of the TB research community are leaving the movement altogether, while others are struggling to maintain commitments in the face of fiscal austerity measures, budget cuts, and expiring funding mechanisms.

The next iteration of the *Global Plan* must include detailed thinking on how to save this research movement from collapse—at worst—or another five years of missed targets and flat funding, if current trends hold. This thinking must address the pharmaceutical industry's disappearing act, which at its most pronounced involves companies leaving the field to work on pathogens and conditions where R&D activities hold greater market potential. Other companies remain invested at lower levels of spending, often because they are concluding research on a particular drug with no younger compounds following. Still others offer their compound libraries, technical assistance, or other in-kind support without investing actual capital. Japan's pharmaceutical industry has done this through GHIT, where the compound libraries belong to pharmaceutical companies, but the real money comes from public and philanthropic groups.

Already, the public and philanthropic sectors have offered significant financial inducements for industry to stay involved in TB R&D. NIAID has funded the development of drug compounds owned by Sequella and AstraZeneca, and the NIH and the U.S. Department of Defense have done the early work on the technology behind GeneXpert. In his remarks in Melbourne, Dr. Fauci pointed out that NIAID has been involved in the development of most of the TB drugs in the pipeline.[56] Rifapentine, one of the few drugs NIAID has not funded, has received over a decade of support from the CDC. The CDC has invested more money in the clinical development of rifapentine, a drug owned by Sanofi, than has the company itself.[57] The EDCTP has partnered with Bayer, Sequella, and Sanofi on TB drug trials through its PanACEA research network.[58] The TB Alliance owns the rights, and therefore will assume the costs, to develop Janssen's bedaquiline for DS-TB and now owns Novartis's TB drug compounds as well.[59] The list goes on; none of it has been enough to stem the private sector's withdrawal. Meeting industry halfway has not worked, and the authors of the next *Global Plan* should acknowledge this and propose alternative paths forward.

The current R&D system is not working for TB diagnostic, drug, or vaccine research. For many of the new technologies that have emerged since 2006, the public has been asked to pay twice—first to fund the research of a product owned by a private corporation and then again to buy it at a price set by that same company that benefitted from public research dollars. This is what happened with GeneXpert globally and with rifapentine in the United States before advocacy led Cepheid and Sanofi, respectively, to lower prices.[60,61] In other situations, patients have been denied access to potentially lifesaving technologies due to either nonexistent compassionate use programs or slow moves by companies to file for product registration. A disturbing oversight has become commonplace: many companies with new products or new indications for existing products have not filed for registration in countries that hosted the clinical trials that made these advances possible. This is a breach of global health equity exacerbated by a harsh funding landscape in which researchers from all sectors are asked to confront a sizeable epidemic with shrinking resources.

The world needs a TB research movement with muscle, money, and political commitment—one that can command the resources required to develop new technologies and hold governments and developers accountable to making them available quickly and justly to all patients in need. The goal of the next *Global Plan* should be to design this movement, create specific milestones for success, assess the costs of future research needs and empower countries and communities to hold R&D funders accountable. This should be done with an eye toward the WHA resolution approving the post-2015 global TB strategy with its targets to cut new TB cases by 90 percent and reduce TB deaths by 95 percent between 2015 and 2035. The WHA resolution warns that in order to achieve these goals, new tools must be introduced no later than 2025—and preferably much sooner. The *2016–2020 Global Plan* will cover a crucial period; the next five years are too important to risk repeating the last ten. Now that WHO member states have expressed the political will to reach zero TB deaths, new infections, and suffering, the money to make this a reality must follow, and a real research movement must demand it.

Endnotes

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Appendix 1

Top Reporting TB R&D Funders, 2013

2013 Rank	Funding Organization	Funder Type	Total (USD)
1	NIH NIAID	P	$158,797,248
2	Gates Foundation	F	$147,923,878
3	Otsuka Pharmaceuticals	C	$58,717,259
4	NIH Other ICs	P	$36,656,765
5	U.K. Department for International Development	P	$24,640,072
6	USAID	P	$20,429,363
7	EDCTP	P	$18,980,589
8	European Commission	P	$16,858,354
9	CDC	P	$16,078,985
10	Wellcome Trust	F	$14,458,418
11	Company X	C	$13,071,337
12	U.K. Medical Research Council (MRC)	P	$11,956,068
13	NIH National Heart, Lung and Blood Institute (NHLBI)	P	$11,075,642
14	Dutch Directorate-General for International Cooperation	P	$9,721,685
15	Department of Foreign Affairs and Trade (DFAT) (AusAID)	P	$7,197,108
16	Indian Council of Medical Research	P	$7,023,773
17	German Federal Ministry of Education and Research (BMBF)	P	$6,968,480
18	French National Institute of Health and Medical Research (INSERM)	P	$5,964,809
19	Company Y	C	$5,000,000
20	NHMRC Australian	P	$4,935,036
21	Emergent BioSolutions	C	$4,882,000
22	Canadian Institutes of Health Research	P	$4,490,049
23	Company V	C	$4,278,035
24	Qiagen*	C	$4,100,000
25	UNITAID*	M	$3,412,000
26	Global Health Innovative Technology Fund*	M	$3,349,544
27	Norwegian Agency for Development Cooperation	P	$3,176,614
28	Institut Pasteur Paris	F	$3,133,454
29	Eli Lilly and Company	C	$3,100,000
30	Company S	C	$3,063,516
31	Irish Aid	P	$2,646,350

* New TB R&D funder

Basic Science	Diagnostics	Drugs	Vaccines	Operational Research	Infrastructure/ Unspecified
$60,357,403	$15,799,285	$34,680,504	$17,202,047	$13,682,061	$17,075,948
$13,255,042	$16,041,887	$68,696,528	$39,599,146	$10,331,275	$0
$0	$0	$58,717,259	$0	$0	$0
$13,957,509	$1,669,409	$7,074,534	$0	$10,977,466	$2,977,847
$0	$4,258,352	$9,885,460	$3,041,680	$7,454,580	$0
$0	$1,200,000	$8,748,000	$0	$5,652,363	$4,829,000
$0	$2,279,996	$12,494,787	$4,082,007	$0	$123,800
$6,907,002	$0	$6,544,567	$1,513,270	$0	$1,893,515
$0	$2,207,014	$7,970,437	$0	$3,968,429	$1,933,105
$2,713,150	$2,115,383	$1,634,746	$1,682,743	$3,999,501	$2,312,896
$0	$0	$11,640,556	$1,430,781	$0	$0
$6,559,351	$0	$1,696,073	$2,516,682	$1,183,962	$0
$8,712,423	$558,675	$201,716	$1,035,023	$0	$567,805
$0	$3,790,633	$0	$4,348,086	$0	$1,582,965
$0	$0	$2,320,500	$2,320,509	$272,931	$2,283,168
$8,380	$0	$51,846	$0	$53,930	$6,909,618
$4,296,966	$134,228	$47,689	$0	$0	$2,489,597
$5,964,809	$0	$0	$0	$0	$0
$0	$5,000,000	$0	$0	$0	$0
$2,533,294	$170,240	$511,073	$0	$1,720,430	$0
$0	$0	$0	$4,882,000	$0	$0
$1,399,813	$205,604	$943,609	$927,878	$1,013,145	$0
$0	$0	$4,278,035	$0	$0	$0
$0	$4,100,000	$0	$0	$0	$0
$0	$0	$3,412,000	$0	$0	$0
$0	$0	$149,335	$3,200,208	$0	$0
$484,224	$145,662	$0	$1,624,258	$615,235	$307,235
$1,995,812	$182,631	$619,230	$335,781	$0	$0
$0	$0	$3,100,000	$0	$0	$0
$4,959	$0	$1,295,000	$1,763,557	$0	$0
$0	$0	$2,646,350	$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, 2013

2013 Rank	Funding Organization	Funder Type	Total (USD)
32	Carlos III Health Institute	P	$2,427,077
33	Japanese Ministry of Health, Labour and Welfare	P	$2,408,021
34	South African Medical Research Council*	P	$2,248,534
35	U.S. President's Emergency Plan for AIDS Relief (PEPFAR)	P	$2,028,593
36	Alere	C	$2,000,000
37	Swedish Research Council	P	$1,806,504
38	Department of Defense, Medical Research and Development Program*	P	$1,641,914
39	Fondation Mérieux	F	$1,593,370
40	Korea International Cooperation Agency	P	$1,564,244
41	French National Agency for AIDS Research (ANRS)	P	$1,330,238
42	Taiwan Centers for Disease Control*	P	$1,269,563
43	Department of Foreign Affairs, Trade and Development Canada	P	$1,241,067
44	U.S. Food and Drug Administration	P	$1,200,001
45	French National Agency for Research (ANR)	P	$1,199,084
46	Médecins Sans Frontières*	F	$976,833
47	Japan International Cooperation Agency	P	$970,361
48	Grand Challenges Canada	P	$912,475
49	International Centre for Genetic Engineering and Biotechnology	P	$893,746
50	Brazil National TB Program	P	$864,596
51	Health Research Council of New Zealand	P	$853,766
52	Bloomberg Foundation	F	$765,000
53	German Research Foundation	P	$752,237
54	U.K. Department of Health	P	$735,371
55	Australian Research Council	P	$659,845
56	National Science Foundation*	P	$598,710
57	World Health Organization (WHO)	M	$576,514
58	WHO TDR (Special Programme for Research and Training in Tropical Diseases)	M	$545,000
59	Japan BCG Laboratory	C	$437,875
60	Indian Ministry of Health and Family Welfare	P	$418,069
61	Danish Council for Independent Research	P	$414,698
62	Génome Québec	P	$414,457

* New TB R&D funder

Basic Science	Diagnostics	Drugs	Vaccines	Operational Research	Infrastructure/ Unspecified
$1,269,860	$38,025	$635,324	$365,420	$118,448	$0
$332,186	$457,652	$0	$1,108,800	$484,183	$25,200
$75,461	$15,238	$15,238	$0	$901,992	$1,240,606
$0	$0	$0	$0	$2,028,593	$0
$0	$2,000,000	$0	$0	$0	$0
$875,316	$297,980	$499,117	$134,091	$0	$0
$122,049	$749,998	$384,867	$385,000	$0	$0
$0	$32,518	$0	$0	$1,560,852	$0
$0	$0	$0	$0	$0	$1,564,244
$168,577	$343,495	$687,375	$0	$0	$130,791
$0	$112,487	$390,709	$0	$766,366	$0
$0	$0	$0	$0	$1,241,067	$0
$0	$0	$1,200,001	$0	$0	$0
$705,388	$0	$322,656	$171,040	$0	$0
$0	$373,304	$104,057	$0	$499,473	$0
$0	$970,361	$0	$0	$0	$0
$322,050	$429,400	$107,350	$0	$53,675	$0
$554,469	$0	$60,410	$0	$0	$278,866
$0	$0	$0	$0	$864,596	$0
$700,635	$153,131	$0	$0	$0	$0
$0	$0	$0	$0	$765,000	$0
$752,237	$0	$0	$0	$0	$0
$0	$0	$21,344	$441,870	$44,938	$227,219
$118,726	$43,381	$497,738	$0	$0	$0
$150,203	$433,577	$0	$0	$14,931	$0
$0	$472,408	$0	$0	$104,106	$0
$0	$0	$545,000	$0	$0	$0
$437,875	$0	$0	$0	$0	$0
$0	$0	$0	$0	$343,852	$74,218
$0	$0	$0	$414,698	$0	$0
$414,457	$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, 2013

2013 Rank	Funding Organization	Funder Type	Total (USD)
63	République Gabonaise	P	$320,598
64	South African Department of Science and Technology	P	$316,776
65	OPEC Fund for International Development	M	$300,956
66	InnovationsFonden	P	$251,805
67	Indian Ministry of Science and Technology, Department of Biotechnology	P	$235,326
68	Korea Centers for Disease Control and Prevention	P	$232,200
69	Korea Health Industry Development Institute*	P	$227,341
70	World Bank*	M	$199,996
71	Research Council of Norway	P	$181,049
72	BioDuro	C	$180,000
73	Quantimetrix*	C	$172,000
74	Statens Serum Institut	P	$170,060
75	Firland Foundation*	F	$163,598
76	South-Eastern Norway Regional Health Authority	P	$149,119
77	Seegene, Inc.*	C	$147,273
78	South African National Research Foundation*	P	$143,548
79	Danish International Development Agency	P	$115,168
80	Japan Health Sciences Foundation	F	$100,800
81	Howard Hughes Medical Institute*	F	$100,000
82	World Diabetes Foundation	F	$88,646
83	Economic & Social Research Council	P	$81,401
84	Financial Management Corps†	C	$71,380
85	Biofabri	C	$65,036
86	Institut Mérieux*	C	$65,036
87	Nipro Corporation*	C	$50,000

* New TB R&D funder
† As reported by the Korean Institute of Tuberculosis

Basic Science	Diagnostics	Drugs	Vaccines	Operational Research	Infrastructure/ Unspecified
$320,598	$0	$0	$0	$0	$0
$18,175	$0	$0	$0	$298,601	$0
$300,956	$0	$0	$0	$0	$0
$0	$0	$0	$251,805	$0	$0
$11,581	$0	$100,560	$0	$123,185	$0
$0	$86,000	$0	$0	$103,200	$43,000
$0	$227,341	$0	$0	$0	$0
$0	$0	$0	$0	$199,996	$0
$181,049	$0	$0	$0	$0	$0
$0	$0	$180,000	$0	$0	$0
$0	$172,000	$0	$0	$0	$0
$0	$0	$0	$170,060	$0	$0
$20,000	$47,600	$36,000	$0	$59,998	$0
$149,119	$0	$0	$0	$0	$0
$0	$147,273	$0	$0	$0	$0
$143,548	$0	$0	$0	$0	$0
$0	$0	$115,168	$0	$0	$0
$100,800	$0	$0	$0	$0	$0
$100,000	$0	$0	$0	$0	$0
$0	$0	$0	$0	$88,646	$0
$0	$0	$0	$0	$81,401	$0
$0	$0	$0	$0	$71,380	$0
$0	$0	$0	$65,036	$0	$0
$0	$0	$0	$65,036	$0	$0
$0	$50,000	$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, 2013

2013 Rank	Funding Organization	Funder Type	Total (USD)
88	Hain Lifescience*	C	$49,978
89	Oppenheimer Memorial Trust*	F	$48,523
90	State Trustees of Victoria*	P	$45,664
91	Claude Leon Foundation*	F	$42,963
92	Company T	C	$42,606
93	École Polytechnique Fédérale de Lausanne	P	$42,304
94	U.K. Defence Science and Technology Laboratory	P	$38,873
95	Australia-China Council*	P	$36,531
96	FIT Biotech	C	$32,518
97	Japan Science and Technology Agency	P	$30,240
98	Taiwan Ministry of Science and Technology*	P	$30,000
99	Gulbenkian Foundation	F	$29,266
100	ZonMw	P	$28,951
101	National Research Foundation of Korea	P	$27,167
102	Biometrix Technology, Inc.*	C	$25,800
103	Fondation pour la Recherche Médicale*	F	$23,708
104	Individual donors to iM4TB	F	$21,152
105	Japan Society for the Promotion of Science	P	$16,128
106	University College London Hospitals Charitable Foundation*	F	$16,014
107	KNCV Tuberculosis Foundation	F	$14,192
108	Technology Strategy Board	P	$12,136
109	European Centre for Disease Prevention and Control (ECDC)	P	$11,719
110	Faber Daeufer	C	$9,000
111	WHO-Stop TB Partnership	M	$7,000
112	British Society for Antimicrobial Chemotherapy	F	$5,067
113	Thrasher Research Fund	F	$4,209
114	Individual donors to TB Alliance	F	$1,310
	GRAND TOTAL		$676,656,323

* New TB R&D funder

Basic Science	Diagnostics	Drugs	Vaccines	Operational Research	Infrastructure/ Unspecified
$0	$49,978	$0	$0	$0	$0
$48,523	$0	$0	$0	$0	$0
$0	$45,664	$0	$0	$0	$0
$42,963	$0	$0	$0	$0	$0
$0	$42,606	$0	$0	$0	$0
$0	$0	$42,304	$0	$0	$0
$0	$0	$38,873	$0	$0	$0
$0	$36,531	$0	$0	$0	$0
$0	$0	$0	$32,518	$0	$0
$30,240	$0	$0	$0	$0	$0
$0	$0	$0	$30,000	$0	$0
$0	$0	$0	$29,266	$0	$0
$0	$28,951	$0	$0	$0	$0
$0	$0	$27,167	$0	$0	$0
$0	$25,800	$0	$0	$0	$0
$23,708	$0	$0	$0	$0	$0
$0	$0	$21,152	$0	$0	$0
$16,128	$0	$0	$0	$0	$0
$0	$16,014	$0	$0	$0	$0
$0	$0	$14,192	$0	$0	$0
$0	$12,136	$0	$0	$0	$0
$1,194	$0	$0	$0	$10,525	$0
$0	$0	$9,000	$0	$0	$0
$0	$0	$7,000	$0	$0	$0
$0	$0	$5,067	$0	$0	$0
$0	$1,719	$0	$2,490	$0	$0
$0	$0	$1,310	$0	$0	$0
$137,658,205	$67,771,567	$255,428,811	$95,172,788	$71,754,311	$48,870,641

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

Appendix 2

Prevously Reporting Funders Unresponsive in 2013

Brazilian Ministry of Health, Department of Science and Technology
Butantan Institute
Chinese Center for Disease Control and Prevention
Columbia Department for Science and Technology
Colombian Ministry of Social Protection
Consejo Nacional de Ciencia y Tecnología
Damien Foundation
Fundació Clínic per la Recerca Biomèdica
Global Fund to Fight AIDS, TB and Malaria
Irish Health Research Board
Mexican National Institute of Public Health
Pan American Health Organization
Public Health Agency of Canada
Swiss Agency for Development and Cooperation
Swiss National Science Foundation
Vakzine Projekt Management GmbH
Peruvian National Institute of Health
Wellington Medical Research Foundation

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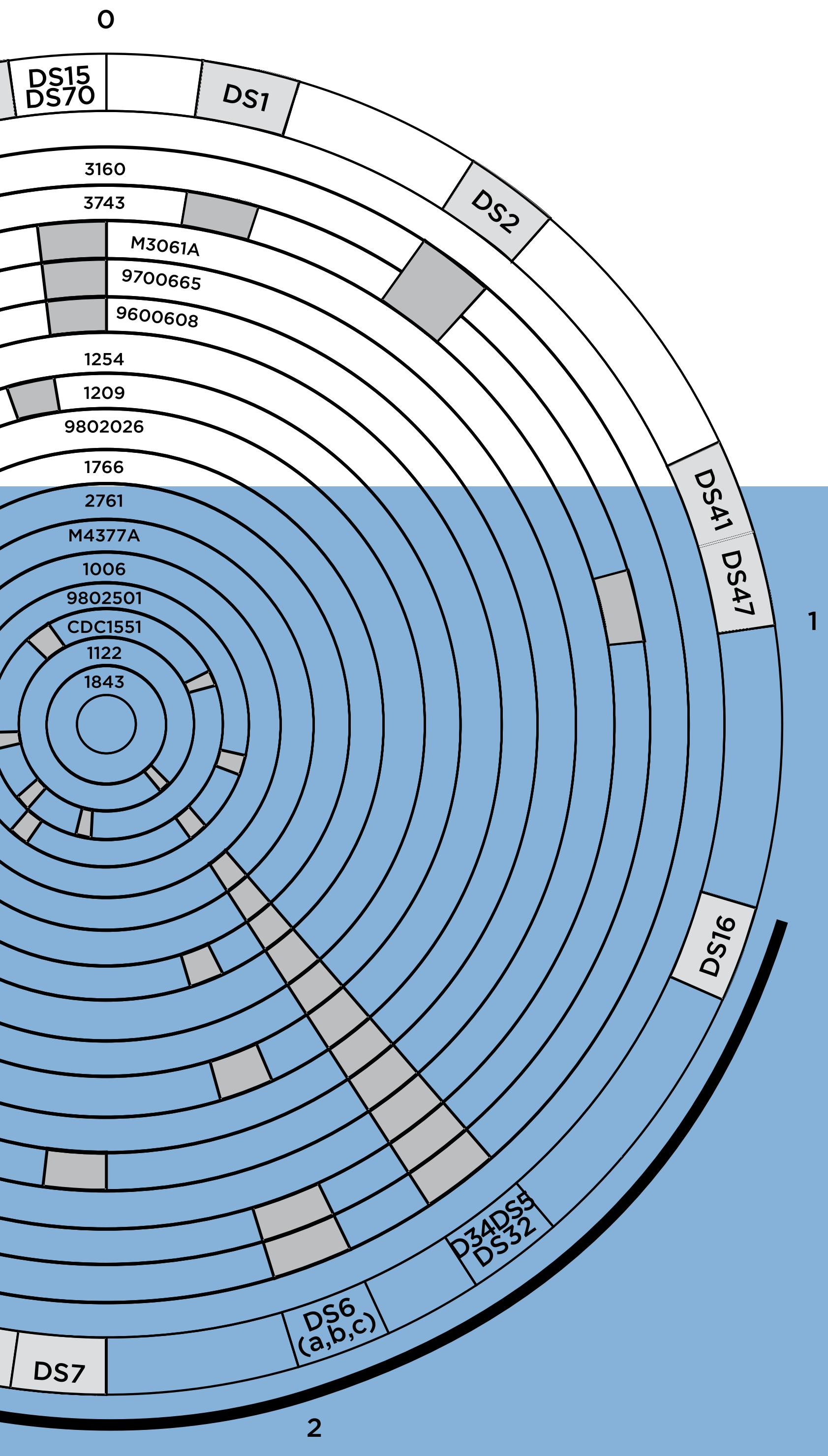

Treatment Action Group