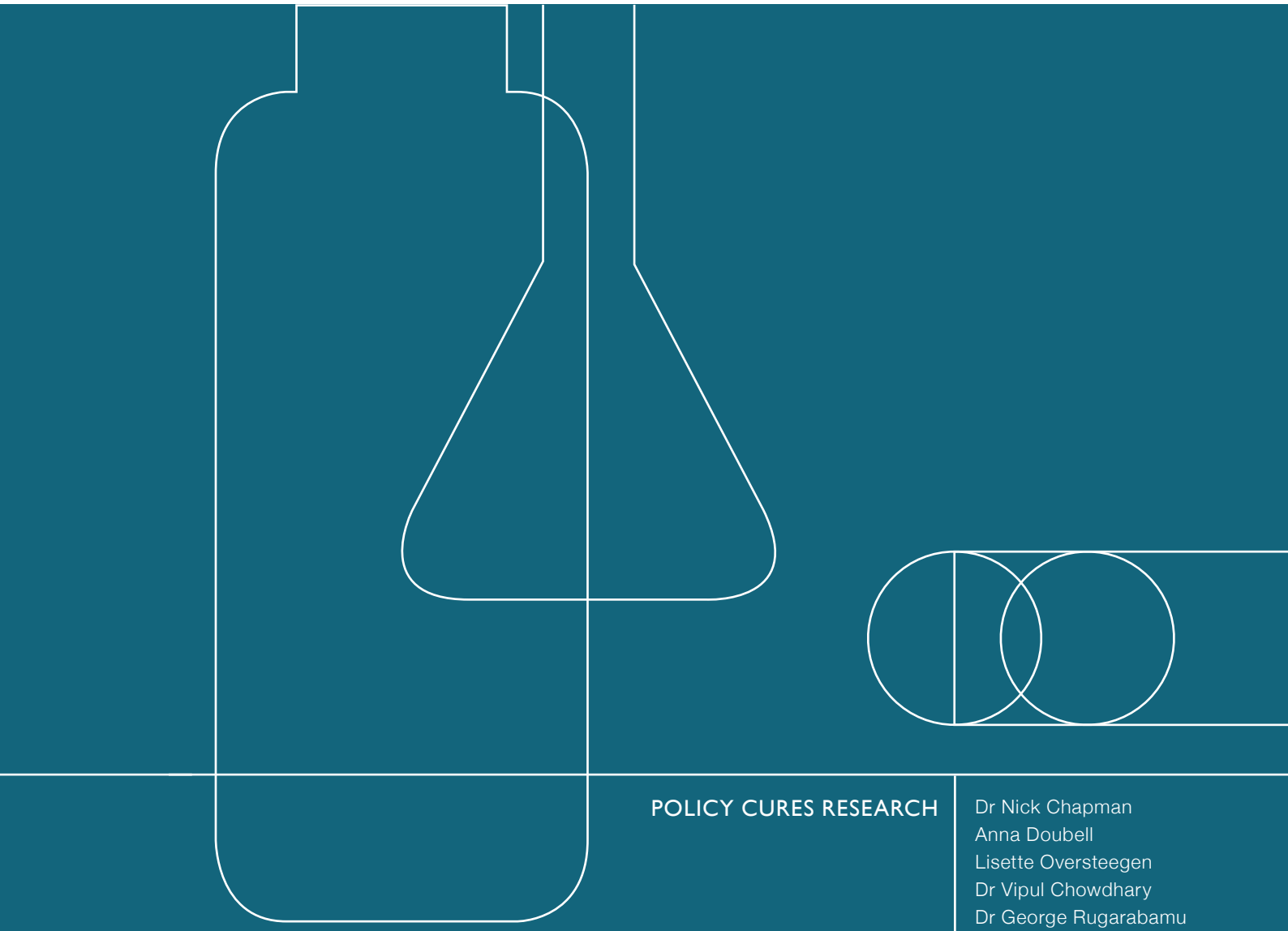
G-FINDER | 2017

POLICY CURES RESEARCH.

NEGLECTED DISEASE RESEARCH AND DEVELOPMENT: **REFLECTING ON A DECADE OF GLOBAL INVESTMENT**



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GLOSSARY

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ACT	Artemisinin-based combination therapy
Aggregate industry	Aggregate pharmaceutical and biotechnology companies
AIDS	Acquired Immune Deficiency Syndrome
AmB	Amphotericin B
ARV	Antiretroviral
Australia - India SRF	Australia - India Strategic Research Fund
Australian ACH^2	Australian Centre for HIV and Hepatitis Virology Research
Australian DFAT	Australian Department of Foreign Affairs and Trade (formerly AusAID)
Australian DIIS	Australian Department of Industry, Innovation and Science
Australian NHF	Australian National Heart Foundation
Australian NHMRC	Australian National Health and Medical Research Council
bNAbs	Broadly neutralising anti-HIV antibodies
Brazilian BNDES	Brazilian Development Bank
Brazilian DECIT	Brazilian Ministry of Health: Department of Science and Technology
Brazilian FAPEMIG	Brazilian Support Foundation for Research in the State of Minas Gerais
Brazilian FAPESP	State of São Paulo Research Foundation
Brazilian FINEP	Brazilian Innovation Agency
Canadian CIHR	Canadian Institutes of Health Research
Chilean FONDECYT	Chilean National Fund for Scientific and Technological Development
CLTRF	Cebu Leprosy and Tuberculosis Research Foundation
Colombian Colciencias	Colombian Department for Science, Technology and Innovation
CORDIS	Community Research and Development Information Service
DAA	Direct-acting antivirals
DAHW	German Leprosy and TB Relief Association
DALY	Disability adjusted life year
DND*i*	Drugs for Neglected Diseases initiative
Dutch DGIS	Dutch Ministry of Foreign Affairs - Directorate General of Development Cooperation
EAggEC	Enteroaggregative *E. coli*
EC	European Commission: Research Directorate-General
EDCTP	European & Developing Countries Clinical Trials Partnership
EID	Emerging infectious disease
EMA	European Medicines Agency
ETEC	Enterotoxigenic *E. coli*
EVI	European Vaccine Initiative
FIND	Foundation for Innovative New Diagnostics

GLOSSARY

Flemish EWI	Flemish Department of Economics, Science and Innovation
French ANR	French National Research Agency
French ANRS	French National Agency for Research on AIDS and Viral Hepatitis
French IRD	French Research Institute for Development
FY	Financial year
Gates Foundation	Bill & Melinda Gates Foundation
Gavi	Gavi, the Vaccine Alliance
GBD	Global Burden of Disease Study
GDP	Gross domestic product
German BMBF	German Federal Ministry of Education and Research
German DFG	German Research Foundation
G-FINDER	Global Funding of Innovation for Neglected Diseases
GHE	Global Health Estimates
GHIT Fund	Global Health Innovative Technology Fund
HCV	Hepatitis C virus
HIC	High-income country
HIV	Human immunodeficiency virus
IAVI	International AIDS Vaccine Initiative
IDC	Innovative developing country
IDRI	Infectious Disease Research Institute
IHME	Institute for Health Metrics and Evaluation
IMF	International Monetary Fund
Indian DBT	Indian Department of Biotechnology
Indian ICMR	Indian Council of Medical Research
IPM	International Partnership for Microbicides
IRS	Indoor residual spraying
ISGlobal	Barcelona Institute for Global Health
IVCC	Innovative Vector Control Consortium
IVI	International Vaccine Institute
LAMP	Loop-mediated isothermal amplification
LLIN	Long-lasting insecticide treated net
LMIC	Low- and middle-income country
LRI	Leprosy Research Initiative
MDR-TB	Multidrug-resistant tuberculosis
MIC	Middle-income country
MMV	Medicines for Malaria Venture
MNC	Multinational pharmaceutical company
MSF	Médecins Sans Frontières
New Zealand HRC	Health Research Council of New Zealand
NTS	Non-typhoidal *Salmonella enterica*
OAR	Office of AIDS Research
OECD	Organisation for Economic Cooperation and Development
OWH	OneWorld Health
PCV	Pneumococcal conjugate vaccine
PDP	Product development partnership
R&D	Research and development
RCDC	US NIH's Research, Condition and Disease Categorization Process
RDT	Rapid diagnostic test
RePORTER	US NIH's Research Portfolio Online Reporting Tools
RT-PCR	Reverse transcription polymerase chain reaction
S&T	Science and technology
SFI	Science Foundation Ireland

GLOSSARY

SME	Small pharmaceutical and biotechnology firms
South African DST	South African Department of Science and Technology
South African MRC	South African Medical Research Council
SSI	Statens Serum Institute
Swedish SIDA	Swedish International Development Agency
Swiss SDC	Swiss Agency for Development and Cooperation
Swiss SERI	Swiss State Secretariat for Education, Research and Innovation
Swiss SNSF	Swiss National Science Foundation
TB	Tuberculosis
TBVI	TuBerculosis Vaccine Initiative
Thailand GPO	Thailand Government Pharmaceutical Organisation
The Union	International Union Against Tuberculosis and Lung Disease
TLMI	The Leprosy Mission International
UK	United Kingdom
UK DFID	UK Department for International Development
UK MRC	UK Medical Research Council
US	United States
US BARDA	US Biomedical Advanced Research and Development Authority
US CDC	US Centers for Disease Control and Prevention
US DOD	US Department of Defense
US FDA	US Food and Drug Administration
US NIAID	US National Institute of Allergy and Infectious Diseases
US NIH	US National Institutes of Health
USAID	US Agency for International Development
VCP	Vector control product
VHF	Viral haemorrhagic fever
WHO	World Health Organization
WHO/TDR	World Health Organization Special Programme for Research and Training in Tropical Diseases
XDR-TB	Extensively drug-resistant tuberculosis
YOY	Year-on-year

EXECUTIVE SUMMARY

The survey

Each year since 2007, the G-FINDER project has provided policy-makers, donors, researchers and industry with a comprehensive analysis of global investment into research and development (R&D) of new products to prevent, diagnose, control or cure neglected diseases in developing countries. It provides an up-to-date analysis of how R&D investments are being allocated across diseases and product types, funding trends over time, and where the potential gaps lie.

This is the tenth annual G-FINDER report. In addition to the previous nine years of funding data, it reports on investments made in financial year 2016. In all, 187 organisations completed the survey for FY2016, which covered 33 neglected diseases and all relevant product types: drugs, vaccines (preventive and therapeutic), diagnostics, microbicides and vector control products (pesticides, biological control agents and vaccines targeting animal reservoirs) – as well as basic research.

In 2016, following a review by the G-FINDER Advisory Committee, the bacterial pneumonia & meningitis category was expanded to include developing country-focused basic research for both *Streptococcus pneumoniae* and/or *Neisseria meningitidis*. Developing country-specific research into therapeutic vaccines for HIV/AIDS was also added as a restricted category.

While included in the last two G-FINDER reports, analysis of R&D funding for African viral haemorrhagic fevers (including Ebola) was separated from the neglected disease funding analysis in 2016. A separate scope definition has been developed to identify investments in R&D for all priority emerging infectious diseases identified in the World Health Organization R&D Blueprint for action to prevent epidemics. EID data is not included in this G-FINDER neglected disease report, and will be reported separately.

Findings

In 2016, a reported $3,203m was invested in neglected disease R&D, consisting of $3,024m from repeat survey participants (called year-on-year – YOY – funders) and $179m from irregular survey participants. Total YOY funding for neglected disease R&D increased for the first time since 2012 (up $99m, 3.4%).

FUNDING BY DISEASE

Global funding for neglected disease R&D increased for the first time since 2012

As in previous years, three diseases – HIV/AIDS, malaria and tuberculosis (TB) – collectively received more than two-thirds ($2,247m, 70%) of all global funding for neglected disease R&D in 2016. Overall funding to this group of diseases increased slightly (up $60m, 2.9%), driven by increased investment in HIV/AIDS (up $83m, 8.3%). Funding for malaria increased modestly (up $13m, 2.5%), while investment in TB fell by $37m (down 6.8%).

Diseases in the second funding tier receive between 0.5% and 6.0% of total funding each year. This group includes diarrhoeal diseases, kinetoplastids, dengue, bacterial pneumonia & meningitis, *Salmonella* infections, helminths and hepatitis C (genotypes 4, 5 & 6). Funding for this tier was essentially unchanged from the previous year (up $0.9m, 0.2%). Only three second tier diseases saw funding increases in 2016: *Salmonella* infections (up $21m, 32%), kinetoplastids (up $12m, 12%) and dengue (up $8.4m, 8.7%). Funding fell for all other second tier diseases, with the largest drop being for diarrhoeal diseases (down $21m, -14%), followed by hepatitis C (down $12m, -36%), helminths (down $3.9m, -5.5%) and bacterial pneumonia & meningitis (down $3.1m, -3.8%). The most poorly funded neglected diseases covered by the G-FINDER survey – those in the third tier of funding – each receive less than 0.5% of global funding. This tier includes leprosy, cryptococcal meningitis, Buruli ulcer, leptospirosis, trachoma and rheumatic fever. In 2016, leprosy was the best-funded of these diseases ($11m, 0.3%), while rheumatic fever received less than any other neglected disease ($1.3m, <0.1%).

Non-disease-specific investment increased to $261m in 2016, an increase of $37m (up 17%). Core funding – non-earmarked funds given to organisations working on multiple neglected diseases – accounted for just over half ($136m, 52%) of all non-disease-specific investment in 2016, an increase of $15m (up 14%). Platform technologies – tools that can potentially be applied to a range of areas, but which are not yet focused on a specific product or disease – received $52m in 2016 (20% of all non-disease-specific funding); the largest investment ever reported for this area.

FUNDERS

All three sectors increased their funding for neglected disease R&D in 2016. This was the first increase in several years from both the public sector (up $49m, 2.6%) and the philanthropic sector (up $28m, 4.4%), while industry (up $22m, 5.3%) increased its investment for the fifth year in a row. The public sector remained the most significant source of neglected disease R&D funding in 2016, contributing just under two-thirds ($2,034m, 64%) of the global total. As in previous years, most public sector funding came from HIC governments and multilaterals ($1,951m, 96%).

The top three public funders in 2016 were the US, the UK and the European Commission (EC)[1], with the US contributing nearly three-quarters of all public investment in neglected disease R&D ($1,490m, 73%). The US also provided the largest increase in public funding (up $78m, 5.5%), followed by the Netherlands (up $18m, 447%) and the UK (up $9.3m, 10%). All of the notable decreases in public funding for neglected disease R&D in 2016 came from European funders. The most significant reduction came from the EC (down $49m, -39%), although this was largely linked to uneven disbursements to the European and Developing Countries Clinical Trials Partnership (EDCTP). Nearly two-thirds (59%) of all HIC government and multilateral funding went to basic and early stage research, with only a quarter (27%) going to clinical or field development and post registration studies.

The philanthropic sector provided $671m for neglected disease R&D in 2016, representing 21% of total global funding. The Gates Foundation and the Wellcome Trust collectively provided the vast majority ($642m, 96%) of all philanthropic funding, and both increased their investment in 2016 (up $12m, 2.3% and up $17m, 21%, respectively). A third (34%) of all philanthropic funding for neglected disease R&D was for basic and early stage research, most of which was for discovery and pre-clinical R&D, a quarter (26%) was for clinical or field development and post registration studies, and the remaining 40% was largely provided in a portfolio-based approach, to support product development from discovery through to registration.

[1] The term 'EC' refers to funding from the EU budget that is managed by the European Commission or related EU partnerships and initiatives, such as the European & Developing Countries Clinical Trials Partnership and Innovative Medicines Initiative

Two-thirds of funding to researchers and developers was for basic and early stage research

The private sector invested $497m in neglected disease R&D in 2016, accounting for 16% of total global funding. For the second year in a row, the increase in industry investment was entirely driven by small pharmaceutical and biotechnology firms (SMEs, up $23m, 30%). Most of this increase came from SMEs in innovative developing countries (IDCs), and was directed towards bacterial pneumonia & meningitis (up $10m, 43%) and *Salmonella* (up $9.4m, 86%). More than three-quarters of all SME investment was in clinical or field development and post registration studies ($82m, 78%), with most of the remainder invested in basic and early stage research ($16m, 15%).

FUNDING FLOWS

Almost three-quarters ($2,352m, 73%) of all neglected disease R&D funding in 2016 was external investment in the form of grants. Of this funding, 79% ($1,851m) went directly to researchers and developers, 18% ($420m) was for product development partnerships (PDPs), and the remaining $80m (3.4%) was channelled through other intermediary organisations. Direct YOY funding to researchers and developers increased for the first time since 2012 (up $147m, 9.1%), driven by both S&T agencies and philanthropic organisations. Funding to PDPs decreased by $29m (-6.8%), to the lowest level recorded in the history of the G-FINDER survey, although most of the drop in 2016 could be attributed to the highly cyclical nature of grant funding to PDPs, especially from the Gates Foundation. Funding to other intermediary organisations decreased by $23m (-25%), primarily due to lower funding from the EC to EDCTP.

Almost two-thirds (62%) of all funding given directly to researchers and developers went to basic and early stage research, with just 22% for clinical or field development and post registration studies. The very different pattern of funding given to PDPs reflects their product-development focus. More than two-fifths (42%) of all funding to PDPs was for clinical or field development and post registration studies, more than double the amount (19%) that was for basic and early stage research (essentially all of which was for discovery and pre-clinical R&D, rather than basic research).

Internal investment accounted for $851m (27%) of total neglected disease R&D funding. This was essentially steady (up $4.7m, 0.6%), with ongoing growth in industry investment (up $20m, 4.6%), particularly from SMEs, offset by internal investment by government agencies (down $19m, -5.1%). The allocation of internal investment depended on the type of organisation; where two-thirds (66%) of industry self-funding was for clinical or field development and post registration studies, non-industry self-funding was focused more on basic and early stage research (49%).

DISCUSSION

Global funding for neglected disease R&D increased for the first time since 2012, driven by an increase in funding from the US government

- Global funding for neglected disease R&D increased (up $99m, 3.4%) to $3,203m in 2016. This was the first increase in global funding since 2012, and was driven by increased investment from the US government (up $78m, 5.5%).
- The US government was not alone in increasing funding for neglected disease R&D in 2016. The philanthropic sector and the pharmaceutical industry (particularly SMEs) also increased their investment, as did the UK, Dutch and a number of non-European governments, which – in conjunction with the US government increase – was enough to result in an overall increase in public funding, despite lower investment from the EC and several other European governments.
- However, as the largest funder, the US government is the primary driver of changes in global funding for neglected disease R&D: every increase or decrease in US government funding over the last decade has been accompanied by a corresponding change in global investment.

An overreliance on US government funding is defining the shape of R&D for neglected diseases

- The US government's investment of $1,490m in 2016 was triple the combined investment of the rest of the world's governments, and fifteen times larger than that of the next biggest government funder (the UK, with $101m).
- 82% of all US government funding for neglected disease R&D in 2016 – and consequently 70% of all global funding – was for HIV/AIDS, TB and malaria.
- Excluding the quarter of a billion dollars the US government invested in HIV vaccine clinical trials in 2016, 80% of all remaining US government funding for neglected disease R&D – and 70% of all funding from HIC governments – was for basic and early stage research, compared to just 14% for clinical or field development and post registration studies.

The sustained growth in industry investment in neglected disease R&D – lately driven by SMEs – continues to be a good news story

- Industry investment in neglected disease R&D has increased in every one of the last five years, and reached new record highs in each of the last three years. Since 2008, reported industry investment has increased by nearly 50%, while funding from both the public and philanthropic sectors has fallen.
- The vast bulk of industry investment – and the majority of the increase in industry funding since 2008 – has come from MNCs. Since 2014 however, MNC investment has essentially plateaued, with annual increases of less than 1% in both 2015 and 2016.
- Increased investment by SMEs since 2012, particularly from those in India, has helped to sustain the growth of overall industry investment. Importantly, much of this investment growth has also been in new areas: two-thirds of all SME investment in 2016 was for bacterial pneumonia & meningitis, *Salmonella* infections and diarrhoeal diseases.

In addition to SMEs, a number of other funders have been making a small but growing contribution in areas of need

- A number of key global health initiatives – Unitaid, MSF and Gavi – have expanded their focus to include support for neglected disease R&D, particularly for clinical or field development and post registration studies.
- The Japanese government – along with Japanese pharmaceutical companies – is increasingly investing in neglected disease product development following the establishment of the GHIT Fund, recording its highest ever investment in 2016.
- Funding from LMIC governments grew by $18m (up 30%) in 2016, to $84m, with India becoming the fourth largest government funder of neglected disease R&D, ahead of both France and Germany.

Conclusion

The US government's contribution to neglected disease R&D funding is unparalleled. But an overreliance on US government funding is reflected in the heavy concentration of global funding on HIV/AIDS, malaria and TB, and the overwhelming focus of HIC government funding on basic and early stage research. The growth of non-traditional funders is promising, but their collective contribution is still just a fraction of overall global funding. And while Gates Foundation investment in product development has consistently been relied on to balance the public sector focus on basic research – it has provided 55% of all funding to PDPs and 47% of all funding for platform technologies over the last decade – this is again a reflection of overreliance on a single funder. The world can ill afford to keep relying on the US government and the Gates Foundation to provide two-thirds of all global funding for neglected disease R&D over the next ten years, as they have done for the last decade.

INTRODUCTION

Background to the G-FINDER survey

Each year since 2007, the G-FINDER project has provided policy-makers, donors, researchers and industry with a comprehensive analysis of global investment into research and development (R&D) of new products to prevent, diagnose, control or cure neglected diseases in developing countries. It provides an up-to-date analysis of how R&D investments are being allocated across diseases and product types, funding trends over time, and where the potential gaps lie. G-FINDER is the primary source of neglected disease R&D funding data for both the World Health Organization's (WHO) Global Observatory on Health R&D and Donor Tracker, and helps support the work of many other groups in the broader global health community.

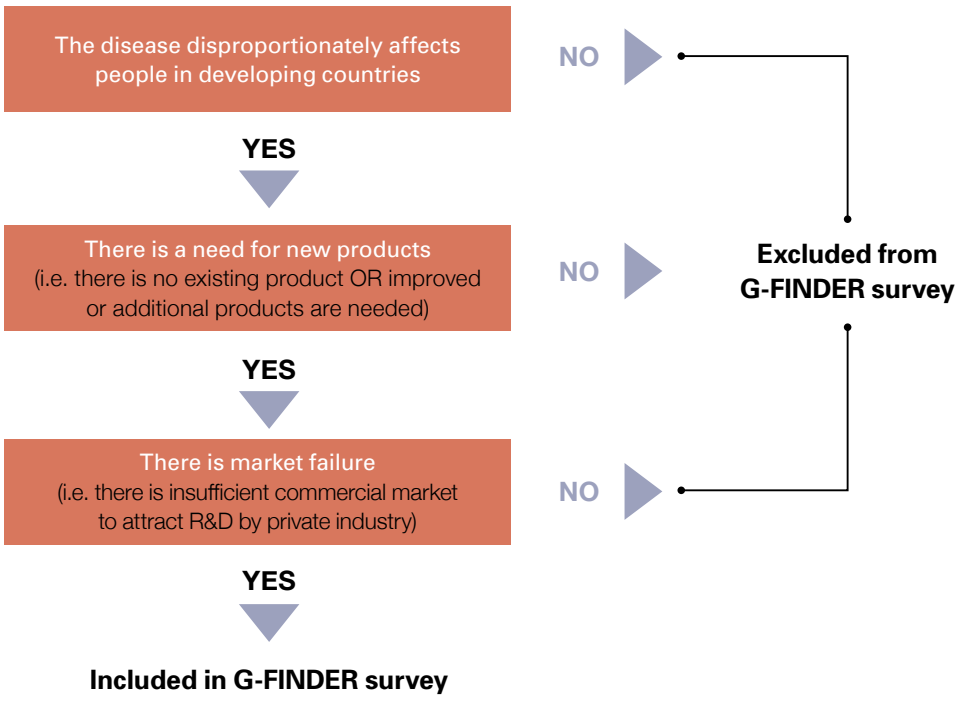
This is the tenth annual G-FINDER report; in addition to the previous nine years of funding data, it reports on investments made in financial year 2016, referred to as 2016 in the text.

The survey scope

DEFINING NEGLECTED DISEASES AND PRODUCTS

The scope of the G-FINDER survey is determined in consultation with the G-FINDER Advisory Committee, which is made up of a broad cross-section of international experts in neglected diseases and product development (see Annexe 1 for the list of current Advisory Committee members). When defining the G-FINDER scope at the project's inception, and at all subsequent reviews, three key criteria (see Figure 1) have been applied in order to establish a list of neglected diseases and products for which R&D would cease or wane if left to market forces.

Figure 1. Filter to determine G-FINDER inclusions



Although all relevant product types – drugs, vaccines (preventive and therapeutic), diagnostics, microbicides and vector control products (pesticides, biological control agents and vaccines targeting animal reservoirs) – as well as basic research were considered for all diseases, it is important to note that not all product types are included in the G-FINDER scope for all diseases, and some are included only with restrictions. For example, pneumonia drugs are excluded because there is a sufficient commercial market; while pneumonia vaccine investments are only included if they meet G-FINDER requirements for strain, vaccine type and target age group.

Platform technologies (adjuvants, diagnostic platforms and delivery devices) are also included in the scope of G-FINDER. Platform technologies can potentially be applied to a range of neglected diseases and products, but have not yet been attached to a specific product for a specific disease.

Investments that do not meet the G-FINDER scope are excluded from the results. This includes activities such as advocacy and behavioural research, which are important and critical to effect change, however are distinct from product development and fall outside the G-FINDER criteria.

A comprehensive explanation of all inclusions, exclusions and restrictions is outlined in the detailed G-FINDER R&D scope document, which is available online. A matrix summarising the neglected diseases, products and technologies included in this year's G-FINDER report is shown in Table 1.

CHANGES TO THE G-FINDER R&D SCOPE FOR NEGLECTED DISEASES

Although it is important to maintain a consistent scope in order to allow comparable, long-term analysis of multi-year R&D funding trends, the scope of the G-FINDER survey is reviewed annually in consultation with the Advisory Committee.

In year two of the G-FINDER survey (FY2008), the typhoid and paratyphoid fever disease category was expanded to include non-typhoidal *Salmonella enterica* (NTS) and multiple *Salmonella* infections, and R&D for lymphatic filariasis diagnostics was added.

In FY2013 (the seventh survey year), the survey was expanded to include three additional diseases: cryptococcal meningitis, hepatitis C (genotype 4) and leptospirosis. Dengue vaccines were determined to no longer fit the criteria for inclusion in the G-FINDER survey given the emergence of a commercial market, and dengue vaccine R&D funding (including all previously reported investment) was removed from the survey. All other dengue product areas were retained.

In FY2014 (the eighth survey year), the hepatitis C category was expanded to capture investment in R&D for two additional genotypes (genotypes 5 and 6) that disproportionately affect people in developing countries.

This year (FY2016, the tenth year of the survey), the bacterial pneumonia & meningitis category was expanded to include developing country-focused basic research for both *Streptococcus pneumoniae* (*S. pneumoniae*) and/or *Neisseria meningitidis* (*N. meningitidis*). Developing country-specific research into therapeutic vaccines for HIV/AIDS was also added as a restricted category, reflecting emerging research into broadly neutralising anti-HIV antibodies (bNAbs) and their potential use in developing countries.

Table 1. G-FINDER neglected diseases, products and technologies

Disease		Basic research	Drugs	Vaccines (preventive)	Vaccines (therapeutic)	Diagnostics	Microbicides	Vector control products
HIV/AIDS		Restricted	Restricted	✓	Restricted	✓	✓	-
Malaria	*P. falciparum*	✓	✓	✓	-	✓	-	✓
	P. vivax	✓	✓	✓	-	✓	-	✓
	Multiple and/or other malaria strains	✓	✓	✓	-	✓	-	✓
Tuberculosis		✓	✓	✓	✓	✓	-	-
Diarrhoeal diseases	Rotavirus	-	-	Restricted	-	-	-	-
	Shigella	✓	Restricted	✓	-	✓	-	-
	Cholera	✓	Restricted	✓	-	✓	-	-
	Cryptosporidium	✓	Restricted	✓	-	✓	-	-
	Enterotoxigenic *E. coli* (ETEC)	-	-	✓	-	✓	-	-
	Enteroaggregative *E. coli* (EAggEC)	-	-	✓	-	✓	-	-
	Giardia	-	-	-	-	✓	-	-
	Multiple diarrhoeal diseases	✓	Restricted	✓	-	✓	-	-
Kinetoplastids	Leishmaniasis	✓	✓	✓	✓	✓	-	-
	Sleeping sickness (HAT)	✓	✓	✓	-	✓	-	✓
	Chagas' disease	✓	✓	✓	✓	✓	-	✓
	Multiple kinetoplastid diseases	✓	✓	✓	✓	✓	-	✓
Dengue		✓	✓	-	-	✓	-	✓
Bacterial pneumonia & meningitis	*S. pneumoniae*	Restricted	-	Restricted	-	✓	-	-
	N. meningitidis	Restricted	-	Restricted	-	✓	-	-
	Both *S. pneumoniae* and *N. meningitidis*	Restricted	-	-	-	✓	-	-
***Salmonella* infections**	Typhoid and paratyphoid fever (*S.* Typhi, *S.* Paratyphi A)	✓	✓	✓	-	✓	-	-
	Non-typhoidal *S. enterica* (NTS)	✓	✓	✓	-	✓	-	-
	Multiple *Salmonella* infections	✓	✓	✓	-	✓	-	-
Helminth infections (worms & flukes)	Schistosomiasis (bilharziasis)	✓	✓	✓	-	✓	-	✓
	Lymphatic filariasis (elephantiasis)	✓	✓	-	-	✓	-	✓
	Onchocerciasis (river blindness)	✓	✓	✓	-	✓	-	✓
	Hookworm (ancylostomiasis & necatoriasis)	✓	✓	✓	-	-	-	-
	Tapeworm (taeniasis/cysticercosis)	✓	✓	-	-	-	-	✓
	Whipworm (trichuriasis)	✓	✓	-	-	-	-	-
	Strongyloidiasis & other intestinal roundworms	✓	✓	✓	-	✓	-	-
	Roundworm (ascariasis)	✓	✓	-	-	-	-	-
	Multiple helminth infections	✓	✓	✓	-	✓	-	✓
Hepatitis C (genotypes 4, 5 & 6)		-	Restricted	✓	-	✓	-	-
Leprosy		✓	✓	-	-	✓	-	-
Cryptococcal meningitis		-	✓	-	-	-	-	-
Buruli ulcer		✓	✓	✓	-	✓	-	-
Leptospirosis		-	-	-	-	Restricted	-	-
Trachoma		-	-	✓	-	✓	-	-
Rheumatic fever		-	-	✓	-	-	-	-

Other investment applicable to more than one neglected disease			
Platform technologies			Core funding of a multi-disease R&D organisation
General diagnostic platforms	Adjuvants and immunomodulators	Delivery technologies and devices	
Restricted	Restricted	Restricted	✓

HANDLING OF EMERGING INFECTIOUS DISEASES

In response to the 2014 West African Ebola epidemic, the FY2014 (year eight) G-FINDER survey scope was expanded to capture investments in Ebola R&D for diagnostics, drugs and preventive vaccines, as well as basic research. For FY2015 (year nine), the survey scope was further expanded to include other African viral haemorrhagic fevers (VHFs). In addition to Ebola, this new category allowed respondents to report R&D funding for Marburg and other African VHFs.

Because of the unique nature of the Ebola threat and global response, and its distorting effect on analysis of the R&D funding landscape for neglected diseases, R&D funding for Ebola and other African VHFs was analysed separately in the year nine G-FINDER report.

The separation of emerging infectious diseases (EIDs) and neglected diseases was formalised this year. For the FY2016 (year ten) survey, a separate scope definition was developed to identify investments in R&D for all priority EIDs identified in the WHO R&D Blueprint for action to prevent epidemics. EID data is not included in this G-FINDER neglected disease report, and will be reported separately.

TYPES OF RESEARCH INCLUDED

The purpose of G-FINDER is to track and analyse global investment in the research and development of new health technologies for neglected diseases. It does not, and is not intended to, capture investment in the entire spectrum of neglected disease research. There is a broad range of research activities that are extremely important for improving global health, but which are excluded from this report because they are not related to the development of new tools for neglected diseases, including health systems and operations/implementation research (for example, research into health systems or policy issues, or research into the programmatic delivery of non-product interventions, or existing health technologies), and sociological, behavioural and epidemiological research not related to the development of new health technologies. We also exclude investment into non-pharmaceutical tools such as untreated bed nets, or interventions such as circumcision. General therapies such as painkillers or nutritional supplements are excluded, as these investments cannot be ring-fenced to neglected disease treatment only. Investment that is not research-related is similarly excluded: although we recognise the vital importance of activities such as health programme delivery, advocacy, routine disease surveillance programmes, community education and general capacity building to address neglected diseases, investment in these activities falls outside the scope of G-FINDER.

G-FINDER quantifies neglected disease R&D investments into two overarching categories, each broken down into a number of further categories:

- Basic and early stage research, including:
  - Basic research
  - Product discovery and pre-clinical development
- Clinical and field development and post registration studies, including
  - Baseline epidemiology in preparation for product trials
  - Clinical or field product development
  - Phase IV/pharmacovigilance studies of new products

A detailed explanation of what types of R&D activities are included in each of these categories, as well as specific inclusions and exclusions related to the G-FINDER scope, is provided in the G-FINDER neglected disease R&D scope document.

Survey methodology

DATA COLLECTION

Over the past decade, the G-FINDER survey has operated according to two key principles: capturing and analysing data in a manner that is consistent and comparable across all funders and diseases; and presenting funding data that is as close as possible to 'real' investment figures.

G-FINDER was originally designed as an online survey. An online survey platform was developed to capture grant data and is still used by the majority of survey participants. An offline grant-based reporting tool is also available. Industry (pharmaceutical companies and biotechnology firms) investment in R&D is not grant-based, so the reporting tool has been tailored for these participants. Instead of grants, companies enter the number of staff working on neglected disease programmes, their salaries, and direct project costs related to these programmes. Companies are required to exclude 'soft figures' such as in-kind contributions and costs of capital.

For some organisations with very large datasets, the online survey and equivalent offline reporting tool are difficult to use. The G-FINDER team was therefore asked to use publicly available databases to identify the relevant funding. For the US National Institutes of Health (NIH), grants were collected using the Research Portfolio Online Reporting Tools (RePORTER) and the Research, Condition and Disease Categorization (RCDC) process. For the Biomedical Advanced Research and Development Authority (BARDA), funding information was identified using the international and domestic 'Project Maps' retrieved from the Medical Countermeasures website. Funding from the European Commission (EC)[^] was retrieved from the Community Research and Development Information Service (CORDIS) public database and Innovative Medicines Initiative's (IMI) online project list. Supplementary data was provided by the EC.

All participating organisations were asked to only include disbursements (or receipts), rather than commitments made but not yet disbursed. In general, only primary grant data was accepted; the only exception is in the case of data collection collaborations between G-FINDER and other R&D funding surveys, such as AVAC. Data from all sources was subject to verification using the same processes and inclusion criteria.

VALIDATION

All entries over $0.5m were verified against the inclusion criteria. Cross-checking was conducted using automated reconciliation reports – which match investments reported as disbursed by funders with investments reported as received by intermediaries and product developers – followed by manual grant-level review of the report outputs. Any discrepancies were resolved by contacting both groups to identify the correct figure. For grants from the US NIH, funding data was supplemented and cross-referenced with information received from the Office of AIDS Research (OAR) and the National Institute of Allergy and Infectious Diseases (NIAID).

UNSPECIFIED FUNDING

Around 2.3% ($73m) of funding was reported to the survey as 'unspecified', usually for multi-disease programmes where funds could not easily be apportioned by disease. A proportion of funding for some diseases was also 'unspecified', for instance, when funders reported a grant for research into tuberculosis (TB) basic research and drugs without apportioning funding to each product category. This means that reported funding for some diseases and products will be slightly lower than actual funding, with the difference being included as 'unspecified' funding.

[^] The term 'EC' used here and throughout the report refers to funding from the European Union budget that is managed by the European Commission or related European Union partnerships and initiatives, such as the European & Developing Countries Clinical Trials Partnership (EDCTP) and Innovative Medicines Initiative (IMI)

A further 4.2% ($136m) was given as core funding to R&D organisations that work in multiple disease areas, for example, the European & Developing Countries Clinical Trials Partnership (EDCTP) and the Foundation for Innovative New Diagnostics (FIND). As this funding could not be accurately allocated by disease it was reported as unallocated core funding. In cases where grants to a multi-disease organisation were earmarked for a specific disease or product, they were included under the specific disease-product area.

DATA AGGREGATION

All pharmaceutical industry funding data has been aggregated and anonymised for confidentiality purposes. Rather than being attributed to individual companies, pharmaceutical company investment is instead reported according to the type of company, with a distinction made between multinational pharmaceutical companies (MNCs) and small pharmaceutical and biotechnology companies (SMEs).

INFLATION ADJUSTMENTS

Funding data has been adjusted for inflation and converted to US dollars (US$) to eliminate artefactual effects caused by inflation and exchange rate fluctuations, allowing accurate comparison of annual changes. Due to these adjustments, historical G-FINDER data in tables and figures in this report will differ to data in previous G-FINDER reports. All funding data in this report is in 2016 US$.

LIMITATIONS

While the survey methodology has been refined over the past decade, there are limitations to the data presented, including survey non-completion, time lags in the funding process, an inability to disaggregate some investments, and non-comparable or missing data. Please see the G-FINDER methodology document, available online at www.policycuresresearch.org/g-finder-2017, for a more in-depth discussion of these limitations.

Reading the G-FINDER report

STRUCTURE

The G-FINDER report is structured in four main parts: 1) analysis of funding by neglected disease; 2) analysis of neglected disease funders; 3) analysis of funding flows; and 4) discussion of key findings.

YEARS

Throughout the text, references to years, other than survey years, refer to financial years.

YEAR-ON-YEAR CHANGES

It is important when comparing figures between survey years to distinguish between genuine changes in funding and apparent changes due to fluctuating numbers of survey participants. Therefore, to clearly demonstrate genuine funding changes, any increases or decreases in funding explicitly described in the report rely only on data from organisations that have participated in every year of the survey, referred to as 'year-on-year (YOY) funders'. New funding streams, for example the introduction of the Global Health Innovative Technology Fund (GHIT), are also included in YOY analysis. The YOY amounts reported may not always match the YOY amounts reported in previous years due to participation changes.

COUNTRY GROUPINGS

For brevity, we use the terms 'LMICs' and 'developing countries' to denote low- and middle-income countries and 'HICs' to denote high-income countries as defined by the World Bank.[1] Innovative developing countries (IDCs) are developing countries with a strong R&D base, which in the context of this report refers to Brazil, India and South Africa.

BURDEN OF DISEASE FIGURES

Estimating the burden of disease is a complex process, and estimates may differ substantially between sources depending on the data and methodology used. This report presents disease burden estimates from two key sources: the Institute for Health Metrics and Evaluation's (IHME) Global Burden of Disease Study 2015 (GBD 2015),[2] and the World Health Organization's Global Health Estimates 2015 (GHE 2015).[3] Estimates of mortality and disability-adjusted life years (DALYs) in LMICs from GBD 2015 are presented for all G-FINDER neglected diseases, where available. Estimates of global and LMIC mortality from GHE 2015 are also included, where available. We note some GBD 2015 estimates may differ from those published in previous G-FINDER reports due to updates to IHME's methodology.[4]

Pathogen specific diagnosis for diarrhoeal diseases, and bacterial pneumonia & meningitis is challenging, which affects estimates for burden of disease. The diarrhoeal disease group in GBD 2015 is presented by cause and includes diseases outside the scope of G-FINDER, and does not include estimates for Giardia. Therefore, estimates of mortality and DALYs for the diarrhoeal disease group presented in this report have been calculated by subtracting pathogens identified by aetiology as out of scope from the GBD 2015 diarrhoeal disease grouping by cause totals. GBD 2015 includes an 'Other meningitis' aetiology category that is not disaggregated to a level where it can be established what proportion of the data falls in or out of the scope of G-FINDER. Estimates of mortality and DALYs for bacterial pneumonia & meningitis presented in this report include 'Other meningitis', and may therefore include some burden of disease caused by pathogens outside the scope of G-FINDER. For helminth infections (worms and flukes), GBD 2015 figures presented in this report do not include estimates for strongyloidiasis.

The latest G-FINDER survey

The tenth G-FINDER survey was open for a seven-week period from June to July 2017. Intensive follow-up and support for key participants led to a total of 10,144 recorded entries in the database for financial year 2016. An overview of funding for G-FINDER neglected disease R&D from FY2016 is at Figure 2.

PARTICIPANTS

G-FINDER is primarily focused on funding, and therefore the emphasis is on surveying funding organisations. A total of 187 organisations participated in the G-FINDER survey in 2017, reporting on behalf of 194 organisations. 123 of the 187 direct participants were funders. A wide range of funding intermediaries, product development partnerships (PDPs), and researchers and developers who received funding also participated. Data from funding recipients was used to collect data on investments from funders who did not participate in the survey; to better understand how and where R&D investments were made; to track funding flows through the system; to prevent double counting; and to verify reported data.

Participants originated from 32 countries. Organisations included:

- Public, private and philanthropic funders from 21 HICs
- The EC
- Public funders in three IDCs (Brazil, India and South Africa)
- Public funders in an additional four MICs (Argentina, Colombia, Mexico and Thailand)
- Private sector funders in two MICs (Brazil and India)
- Academic organisations from six MICs.

ONLINE SEARCH TOOL

All of the data behind the G-FINDER report is available through the online search tool at **https://gfinder.policycuresresearch.org/PublicSearchTool**

Table 2. Disease and product R&D funding 2016 (US$ millions)

Disease or R&D area	Basic research	Drugs	Vaccines (preventive)	Vaccines (therapeutic)	Diagnostics	Microbicides	Vector control products	Unspecified	Total
HIV/AIDS	169.87	24.26	724.29	9.18	28.91	124.59		21.21	1,102.30
Malaria	138.90	218.11	115.54		20.53		59.89	23.42	576.40
P. falciparum	68.78	89.76	73.98		8.04		6.99	7.11	254.66
P. vivax	9.73	59.49	7.02		5.97		0.47	0.48	83.15
Multiple and/or other malaria strains	60.40	68.87	34.54		6.53		52.42	15.83	238.58
Tuberculosis	151.84	262.19	74.34	5.81	51.33			22.60	568.11
Diarrhoeal diseases	34.14	6.83	84.75		11.90			7.78	145.39
Rotavirus			37.94					0.92	38.86
Shigella	5.67	0.42	15.44		1.36			0.99	23.89
Cholera	15.19	0.54	6.46		1.10			0.07	23.37
Cryptosporidium	6.24	5.74	1.01		0.25			0.26	13.50
Enterotoxigenic *E. coli* (ETEC)			9.18		0.41			0.09	9.68
Enteroaggregative *E. coli* (EAggEC)			0.54		0.21			0.08	0.82
Giardia					0.02			0.12	0.14
Multiple diarrhoeal diseases	7.04	0.12	14.19		8.56			5.25	35.16
Kinetoplastids	50.30	61.10	6.40	2.00	4.70		0.78	5.88	131.17
Leishmaniasis	15.81	14.35	4.91	0.30	1.79			4.09	41.25
Sleeping sickness (HAT)	19.00	13.88	0.59		0.96		0.72	1.39	36.54
Chagas' disease	12.07	7.85	0.89	1.70	1.93		0.06	0.05	24.55
Multiple kinetoplastid diseases	3.43	25.02	0.01	-	0.02		-	0.35	28.82
Dengue	49.92	28.43			9.38		19.73	5.36	112.82
Bacterial pneumonia & meningitis	9.29		81.39		0.86			-	91.55
S. pneumoniae	7.52		57.87		0.71			-	66.10
N. meningitidis	0.98		23.52		0.07			-	24.58
Both *S. pneumoniae* and *N. meningitidis*	0.79				0.08			-	0.87
***Salmonella* infections**	45.49	3.77	36.84		4.22			1.14	91.46
Typhoid and paratyphoid fever (*S.* Typhi, *S.* Paratyphi A)	31.13	2.99	34.53		2.77			-	71.42
Non-typhoidal *S. enterica* (NTS)	2.96	0.48	0.41		0.81			-	4.66
Multiple *Salmonella* infections	11.40	0.30	1.91		0.64			1.14	15.38
Helminth infections (worms & flukes)	29.49	30.90	7.70		2.46		0.10	3.90	74.56
Schistosomiasis (bilharziasis)	10.13	2.90	2.24		1.45		0.07	1.58	18.37
Lymphatic filariasis (elephantiasis)	6.64	7.27			0.12		0.02	1.78	15.82
Onchocerciasis (river blindness)	1.31	7.36	0.45		0.65		0.02	0.48	10.25
Hookworm (ancylostomiasis & necatoriasis)	0.27	0.85	2.71					0.05	3.87
Tapeworm (taeniasis/cysticercosis)	1.76	1.85					-	-	3.61
Whipworm (trichuriasis)	0.87	0.94						-	1.81
Strongyloidiasis & other intestinal roundworms	0.68	0.47	<0.01		0.24			-	1.39
Roundworm (ascariasis)	0.83	0.45						-	1.28
Multiple helminth infections	7.01	8.82	2.30		-		-	0.02	18.15

Disease or R&D area	Basic research	Drugs	Vaccines (preventive)	Vaccines (therapeutic)	Diagnostics	Microbicides	Vector control products	Unspecified	Total
Hepatitis C (genotypes 4, 5 & 6)		11.92	3.47		6.95			0.03	22.37
Leprosy	6.57	0.18			0.39			3.91	11.06
Cryptococcal meningitis		5.64							5.64
Buruli ulcer	1.05	1.17	-		0.48			0.05	2.76
Leptospirosis					2.31				2.31
Trachoma			1.19		0.22			0.76	2.18
Rheumatic fever			1.18					0.10	1.28
Core funding of a multi-disease R&D organisation									135.99
Unspecified disease									73.18
Platform technologies	General diagnostic platforms			Adjuvants and immunomodulators			Delivery technologies and devices		
	18.30			17.68			16.23		52.21
Total R&D funding									**3,202.74**

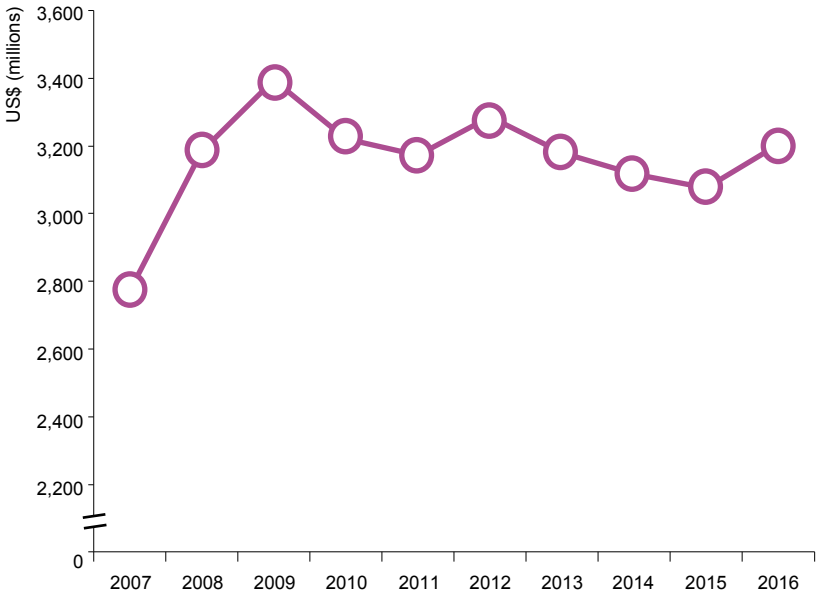
- No reported funding

Category not included in G-FINDER

FUNDING BY DISEASE

Global investment in R&D for neglected diseases in 2016 was $3,203m. Of this total, $3,024m was reported by regular survey participants (called year-on-year – YOY – funders), and the remaining $179m by irregular participants. YOY funding for neglected disease R&D increased for the first time since 2012 (up $99m, 3.4%).

Figure 2. Total R&D funding for neglected diseases 2007-2016



Neglected diseases can be grouped into three distinct tiers according to the amount of R&D funding that each disease receives annually (noting that this does not necessarily reflect the relative burden or funding need of each disease). HIV/AIDS, malaria and tuberculosis (TB) represent the 'top tier' of diseases based on the amount of funding received. These three diseases collectively accounted for more than two-thirds ($2,247m, 70%) of total global neglected disease R&D funding in 2016, with HIV/AIDS receiving 34%, and malaria and TB 18% each. Overall funding for top tier diseases increased slightly (up $60m, 2.9%), mainly due to an increased investment in HIV/AIDS (up $83m, 8.3%). Funding for malaria increased modestly (up $13m, 2.5%), while investment in TB fell by $37m (-6.8%).

'Second tier' diseases are those that receive between 0.5% and 6.0% of total funding. This group includes diarrhoeal diseases, kinetoplastids, dengue, bacterial pneumonia & meningitis, *Salmonella* infections, helminth infections and hepatitis C (genotypes 4, 5 & 6). Funding for second tier diseases represented one-fifth ($670m, 21%) of all neglected disease R&D funding in 2016, and total investment in this tier was essentially unchanged from the previous year (up $0.9m, 0.2%). Only three second tier diseases saw funding increases in 2016: *Salmonella* infections (up $21m, 32%), kinetoplastids (up $12m, 12%) and dengue (up $8.4m, 8.7%). Funding fell for all other second tier diseases, with the largest drop being for diarrhoeal diseases (down $21m, -14%), followed by hepatitis C (down $12m, -36%), helminths (down $3.9m, -5.5%) and bacterial pneumonia & meningitis (down $3.1m, -3.8%).

Table 3. R&D funding by disease 2007-2016^

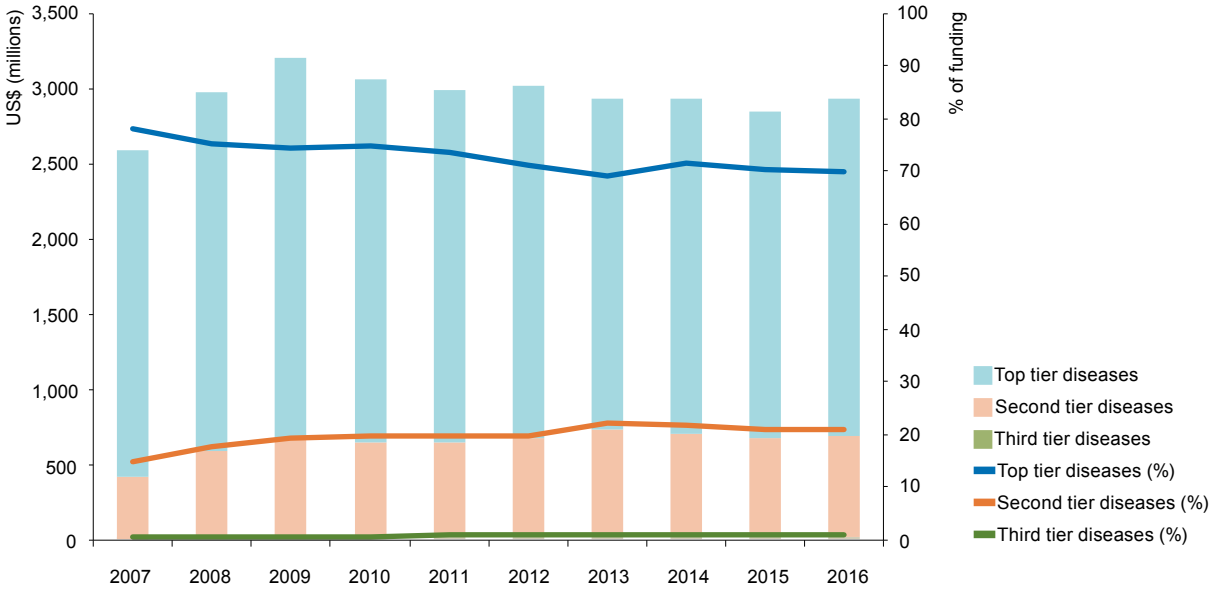
Disease or R&D area	US$ (millions)										2016 % of total
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	
HIV/AIDS	1,225	1,316	1,285	1,216	1,171	1,207	1,110	1,081	1,031	1,102	34.4
Malaria	492	585	641	567	590	577	531	577	563	576	18.0
Tuberculosis	452	495	605	622	577	553	564	569	576	568	17.7
Diarrhoeal diseases	128	149	204	177	167	169	200	175	161	145	4.5
Kinetoplastids	133	149	173	156	139	141	119	139	114	131	4.1
Dengue	51.5	52.7	79.9	68.7	79.3	79.8	76.0	85.9	101	113	3.5
Bacterial pneumonia & meningitis	33.0	99.9	75.1	102	106	110	102	74.8	93.3	91.5	2.9
Salmonella infections	10.4	44.5	44.2	48.8	48.3	58.1	65.5	66.1	69.1	91.5	2.9
Helminth infections (worms & flukes)	56.7	75.2	87.2	80.8	87.0	92.2	92.8	92.8	78.1	74.6	2.3
Hepatitis C (genotypes 4, 5 & 6)							47.3	45.4	34.1	22.4	0.7
Leprosy	6.2	10.9	11.9	10.3	8.9	15.1	12.9	10.7	11.0	11.1	0.3
Cryptococcal meningitis							3.1	5.6	5.6	5.6	0.2
Buruli ulcer	2.4	1.9	1.9	5.5	5.7	6.0	6.4	3.7	1.9	2.8	0.1
Leptospirosis							0.4	1.3	1.3	2.3	0.1
Trachoma	1.4	1.8	1.3	3.5	5.9	2.1	2.2	1.4	1.2	2.2	0.1
Rheumatic fever	1.9	2.5	3.4	2.0	0.9	1.0	0.9	1.3	2.3	1.3	<0.1
Platform technologies	9.8	17.8	24.6	30.6	18.2	50.6	44.7	22.8	33.7	52.2	1.6
General diagnostic platforms	5.2	5.9	9.9	10.6	10.6	17.4	16.9	9.8	13.8	18.3	0.6
Adjuvants and immunomodulators	2.6	2.6	5.6	10.3	5.8	28.3	21.7	8.6	12.2	17.7	0.6
Delivery technologies and devices	2.0	9.3	9.0	9.7	1.9	5.0	6.2	4.4	7.6	16.2	0.5
Core funding of a multi-disease R&D organisation	108	97.2	70.6	73.1	87.5	105	107	88.2	115	136	4.2
Unspecified disease	59.2	85.6	85.0	55.3	76.0	110	91.8	70.4	79.9	73.2	2.3
Total	2,771	3,185	3,393	3,219	3,168	3,277	3,177	3,112	3,073	3,203	100

New disease added to G-FINDER in 2013

^ Please note that some of the diseases listed are actually groups of diseases, such as the diarrhoeal illnesses and helminth infections. This reflects common practice and also the shared nature of research in some areas. For example, *Streptococcus pneumoniae* R&D is often targeted at both pneumonia and meningitis

The most poorly funded neglected diseases covered by the G-FINDER survey – those in the third tier of funding – each receive less than 0.5% of global funding. This tier includes leprosy, cryptococcal meningitis, Buruli ulcer, leptospirosis, trachoma and rheumatic fever. Total funding for this third tier made up just under one percent ($25m, 0.8%) of global investment, unchanged from 2015. Leprosy received the most funding of all third tier diseases ($11m, 0.3%) while rheumatic fever received the least ($1.3m, <0.1%). Due to the small numbers of funders and grants for each of these diseases in any given year, it is not possible to meaningfully comment on funding trends.

Figure 3. Funding distribution 2007-2016^



^ Percentages do not add to 100% because of non-disease specific and unclassified funding

Non-disease-specific R&D investment totalled $261m in 2016 (8.2% of global funding), with YOY funding for this category increasing by $37m (up 17%). Core funding accounted for just over half ($136m, 52%) of all non-disease-specific investment in 2016, and increased by $15m (up 14%). Notably, this increase occurred despite a significant drop in core funding from the EC (down $32m, -79%), which was the result of a number of extraordinary payments to EDCTP in 2015 that would otherwise have been made in 2014 and 2016. The largest increases in core funding came from the Wellcome Trust, with a nearly seven-fold increase (up $32m, 588%), largely to its own clinical research collaborations in LMICs; and the UK Department for International Development (DFID, up $6.2m, 34%), particularly to FIND and EDCTP.

Platform technologies – tools that can potentially be applied to a range of areas, but which are not yet focused on a specific product or disease – received $52m in 2016 (20% of all non-disease specific funding); the largest investment ever reported for this area. Funding for platform technologies was evenly distributed between diagnostic platforms ($18m, 35%), adjuvants and immunomodulators ($18m, 34%) and delivery technologies ($16m, 31%). Funding increased for all three areas: investment in delivery technologies rose by $8.6m (up 113%), almost entirely due to increased funding from the Gates Foundation (up $8.0m, 138%); investment in adjuvants and immunomodulators increased by $5.3m (up 44%), driven by the US NIH (up $6.9m, from a low base); and diagnostic platform investment rose slightly (up $3.8m, 29%), due to a $7.7m (138%) increase in Gates Foundation funding to SMEs.

HIV/AIDS

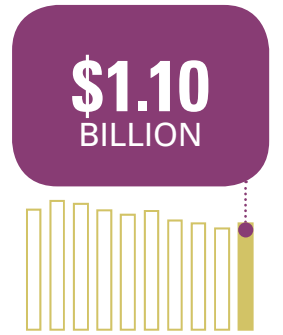
The Human Immunodeficiency Virus (HIV) attacks and destroys CD4 cells in the human immune system. Without treatment, HIV-infected individuals gradually become more susceptible to other diseases, and eventually develop the Acquired Immunodeficiency Syndrome (AIDS); people with AIDS often die from opportunistic infections like TB or cryptococcal meningitis, or cancers like Kaposi's sarcoma.[5]

According to the IHME Global Burden of Disease study, HIV/AIDS ranked as the second highest cause of mortality and morbidity of all the G-FINDER neglected diseases in 2015, causing 1.2 million deaths and 66 million DALYs in developing countries.[2] The WHO Global Health Estimates suggest a slightly lower mortality figure, estimating that HIV/AIDS was responsible for 1.1 million deaths in developing countries in 2015.[3]

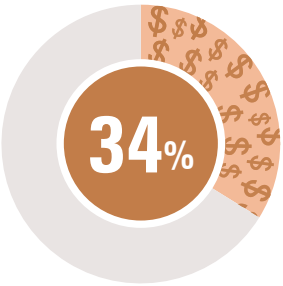
There is currently no vaccine against HIV, and the rapid mutation of the HIV virus has posed a significant challenge to vaccine development. The most advanced vaccine candidates to date demonstrated only modest efficacy in the RV144 Phase III clinical trials in 2009.[6] HVTN 702, a Phase IIb/III trial investigating a modified version of the RV144 vaccine regimen, started in South Africa in 2016.[7] There are several other preventive approaches in Phase I and II trials: NIAID's VRC01 candidate, currently in Phase IIb, is based on broadly neutralising anti-HIV antibodies (bNAbs), a new area of investigation for HIV vaccines.[8] bNAb-based approaches are also being investigated for use as therapeutic vaccines, which are designed to control HIV infection by boosting the body's natural immunity; developing country-specific therapeutic vaccine R&D was included in the G-FINDER scope for the first time this year. Several therapeutic vaccine candidates are in Phase I and II clinical trials, including plasmid and viral vector DNA vaccines, and bNAb immunotherapies.[9,10]

Commercially-driven R&D of antiretroviral (ARV) drugs is excluded from the G-FINDER scope; only R&D targeting the unmet needs of developing countries (for example, paediatric formulations or long-acting injectable drugs for PrEP) is included. The Drugs for Neglected Diseases initiative (DND*i*) is developing two '4-in-1' taste-masked fixed-dose formulations designed specifically for children which combine LPV/r with two NRTIs; these are currently in Phase I trials.[11] One long-acting injectable PrEP candidate, cabotegravir, is in Phase IIb/III trials.[12] Microbicides are preventive tools designed to block transmission of HIV through the vaginal and/or rectal mucosa; the International Partnership for Microbicides' (IPM) dapivirine ring has completed Phase III trials, and is currently undergoing regulatory review by the European Medicines Agency (EMA).[13]

Current methods for early diagnosis are often not adapted to, or suitable for, developing countries, especially for early infant diagnosis. There has been progress towards robust, simple, rapid point-of-care diagnostics, with several promising candidates in development. These include Alere's q HIV-1/2 Detect and Cepheid's Xpert HIV-1 Qual Assay, both of which are WHO prequalified for early infant diagnostic use and are currently undergoing field evaluations.[14]



TOTAL SPEND ON HIV/AIDS R&D IN 2016



OF GLOBAL R&D FUNDING

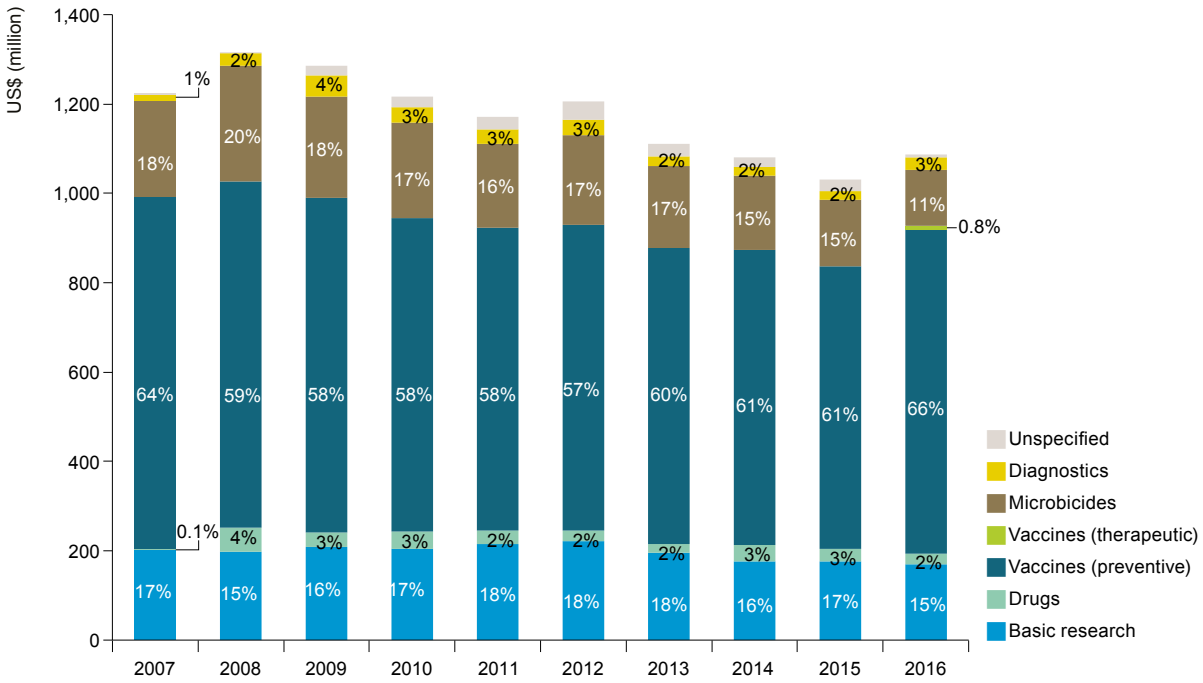
BASIC RESEARCH	RESTRICTED
DRUGS	RESTRICTED
VACCINES (PREVENTIVE)	IN SCOPE
VACCINES (THERAPEUTIC)	RESTRICTED
DIAGNOSTICS	IN SCOPE
VCPs	OUT OF SCOPE
MICROBICIDES	IN SCOPE

Global funding for HIV/AIDS R&D in 2016 was $1,102m. This was the most of any neglected disease, and represented one-third (34%) of all neglected disease R&D investment in 2016. Regular survey participants (YOY funders) increased their investment by $83m (up 8.3%) to $1,092m, ending a three year decline in HIV/AIDS funding and restoring investment to 2013 levels. Irregular participants provided the remaining $10m.

Around two-thirds of HIV/AIDS R&D funding in 2016 went to preventive vaccines ($724m, 66%), with most of the remainder going to basic research ($170m, 15%) and microbicides ($125m, 11%). Diagnostics ($29m, 2.6%) and developing country-focused drug R&D ($24m, 2.2%) each received relatively little funding in comparison. R&D for therapeutic vaccines specifically meeting developing country needs – a product category included for the first time in this year's G-FINDER report – received $9.2m (0.8%), mainly from the Gates Foundation.

There was a major funding increase for preventive vaccine R&D (up $97m, 16%), resulting in the largest investment in this product area since 2009, and its highest share of total HIV/AIDS R&D funding since the start of the survey. Almost all of this increase came from three sources: the US National Institutes of Health (NIH, up $35m, 8.2%), for the pre-clinical development of HIV vaccine candidates; and industry (up $27m, 65%) and the Gates Foundation (up $23m, 32%), for clinical trials. Diagnostics was the only other product area to receive more funding than last year (up $9.8m, 55%), due to increases from the US NIH (up $6.4m, 60%) and the Gates Foundation (up $4.4m, from a low base). In contrast, funding for microbicides fell to historically low levels (down $24m, -16%), with reduced investment by the two main funders of this area – the US NIH (down $12m, -12%) and the US Agency for International Development (USAID, down $11m, -37%) – reflecting the conclusion of Phase III trials for the dapivirine ring. Funding for drug development also fell (down $3.2m, -14%), while basic research investment remained essentially steady (down $1.9m, -1.1%).

Figure 4. HIV/AIDS R&D funding by product type 2007-2016



Just over half of all HIV/AIDS R&D funding in 2016 was for basic and early stage research ($559m, 51%), with most of the remainder going to clinical development and post registration studies ($455m, 41%). Other funding was not allocated to a specific product or R&D stage ($89m, 8.0%). The US NIH provided the vast majority of funding for discovery and pre-clinical R&D ($311m, 80% for this type of research), and more than half of the funding for clinical development and post registration studies ($253m, 56%). The sheer scale of US NIH investment in HIV/AIDS R&D defines the global funding landscape for this disease; the rest of the world actually invested more in HIV clinical trials and post registration studies ($203m, 52% of non-US NIH investment), than in basic and early stage research ($116m, 30%).

The top 12 funders in 2016 provided 97% of all funding for HIV/AIDS R&D, with the top three funders (the US NIH, the Gates Foundation and industry) providing 84% ($921m) of total investment. The US NIH alone provided just under two-thirds of all HIV/AIDS R&D funding ($710m, 64%), an increase of $31m (up 4.6%) compared to 2015, which was driven by increased funding for preventive vaccines (up $35m, 8.2%). Industry's strong growth (up $29m, 56%) earned it a place in the top three funders for the first time. After seven years of declining HIV/AIDS investments, the Gates Foundation increased funding (up $19m, 17%), primarily for preventive vaccine development through large grants to the International AIDS Vaccines Initiative (IAVI) and Fred Hutchinson. Funding increases from the Dutch Ministry of Foreign Affairs (DGIS), reflecting the launch of its PDP III fund, placed it in the top 12 funders list (up $7.7m, from a low base). Other funding increases came from the US Department of Defense (DOD) (up $6.3m, 22%, following last year's decrease), the Swedish Research Council (up $5.7m, from a low base, reflecting better reporting), and the EC (up $4.0m, 33%). USAID had the largest funding decrease (down $12m, -20%) reflecting the end of dapivirine Phase III trials and, as a result, it dropped out of the top three funders. The Wellcome Trust also decreased funding in 2016 (down $5.2m, -31%).

Table 4. Top HIV/AIDS R&D funders 2016

Funder / US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
US NIH	796	755	808	771	740	761	692	682	678	710	64
Gates Foundation	108	188	140	139	130	128	125	114	109	128	12
Aggregate industry	20	50	38	32	24	23	16	47	56	84	7.6
USAID	79	80	80	80	76	75	68	60	59	48	4.3
US DOD	33	29	40	37	49	54	57	64	29	35	3.2
EC	24	25	26	19	20	15	16	13	12	16	1.5
Wellcome Trust	5.8	8.2	8.2	9.6	14	23	19	21	17	11	1.0
Inserm	0.3	1.1	12	13	13	12	12	11	11	10	0.9
Dutch DGIS	12	8.2	6.7	3.6	5.6	3.7	7.2	5.9	1.3	8.9	0.8
Swedish Research Council		1.4	2.0	0.6	0.7	1.2	0.8	0.7	0.5	6.2	0.6
Canadian CIHR	3.2	1.8	5.1	8.1	7.6	7.3	7.7	7.8	6.2	6.2	0.6
German BMBF			-	2.4	0.9	1.6	2.1	1.9	3.7	5.9	0.5
Subtotal of top 12^	1,154	1,223	1,214	1,147	1,104	1,132	1,039	1,040	991	1,069	97
Disease total	1,225	1,316	1,285	1,216	1,171	1,207	1,110	1,081	1,031	1,102	100

^ Subtotals for 2007–2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016

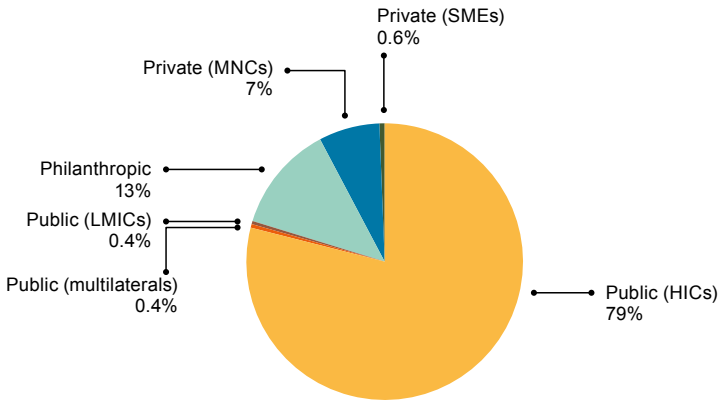
\- No reported funding

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

The public sector provided most HIV/AIDS R&D funding ($877m, 80%), of which $771m (88%) came from S&T agencies, and $65m (7.4%) from aid agencies. Almost all of public sector funding was from HICs ($869m, 99%), with most of this coming from the US NIH ($710m, 82%). The philanthropic sector provided $141m (13%) and industry invested $84m (7.6%), mostly from MNCs ($77m, 92% of industry funding).

YOY funding increased for all sectors. The largest increase came from public funders (up $40m, 4.9%), three-quarters of which was due to the US NIH. Industry investment increased (up $29m, 56%), continuing its rapid and sustained growth since 2013, driven entirely by increased investment from MNCs (up $30m, 62%). Following last year's historical low, the philanthropic sector increased funding in 2016 (up $14m, 11%).

Figure 5. HIV/AIDS R&D funding by sector 2016



A decade of investment in HIV/AIDS R&D

- Despite still receiving by far the most R&D funding of all the neglected diseases, HIV/AIDS is one of only three diseases to receive less funding in 2016 than it did in 2007 (the others being kinetoplastids and rheumatic fever). Global funding for HIV/AIDS R&D has steadily declined since its peak in 2008, with just two annual increases during this time (in 2012 and 2016, both driven by the US government). Notably, funding for microbicides halved over this period (from $259m in 2008 to $125m in 2016), with the failure of several late stage candidates prior to the regulatory submission (in 2017) of IPM's dapivirine ring.
- Nearly three-quarters ($8.6bn, 73%) of all global investment in HIV/AIDS R&D over the past decade came from the US government, a far higher proportion than in any other neglected disease. The vast majority of US government funding for HIV/AIDS came from the US NIH ($7.4bn, 86%), with the remainder largely from USAID ($704m, 8.2%) and the US DOD ($427m, 5.0%).
- The drop in funding for HIV/AIDS R&D over the last decade came entirely from the public sector, with philanthropic funding essentially steady, and industry investment increasing substantially (although still accounting for just 3.3% of all funding over the decade).

MALARIA

Malaria is a parasitic disease transmitted through the bite of an infected female *Anopheles* mosquito.[15] The two most common types of malaria are caused by *Plasmodium falciparum* and *Plasmodium vivax*. Left untreated, malaria can cause severe illness and death. Children and pregnant women are among the most vulnerable, with 70% of all malaria deaths occurring in children under five years of age.[15]

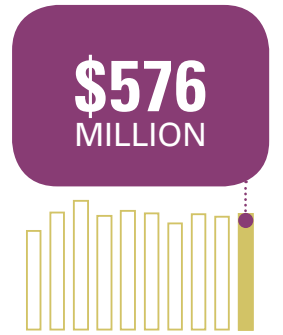
According to the IHME Global Burden of Disease study, malaria was the fifth highest cause of mortality and third highest cause of morbidity of all the G-FINDER neglected diseases in 2015, causing 730,290 deaths and 56 million DALYs in developing countries.[2] The WHO Global Health Estimates of mortality were lower, estimating that malaria was responsible for 439,025 deaths in developing countries in 2015.[3]

The most advanced malaria vaccine candidate, RTS,S, received a positive opinion from the EMA, with large-scale pilot implementations planned in three countries in 2018.[16] New vaccines are needed that have greater efficacy than RTS,S; provide protection against both P. *falciparum* and P. *vivax*; and can prevent transmission.[17] The next most advanced malaria vaccine candidate, Sanaria's PfSPZ, is currently in Phase II trials.[18,19]

Ten new malaria drugs have been approved since G-FINDER began in 2007,[20] including two artemisinin-based combination therapy (ACT) formulations designed specifically for children.[21,22] Nevertheless, new malaria drugs are needed in response to the emergence of resistance to ACTs. A number of promising drugs are in late stage development: tafenoquine, to prevent relapse of P. vivax malaria, has completed Phase III clinical trials;[23] artefenomel/ferroquine (previously OZ439/FQ), which has shown potential as a single-exposure, radical cure, is in Phase IIb trials;[24] and KAF156, also in Phase IIb trials, is the most advanced antimalarial candidate to come from a completely novel compound class.[25]

Cheap, sensitive and specific rapid diagnostic tests (RDTs) exist, although heat instability can be an issue in hot climates.[26] Improved, more sensitive diagnostics are needed to identify non-falciparum species; to distinguish malaria from other febrile illnesses; to detect asymptomatic cases; and to diagnose G6PD enzyme deficiency (key to safely treating P. vivax malaria).[26] Diagnostics in the pipeline include Alere's Malaria Ag P.f, which can detect asymptomatic infections and is undergoing field evaluations,[27] and PATH's point-of-care diagnostic for G6PD deficiency, currently in late development.[28]

Next-generation vector control products (VCPs) are urgently needed in response to emerging pyrethroid resistance. Currently, Syngenta's Actellic CS is the only non-pyrethroid-based indoor residual spraying (IRS) formulation;[29] BASF's chlorfenapyr (a crop protection ingredient being re-purposed for IRS) and next-generation long-lasting insecticide treated bed nets (LLINs) such as BASF's Interceptor G2 and Sumitomo's Olyset Duo are currently in development. Vector manipulation approaches to reduce mosquito fertility are also being investigated, including a sterile insect technique and *Wolbachia*-infected mosquitoes.[30]



TOTAL SPEND ON MALARIA R&D IN 2016

OF GLOBAL R&D FUNDING

BASIC RESEARCH	IN SCOPE
DRUGS	IN SCOPE
VACCINES (PREVENTIVE)	IN SCOPE
VACCINES (THERAPEUTIC)	OUT OF SCOPE
DIAGNOSTICS	IN SCOPE
VCPs	IN SCOPE

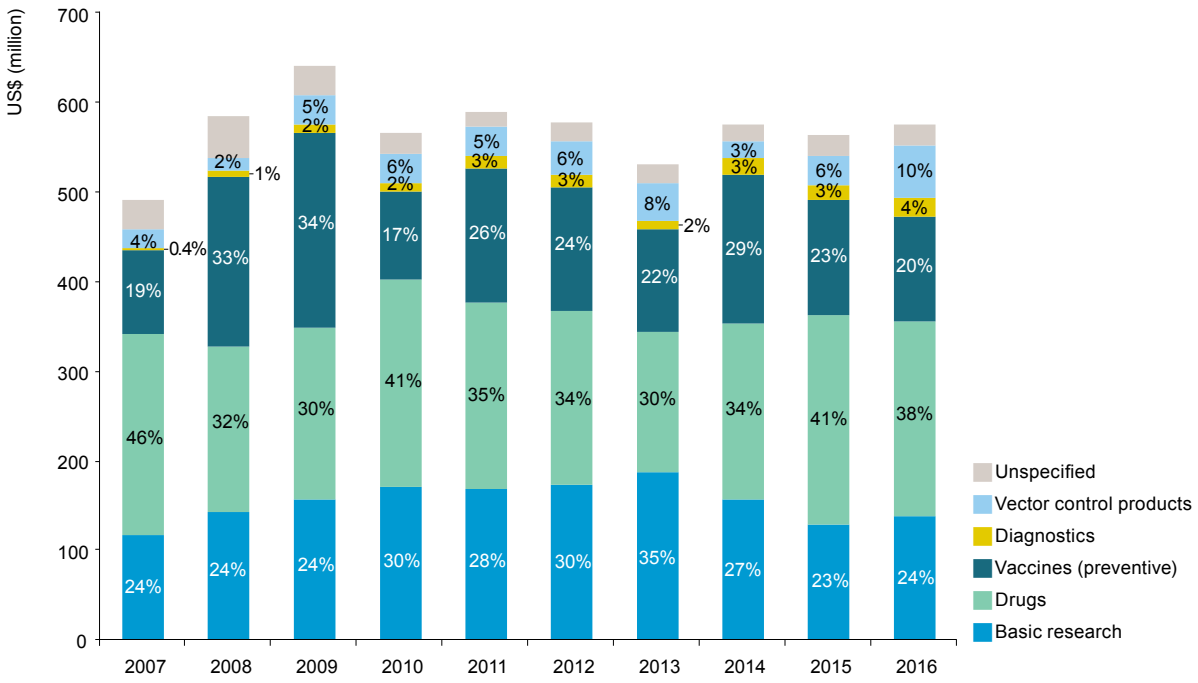
Global funding for malaria R&D in 2016 was $576m, making it the second-highest funded neglected disease once again (after having lost this position to TB in 2015). Investment by regular survey participants (YOY funders) increased by $13m (up 2.5%), with irregular survey participants reporting the remaining $24m.

More than a third of all malaria R&D funding in 2016 was for the development of new drugs ($218m, 38%), followed by basic research ($139m, 24%) and vaccine development ($116m, 20%). Vector control product R&D received $60m (10%) and malaria diagnostics $21m (3.6%).

The largest increase in funding was for vector control products (up $28m, 97%). This near-doubling, which took investment in vector control products for malaria to the highest level ever recorded in the G-FINDER survey, was entirely due to the Gates Foundation almost tripling its funding for this area (up $30m, 193%). This came as the Foundation increased its funding to the Innovative Vector Control Consortium (IVCC) for the second year in a row (up $17m, 156%), and started funding Imperial College London for the first time ($13m in 2016). After declining over the previous two years, investment in basic research increased modestly in 2016 (up $7.3m, 5.9%). Malaria diagnostics was the only other area to receive increased funding (up $3.8m, up 28%), which came from various organisations, including the US NIH (up $1.9m, 75%) and the Gates Foundation (up $1.4m, 17%, mostly towards PDPs). The increase resulted in malaria diagnostics also receiving the largest investment in this area ever recorded in the history of the G-FINDER survey, although this remains a small proportion of overall malaria R&D investment.

Funding for malaria vaccines decreased by $15m (-12%), largely driven by two funders: the Gates Foundation (down $6.5m, -35%), reflecting the progression of RTS,S; and industry (down $5.8m, -15%), whose investment in malaria vaccine discovery programmes was lower than in previous years. Funding for drug development decreased by $11m (-5.1%), after two years of successive increases, partially due to cyclical funding from the Gates Foundation to the Medicines for Malaria Venture (MMV, down $13m, -27%). Industry investment in malaria drugs was essentially steady (up $0.7m, -0.7%), following two years of rapid growth.

Figure 6. Malaria R&D funding by product type 2007-2016



Just under half of all malaria R&D funding in 2016 was for basic and early stage research ($259m, 45%), with a further third going to clinical or field development and post registration studies ($184m, 32%). The remainder ($133m, 23%) was not allocated to a specific product or R&D stage.

The top 12 funders of malaria R&D in 2016 provided 92% of all funding, with the top three funders – the US NIH, the Gates Foundation and industry – collectively accounting for three-quarters ($428m, 74%) of total funding.

Six of the top 12 funders increased their investment in 2016, most notably the Gates Foundation (up $15m, 13%), predominantly for vector control products, followed by the US NIH (up $5.9m, 3.7%), the UK Medical Research Council (MRC, up $2.5m, 30%, from historically low levels in 2015) and the Indian Council of Medical Research (ICMR, up $1.2m, 15%). Inserm (up $0.8m, 16%) re-entered the top 12 funders list for the first time since 2012. The largest reductions in funding came from Unitaid (down $3.1m, -42%), which dropped out of the top 12 due to reduced funding to MMV, likely reflecting the end of studies to support WHO prequalification of rectal artesunate, and the EC (down $6.1m, -43%).

Table 5. Top malaria R&D funders 2016

Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
US NIH	99	123	136	156	143	177	144	153	160	166	29
Aggregate industry	83	85	96	115	93	106	76	118	142	137	24
Gates Foundation	146	204	213	102	170	135	125	146	110	125	22
US DOD	39	36	44	27	21	11	23	19	30	29	5.0
Wellcome Trust	24	23	24	29	27	27	24	22	17	14	2.4
UK DFID	3.4	3.3	3.2	20	18	5.7	25	18	17	12	2.1
UK MRC	16	17	18	19	17	16	16	14	8.2	11	1.9
Indian ICMR		10	7.0	5.0	5.1	6.7	7.5	7.0	7.8	9.0	1.6
USAID	11	9.6	9.6	10	9.1	12	6.6	5.6	9.3	8.7	1.5
EC	20	23	23	23	20	13	20	19	14	8.3	1.4
German BMBF	0.8	0.6	1.6	1.6	2.0	2.6	2.8	3.3	5.8	6.9	1.2
Inserm	0.4	0.4	3.3	4.2	4.7	5.9	5.8	3.8	4.9	5.7	1.0
Subtotal of top 12^	467	551	593	525	542	531	487	541	528	533	92
Disease total	492	585	641	567	590	577	531	577	563	576	100

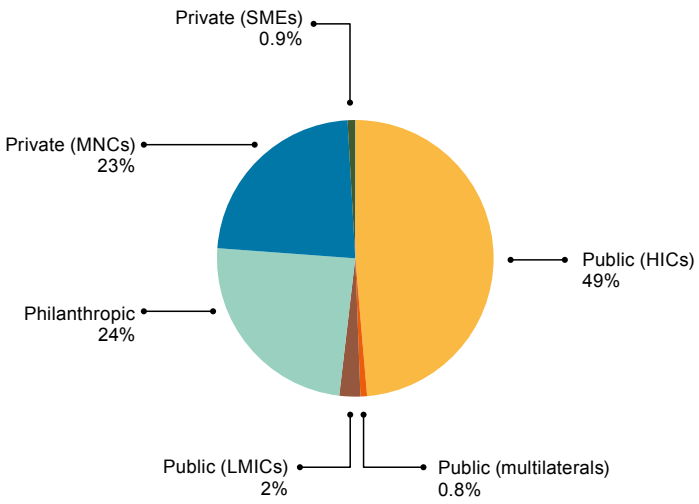
^ Subtotals for 2007-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

Public funders continued to provide more than half of all malaria funding in 2016 ($299m, 52%). The vast majority of public sector funding came from HICs ($280m, 94%), with $166m (59% of total HIC funding) coming from the US NIH. Non-public sector funding for malaria R&D was split almost equally between the philanthropic sector ($140m, 24%) and industry ($137m, 24%). This was a change from 2015, when industry investment in malaria R&D surpassed that of the philanthropic sector for the first time in the history of the G-FINDER survey.

Philanthropic sector funding increased by $12m (up 9.6%), entirely due to increased investment from the Gates Foundation. Public sector funding also increased (up $6.2m, 2.2%), driven by the US NIH across all products. Industry funding dropped its investment slightly (down $5.1m, -3.8%), primarily for vaccine R&D.

Figure 7. Malaria R&D funding by sector 2016



A decade of investment in malaria R&D

- Annual global funding for malaria R&D peaked at $641m in 2009, but since then has been essentially steady within the range of $550-600m per year (although dropping to $531m in 2013). Changes in annual funding have reflected the progression of the R&D pipeline, with a spike in vaccine R&D funding in 2008-2009 related to RTS,S clinical trials, and a subsequent sharp drop. Funding for malaria drug R&D had peaks in 2010 and 2015-2016, with the latter peak reflecting an increased focus on clinical development (which accounted for 40% of total drug funding in 2016, up from 23% in 2007), as product candidates advanced through clinical trials.
- Almost a quarter ($1,287m, 23%) of all malaria funding over the past decade went to PDPs – the equal highest share (with diarrhoeal diseases) of all neglected diseases. Nearly three-quarters (72%) of this PDP funding came from the Gates Foundation.
- The Gates Foundation has been a major contributor to malaria R&D, although its share of annual global funding has fallen from a peak of 35% in 2008 to 22% in 2016. The Foundation was responsible for more than two-thirds ($217m, 69%) of all funding for malaria vector control products over the past ten years, and was the main driver for the record investment in this area ($46m) in 2016. Diagnostic R&D investments were also largely shaped by funding from the Gates Foundation, which provided 43% of all funding for this area over the past decade.

TUBERCULOSIS

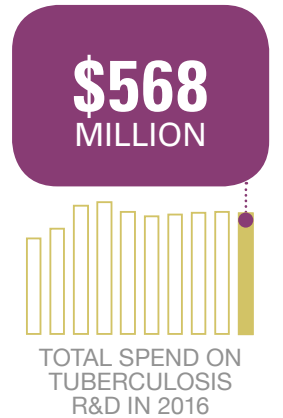
Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, most commonly affects the lungs and is spread via air droplets.[31] Most TB cases are latent and non-infectious, but around 5-15% will progress to active TB if left untreated. Active TB usually causes coughing, fever and weight loss, and is highly infectious.[31] TB is especially dangerous for people with low immunity, and is a leading cause of death among people with HIV/AIDS.

According to the IHME Global Burden of Disease study, TB ranked as the third highest cause of mortality and the fifth highest cause of morbidity of all the G-FINDER neglected diseases in 2015, causing 1.1 million deaths and 40 million DALYs in developing countries.[2] The WHO Global Health Estimates suggest an even higher mortality figure, estimating that TB was responsible for 1.4 million deaths in developing countries in 2015.[3]

Current TB drug regimens are complex and require up to two years of daily treatment, leading to poor compliance, drug resistance and treatment failure. New drugs are needed that act more rapidly, are effective against multidrug-resistant or extensively drug-resistant TB (MDR-TB and XDR-TB), and are safe to use in conjunction with HIV treatments. The world's first fixed-dose combination treatments specifically designed for children, HRZ/HR, were rolled out in over 30 countries in 2016.[32] Two new drugs (delamanid and bedaquiline) have been approved for treatment for MDR-TB under programmatic conditions in several countries, and both drugs were added to the WHO Essential Medicine List in 2015.[33] Despite progress, routine use of these two drugs in high-burden countries remains limited.[34,35] Another novel drug (pretomanid) is being tested in different combinations: TB Alliance's BPaMZ regimen trial is in Phase III,[36] and Médecins Sans Frontières (MSF) is conducting TB-PRACTECAL Phase II/III trials.[37] Sutezolid, now licenced by the Medicines Patent Pool, will be trialled in combination with other TB drugs by the TB Alliance.[38]

The only available TB vaccine, BCG, was developed over 90 years ago. While highly effective against disseminated TB in children, a new safe and more effective vaccine is needed that prevents the progression to active TB for adults.[39] Several candidates are in clinical development, mostly targeting the same antigens as the existing vaccine.[40] VPM1002, specifically developed for infants in endemic areas, is currently in Phase II trials.[37] A Phase IIb trial of M72+AS01E in adults is underway, after Phase II trials found it to be safe for use in infants.[41]

There is a need for more effective and appropriate point-of-care TB tests,[40] tests to diagnose TB in children, and tests for drug resistance and susceptibility.[37] Cepheid's Xpert MTB/RIF diagnostic platform was a major advance, however cost remains a barrier to access despite discounts offered to developing countries.[42] Cepheid's Xpert Ultra, a more sensitive cartridge-based assay, was endorsed by the WHO in 2017,[37] and its GeneXpert Omni point-of-care molecular diagnostic system is expected to undergo field evaluation in 2018.[43] The WHO recently recommended use of a number of newly-developed diagnostics, including initial tests to detect resistance to first- and second-line anti-TB drugs, and a replacement for microscopy of pulmonary TB in adults.[44]



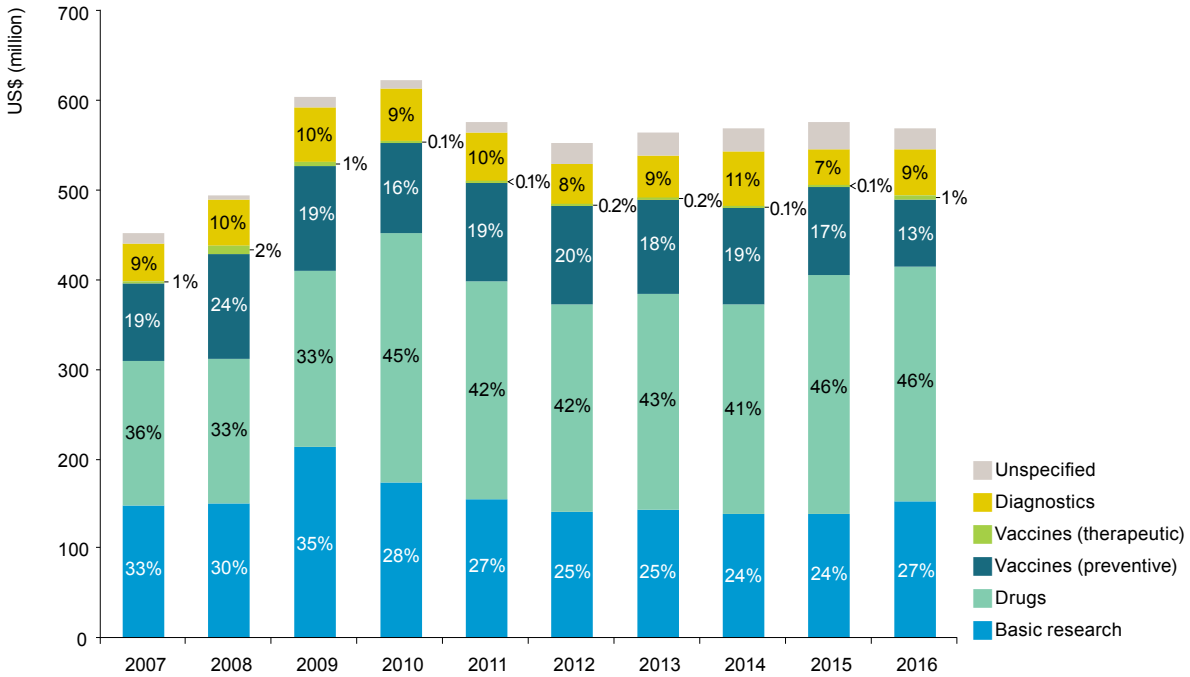
BASIC RESEARCH	IN SCOPE
DRUGS	IN SCOPE
VACCINES (PREVENTIVE)	IN SCOPE
VACCINES (THERAPEUTIC)	IN SCOPE
DIAGNOSTICS	IN SCOPE
VCPs	OUT OF SCOPE

Global funding for TB R&D in 2016 was $568m, making it the third-highest funded neglected disease by a small margin (just behind malaria). Of this total, $508m was from regular survey participants (YOY funders), with irregular survey participants providing the remaining $60m. YOY funding for TB R&D fell by $37m (-6.8%), completely reversing the increase in funding over the preceding three years, and reducing YOY funding to the lowest level since 2008. However this drop in YOY funding does not take into account a $26m increase in funding from Unitaid, which (as a relatively new funder of R&D) is not included in the G-FINDER group of YOY funders. If the Unitaid funding increase is included, the drop in YOY investment for TB would have been considerably smaller (down $10m, -1.9%).

Similarly to previous years, almost half of TB R&D funding in 2016 was for drugs ($262m, 46%), followed by basic research ($152m, 27%), preventive vaccines ($74m, 13%), diagnostics ($51m, 9.0%) and therapeutic vaccines ($5.8m, 1.0%).

Funding for TB drug R&D fell by $33m (-13%) in 2016, almost entirely due to a reduction in Gates Foundation funding to the TB Alliance (down $31m, -68%), associated with the start of a new project cycle; although again, if Unitaid's investment is included the decrease would have been much smaller (down $6.8m, -2.6%). Preventive vaccine investment fell by over a quarter to $74m (down $26m, -28%), to the lowest level ever recorded by the G-FINDER survey. This was in large part due to a halving of industry investment in preventive vaccine R&D (down $11m, -51%), with two candidates approaching the end of Phase II clinical trials, as well as reduced funding from the Gates Foundation (down $8.1m, -20%) and the US NIH (down $4.8m, -31%). These two organisations did however increase their funding of other product areas: the increase in funding for diagnostics (up $12m, 36%) was driven by increased investment in this area by the Gates Foundation (up $11m, 434%); and the increase for basic research (up $11m, 8.5%) was a result of increased investment by the US NIH (up $11m, 12%). Therapeutic vaccine investment increased by $5.6m, after almost no investment in this area in 2015.

Figure 8. TB R&D funding by product type 2007-2016



More than half of all TB R&D funding in 2016 ($329m, 58%) was for basic and early stage research; a further $181m (32%) went towards clinical development and post registration studies, and $58m (10%) was not allocated to a specific product or R&D stage. However, the focus for each product was slightly different, with just under half of all funding for drug R&D going to clinical development ($128m, 49%), while the vast majority of R&D investment in therapeutic vaccines was for the discovery and pre-clinical stages (5.3m, 91%), reflecting the very different state of the R&D pipeline in these two areas.

The top 12 funders provided 92% of total funding for TB R&D, unchanged from 2015. The top three funders collectively contributed just under three quarters of total funding ($404m, 71%): the US NIH invested $210m (37%), the Gates Foundation $99m (17%), and industry $96m (17%).

The largest increase in funding was from Unitaid (up $26m, from a low base), attributable to a large grant to Partners In Health for the endTB project. Smaller increases came from the US NIH (up $9.6m, 4.8%), the Indian ICMR (up $3.9m, 49%) and the German Federal Ministry of Education and Research (BMBF, up $2.6m, 40%). Investment from the Gates Foundation fell significantly (down $33m, -25%), largely reflecting reduced funding to the TB Alliance related to the transition to a new project cycle. Industry investment also fell (down $8.3m, -8.9%), extending the decline in industry investment in TB R&D since 2010. The US Center for Disease Control and Prevention (CDC) dropped out of the top 12, with no reported disbursements to the TB Trials Consortium in 2016.

Table 6. Top TB R&D funders 2016

Funder / US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
US NIH	143	132	192	184	178	186	172	192	200	210	37
Gates Foundation	136	155	114	120	101	106	131	137	132	99	17
Aggregate industry	71	96	136	168	162	140	116	107	104	96	17
Unitaid			6.9			0.4	2.0	0.5	6.1	33	5.7
EC	20	26	28	21	18	11	18	15	22	18	3.1
USAID	4.6	7.7	9.6	9.8	9.6	10	8.9	13	13	16	2.8
Indian ICMR		1.0	2.2	3.5	3.5	6.9	8.3	8.3	8.0	12	2.1
German BMBF	4.1	0.4	4.6	4.0	3.7	4.7	4.8	5.7	6.5	9.1	1.6
UK MRC	11	11	11	13	13	13	11	9.5	7.1	9.1	1.6
Wellcome Trust	2.2	4.8	7.3	11	11	12	12	11	9.6	8.8	1.6
UK DFID	1.5	2.9	15	19	11	1.4	13	14	12	7.6	1.3
Inserm	0.3	0.4	5.4	<0.1	3.0	3.7	5.1	2.6	3.9	5.0	0.9
Subtotal of top 12^	429	458	552	577	529	502	508	525	530	522	92
Disease total	452	495	605	622	577	553	564	569	576	568	100

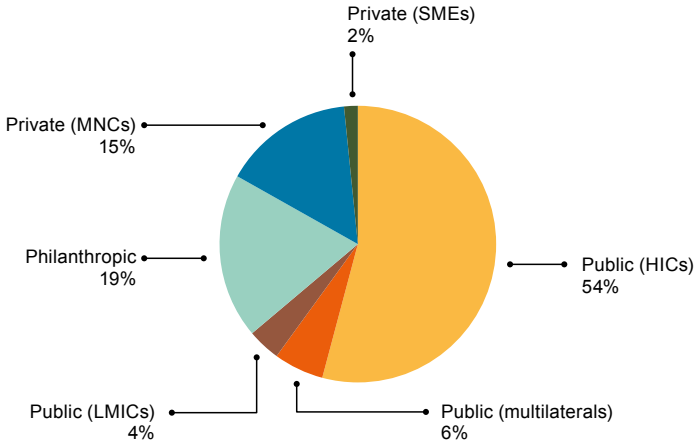
^ Subtotals for 2007-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

In 2016, the public sector provided around two-thirds ($362m, 64%) of total TB R&D investment, with the remainder split relatively evenly between the philanthropic ($110m, 19%) and private sectors ($96m, 17%). The vast majority of public funding was provided by HICs ($307m, 85%); however this level of HIC contribution is actually one of the lowest proportions of all the tier one and tier two diseases. Multilaterals (largely Unitaid) contributed $33m (9.2% of public funding), which is the largest share of total investment in any single neglected disease (5.8% of all TB R&D funding) that this sector has ever contributed in the history of the G-FINDER survey. Most private sector investment was provided by MNCs ($87m, 90%).

Public sector investment remained essentially flat in 2016 (up $5.1m, 1.6%). Philanthropic sector investment fell to the lowest level ever recorded by the G-FINDER survey (down $33m, -24%), due to reduced funding from the Gates Foundation. Industry investment in TB R&D also fell, in this case to the lowest level seen since the first year of the G-FINDER survey, with the drop in 2016 (down $8.3m, -8.9%) due to reduced investment in TB vaccine R&D.

Figure 9. TB R&D funding by sector 2016



A decade of investment in tuberculosis R&D

- Annual global funding for TB R&D over the last decade followed a similar pattern to malaria. It grew strongly between 2007 and 2010, to a peak of $622m, before plateauing within the range of $550-600m per year.
- Drug development accounted for 41% of all TB R&D investment over the decade, and was the only area to have strong investment growth during this time – driven first by industry investment in TB drug development (which peaked in 2011), and subsequently by the public sector, who have offset the decline in industry investment since 2011. Investment in TB basic research peaked in 2009 (driven by US government fiscal stimulus funding) before falling back to pre-existing levels and plateauing there; funding for all other product areas was essentially steady over the decade.
- 2016 marked the highest ever public investment in TB R&D, driven by that sector's highest ever investment in TB drug development. Governments in IDCs have more than doubled their investment since 2008 (from $9.6m, to $21m in 2016), with their collective funding now comparable to that of the EC. In contrast, industry investment in 2016 was its lowest since 2007, and more than 40% lower than its 2010 peak.

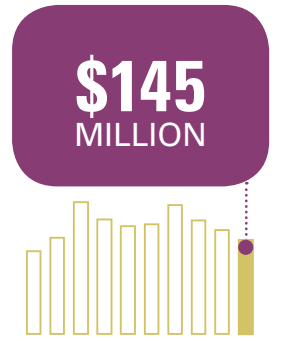
DIARRHOEAL DISEASES

Diarrhoeal diseases are a group of illnesses caused by viruses, bacteria and protozoa that often spread through contaminated food or water. Without treatment, diarrhoeal diseases can cause severe illness and death. Children under the age of five and people with compromised immunity are most at risk.[45] Rotavirus is the most common cause of severe diarrhoeal disease in young children globally, and causes fever, vomiting and watery diarrhoea.[46] Enteroaggregative *Escherichia coli*, also known as EaggEC, and enterotoxigenic *E. coli* (ETEC) can also cause fever and diarrhoea. For some people, cholera (caused by *Vibrio cholerae*) causes no symptoms but for others, infection can cause severe diarrhoea and vomiting, and even kill within hours if left untreated.[47] Shigellosis, caused by the *Shigella* bacterium, is highly contagious.[48] *Giardia* are microscopic parasites found in soil, food and water contaminated by faeces from animals or humans.[49] *Cryptosporidium* is a parasite encased in a hard shell that can survive in soil, food and water, and primarily affects people who work with animals or live in overcrowded settings.[50]

According to the IHME Global Burden of Disease study, diarrhoeal diseases were the fourth highest cause of mortality and morbidity of all the G-FINDER neglected diseases in 2015, resulting in 922,471 deaths and 50 million DALYs in developing countries.[2]

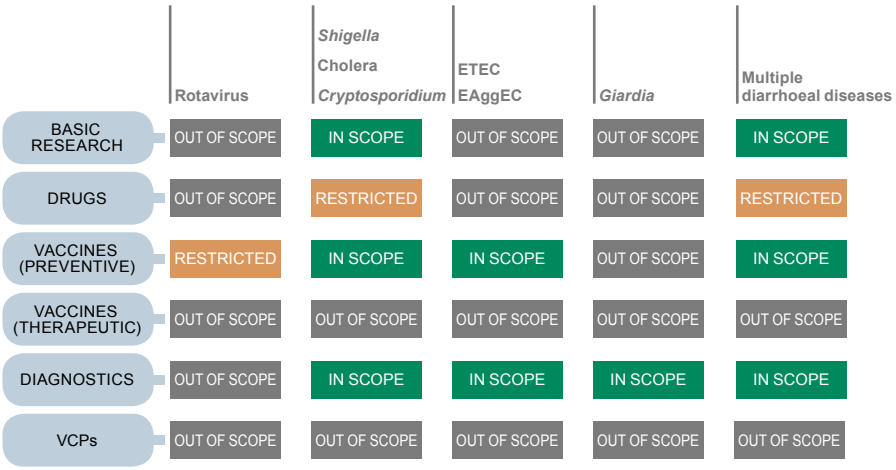
Current vaccines against diarrhoeal diseases are not always suitable for infants under the age of one, and some are relatively ineffective. New bi- and multi-valent vaccines that are suitable for infants and that have long durations of protection are needed for most diarrhoeal diseases. Paxvax's Vaxchora, a cholera vaccine, received US Food and Drug Administration (FDA) approval in 2016, but has not yet been tested in endemic areas and has only been trialled in adults.[51] In March 2016, a $1 rotavirus vaccine (ROTAVAC) was included in India's national immunisation programme. Following an initial rollout in four states, the vaccine will gradually be expanded to cover all of India.[52] Another rotavirus vaccine, ROTASIIL, received regulatory approval from Indian authorities in January 2017 after successfully completing Phase III trials.[53] ROTASIIL has proven to be heat-stable in another Phase III trial.[54] Several vaccine candidates for other diarrhoeal diseases are in Phase I and II trials. Vaccine candidates include ACE527 to address ETEC[55]; and WRSS1 and Sf2aWC (which entered Phase II in 2017) to address *Shigella*.[56, 57]

New safe, effective and affordable drugs are needed to complement supportive interventions such as oral rehydration therapy and zinc supplementation for some diarrhoeal diseases, including for cholera, *Shigella* and *Cryptosporidium*.[58] New, rapid diagnostic tests capable of distinguishing between diarrhoeal diseases are also required, however there are currently no late stage candidates in the diagnostic pipeline.[59]



TOTAL SPEND ON DIARRHOEAL DISEASE R&D IN 2015

OF GLOBAL R&D FUNDING



Global funding for diarrhoeal disease R&D in 2016 was $145m. Funding from regular survey participants (YOY funders) decreased by $21m (-14%) to $134m. Irregular participants provided the remaining $12m.

Over half of all funding for diarrhoeal disease R&D went to rotavirus ($39m, 27%) and multiple diarrhoeal diseases ($35m, 24%), followed by *Shigella* ($24m) and cholera ($23m), which accounted for 16% each. *Cryptosporidium* received $13m (9.3%) and the remaining diarrhoeal diseases collectively received less than 10% of total funding. Funding was either lower or flat for most diarrhoeal diseases in 2016, with the largest reductions seen in rotavirus (down $11m, -24%), multiple diarrhoeal diseases (down $7.2m, -20%) – primarily due to an adjustment to Inserm's reporting*, ETEC (down $6.5m, -40%) and cholera (down $2.0m, -8.4%). As a result, investment in multiple diarrhoeal diseases was the lowest ever recorded in the history of the G-FINDER survey, and investments in rotavirus and cholera reached the lowest levels seen since 2008. *Shigella* (up $6.1m, 35%) was the only diarrhoeal disease to receive a notable funding increase in 2016.

For diseases where all product types are in scope (cholera, *Shigella* and *Cryptosporidium*) funding profiles varied across product areas. For cholera, basic research received almost two-thirds of funding ($15m, 65%) and preventive vaccines under a third ($6.5m, 28%). For *Shigella*, preventive vaccines received $15m (65%) and basic research $5.7m (24%). For *Cryptosporidium*, funding was spread across basic research ($6.2m, 46%) and drugs ($5.7m, 43%).

Table 7. Diarrhoeal disease R&D funding 2016 (US$ millions)^

Disease	Basic research	Drugs	Vaccines (preventive)	Diagnostics	Unspecified	Total	%
Rotavirus			38		0.9	**39**	27
Shigella	5.7	0.4	15	1.4	1.0	**24**	16
Cholera	15	0.5	6.5	1.1	0.1	**23**	16
Cryptosporidium	6.2	5.7	1.0	0.2	0.3	**13**	9.3
Enterotoxigenic *E. coli* (ETEC)			9.2	0.4	0.1	**9.7**	6.7
Enteroaggregative *E. coli* (EAggEC)			0.5	0.2	0.1	**0.8**	0.6
Giardia				<0.1	0.1	**0.1**	0.1
Multiple diarrhoeal diseases	7.0	0.1	14	8.6	5.2	**35**	24
Total	34	6.8	85	12	7.8	145	100

^ Please note that there were strict eligibility conditions on drug and vaccine investments for some diarrhoeal disease products to avoid inclusion of overlapping commercial activity. Due to this, total funding between product categories cannot be reasonably compared

Category not included in G-FINDER

* Inserm, historically one of the top five funders of diarrhoeal disease R&D, reported more detailed data for 2016. Given the greater detail, it is apparent that a portion of Inserm's research reported in 2016 is out of the scope of G-FINDER in this restricted category, and it is possible that Inserm's investment in prior years is overstated. Since the majority of Inserm's funding is non-product specific, and allocated to multiple diarrhoeal disease R&D, this adjustment affects the overall YOY changes but not product totals. The only disease-specific funding reported by Inserm has been unspecified funding for *Shigella*, with a $0.8m (-44%) decrease in 2016.

Preventive vaccine funding (down $8.5m, -9.6%) saw the largest decrease by product area reflecting decreases in funding for rotavirus (down $11m, -24%) and ETEC (down $6.5m, -42%), which offset a smaller increase in vaccine funding for *Shigella* (up $6.0m, 64%). Other decreases were smaller, with basic research down $5.4m (-14%) and diagnostics down $0.9m (-12%). Drug R&D was the only product area to receive more funding in 2016 (up $2.6m, 62%), driven by an increase in funding for *Cryptosporidium* drug development (up $2.0m, 53%).

Just over half of all diarrhoeal disease R&D funding was for basic and early stage research ($82m, 56%), with clinical development and post registration studies accounting for 30% ($44m). Funding for some of the diarrhoeal diseases had a heavier focus on basic and early stage research, particularly cholera (78%), *Cryptosporidium* (76%) and *Shigella* (65%). On the other hand, around half of funding for ETEC and rotavirus was for clinical development and post registration studies (56% and 49%, respectively). Other diarrhoeal disease funding was not allocated to a specific product or R&D stage ($20m, 14% across all diseases).

The top 12 funders in 2016 provided 97% of all funding for diarrhoeal disease R&D. The top three funders alone provided more than three-quarters of all funding, with the Gates Foundation contributing $43m (30%), the US NIH $38m (26%) and industry $30m (21%).

Only three of the top 12 funders increased their investment in diarrhoeal disease R&D in 2016, and even these increases were relatively modest in size: MSF (up $3.0m, 218%), largely due to the start of BRV-PV rotavirus vaccine trials in Niger; Brazilian Development Bank (BNDES, $2.8m), as part of an ongoing multi-year rotavirus vaccine grant to the Butantan Institute that had no reported funding in 2015; and the Gates Foundation (up $2.2m, 5.4%). The largest decrease was a result of the adjustment to Inserm's reporting (down $9.8m, -91%) with additional smaller reductions spread across a number of funders.

Table 8. Top diarrhoeal disease R&D funders 2016

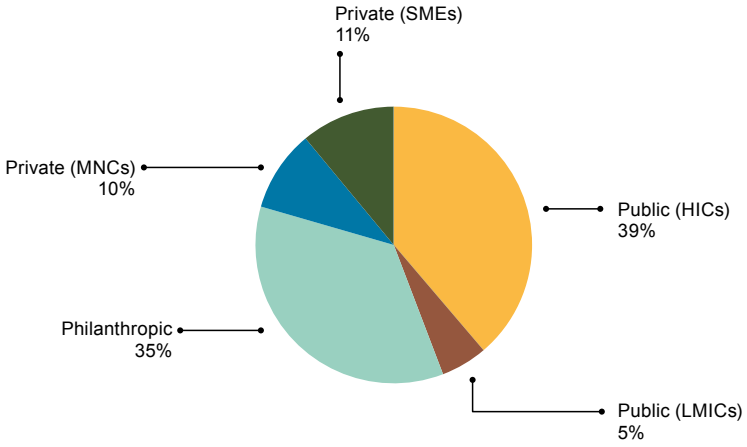
Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
Gates Foundation	52	31	55	53	36	41	52	42	41	43	30
US NIH	36	46	71	59	62	56	48	44	38	38	26
Aggregate industry	13	26	41	33	28	30	45	40	34	30	21
US DOD	6.4	6.9	13	6.9	5.6	8.6	9.6	9.5	7.2	5.8	4.0
Indian ICMR		4.5	3.8	4.8	2.9	2.7	4.7	4.6	5.2	4.9	3.3
MSF							-	-	1.4	4.4	3.0
Institut Pasteur	3.1	3.5	4.8	3.9	4.0	3.8	3.7	3.8	3.6	3.9	2.7
UK DFID	-	-	2.4	4.6	2.6	-	3.2	8.4	4.8	3.5	2.4
Brazilian BNDES								0.7	-	2.8	1.9
Wellcome Trust	0.9	0.4	0.3	0.4	0.4	3.8	2.9	4.7	3.9	2.7	1.9
Gavi	12	17				4.1	7.5		3.4	1.2	0.8
Inserm	0.3	0.3	1.3	1.6	8.0	8.3	12	11	11	1.0	0.7
Subtotal of top 12^	127	143	199	172	161	163	194	172	156	141	97
Disease total	128	149	204	177	167	169	200	175	161	145	100

^ Subtotals for 2007-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016
- No reported funding
Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

Just under half of all funding for diarrhoeal disease R&D in 2016 came from the public sector ($64m, 44%), with the majority of this coming from HIC governments ($56m, 88%). The philanthropic sector contributed just over a third of total funding ($51m, 35%) and industry a fifth ($30m, 21%). SMEs – primarily from innovative developing countries (IDCs) – contributed 54% of industry funding, the third highest share of industry funding among neglected diseases.

Philanthropic funding increased (up $4.0m, 8.8%), due to increases from MSF (up $3.0m, 218%) and the Gates Foundation (up $2.2m, 5.4%). Public sector funding fell by $17m (-22%), although this includes the adjustment to Inserm's reporting (down $9.8m, -91%). The decrease in industry funding (down $8.2m, -26%) reflects reduced industry investment in rotavirus vaccine R&D (down $15m, -49%), which more than offset increased investment in *Shigella* vaccine R&D (up $5.1m, from a low base).

Figure 10. Diarrhoeal disease R&D funding by sector 2016



A decade of investment in diarrhoeal disease R&D

- Funding for diarrhoeal diseases mostly fluctuated between $150m and $200m over the past decade, with peaks in 2009 (related to US government stimulus spending on vaccines and basic research) and 2013 (driven by philanthropic and industry investment in vaccine trials).
- Rotavirus, which has the highest burden of disease of the diarrhoeal diseases included in G-FINDER, received almost half a billion dollars ($495m) in funding for R&D for developing country-specific vaccines. Half of this ($249m, 50%) came from industry, initially driven by MNCs, followed more recently by increased SME investment in early stage research. A slow decline in funding for rotavirus vaccine research since 2013 reflects the registration of new products.
- Almost a quarter ($387m, 23%) of all diarrhoeal disease funding over the past decade went to PDPs – the equal highest share (with malaria) of all neglected diseases. Unlike malaria however, this funding has steadily declined. Funding to PDPs for diarrhoeal disease R&D more than halved since 2007 (from $55m, to just $22m in 2016), with the share falling from 43% of all funding to 15%. PATH – whose portfolio includes rotavirus, ETEC and *Shigella* vaccines – was the largest beneficiary of this funding ($300m, 78% all of funding for PDPs over the decade).

KINETOPLASTIDS

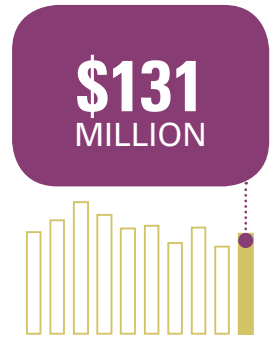
Kinetoplastid infections include three diseases: leishmaniasis; Chagas' disease (also known as American trypanosomiasis); and sleeping sickness (human African trypanosomiasis). Leishmaniasis, spread by sand flies, has three forms: visceral (the most severe form, which is often fatal without treatment); cutaneous (the most common); and mucocutaneous.[60] Chagas' disease is caused by *Trypanosoma cruzi*, and is predominantly spread by the blood-sucking triatomine bug. Chagas' disease has two stages: symptoms in the acute stage are often mild or absent, resulting in widespread under-diagnosis. If left untreated, all infected individuals will progress to chronic Chagas' disease, and around 20-30% will develop life-threatening complications.[61] Sleeping sickness is caused by the parasite *Trypanosoma brucei*, and spread by tsetse flies. It also has two stages, with symptoms of early stage disease often difficult to distinguish from non-specific viral illnesses. Late stage sleeping sickness occurs when the parasite infects the brain and central nervous system, causing confusion and – without treatment – coma and death.[62]

According to available data from the IHME Global Burden of Disease study, kinetoplastids collectively ranked as the ninth highest cause of mortality and the eleventh highest cause of morbidity of all the G-FINDER neglected diseases in 2015, resulting in 35,160 deaths and 1.8 million DALYs in developing countries.[2] The WHO Global Health Estimates provide a similar mortality figure, estimating that kinetoplastids were responsible for 33,974 deaths in developing countries in 2015.[3]

Leishmaniasis needs a vaccine, as well as more effective, oral drug formulations and a diagnostic that can detect early stage disease. At least one vaccine candidate in clinical development is undergoing evaluation for prophylactic and therapeutic indications.[63] There are no novel leishmaniasis drugs in clinical development, although a topical formulation of an existing drug (amphotericin B) is currently in clinical trials for the treatment of cutaneous leishmaniasis.[64] Diagnostics intended for use in resource-limited settings currently in development include a urine-based test, in early stage development, and a LAMP-based test for visceral and cutaneous leishmaniasis currently undergoing demonstration studies in endemic countries.[65]

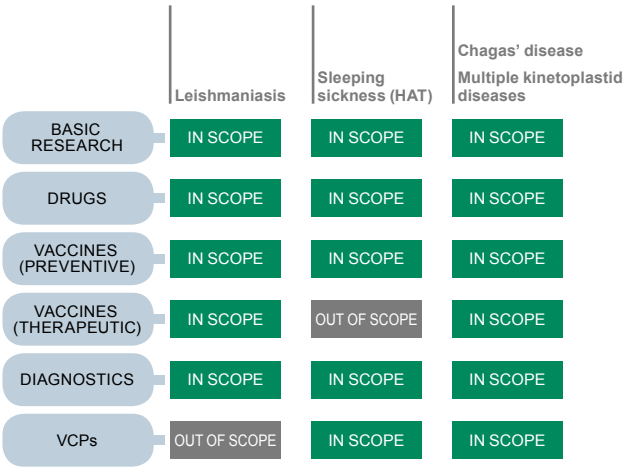
Chagas' disease needs preventive and therapeutic vaccines; safer, more effective drugs that are suitable for children and effective against the chronic form of the disease; and diagnostics that can reliably detect chronic disease and monitor treatment. A paediatric benznidazole formulation was registered in Brazil in 2011[66] and received US FDA approval in 2017.[67] A combination therapy of benznidazole and fosravuconazole (a new chemical entity, previously called E1224) has entered Phase II.[68] A urine-based diagnostic for the detection of congenital Chagas' disease is in late development.[69]

Sleeping sickness needs safe, oral drugs that are active against both stages of the disease to replace the current nifurtimox-eflornithine combination therapy (NECT) injectable treatments[70], as well as an effective vaccine. Fexinidazole, the first potential new drug for the treatment of late stage sleeping sickness in 30 years, is currently in Phase IIIb clinical trials in Africa, and acoziborole (previously SCYX 7158) is in Phase II/III clinical trials.[71] There are currently no vaccine candidates for sleeping sickness in the product pipeline.



TOTAL SPEND ON KINETOPLASTID R&D IN 2016

OF GLOBAL R&D FUNDING



Global funding for kinetoplastid R&D in 2016 was $131m. Regular survey participants (YOY funders) increased funding to $110m (up $12m, 12%), with irregular participants contributed the remaining $21m.

The largest share of funding was for leishmaniasis ($41m, 31%), followed by sleeping sickness ($37m, 28%), and Chagas' disease ($25m, 19%); remaining funding was for multiple kinetoplastid diseases ($29m, 22%). Funding was either higher or steady for all kinetoplastid diseases, with many of the changes reflecting cyclical funding to PDPs from philanthropic organisations and government agencies. Funding for sleeping sickness increased by $6.1m (up 23%), after a big drop in 2015, largely due to cyclical funding from the Gates Foundation to DND*i* ($7.4m in 2016, after no funding in 2015). Funding also increased for Chagas' disease (up $3.6m, 27%), driven by the US NIH (up $4.3m, 61%), and multiple kinetoplastid diseases (up $2.2m, 8.8%), due to increased Dutch DGIS funding to DND*i* (up $3.7m, 470%) following the start of a new PDP funding round. Funding for leishmaniasis remained stable (down $0.1m, -0.3%), with increased funding from the Gates Foundation (up $2.5m, from a low base) offsetting decreases from the US NIH ($1.3m, -9.5%) and the EC ($1.2m, -29%).

Funding increased for all product types with the exception of diagnostics (down $0.7m, -16%), with these changes again being heavily influenced by the pattern of multi-year grant funding to PDPs. Funding for drug R&D increased by $7.8m (up 17%), with the largest increases going to sleeping sickness (up $4.8m, 54%) and leishmaniasis (up $2.1m, 25%), due to an increase in cyclical Gates Foundation funding to DND*i*. Preventive vaccine funding for R&D increased (up $1.9m, 46%) due to cyclical Gates Foundation funding to the Infectious Disease Institute (IDRI). Therapeutic vaccine funding for R&D doubled, albeit from a modest amount (up $0.3m, 126%), split across Chagas' disease (up $0.2m, from a low base) and leishmaniasis (up $0.1m, 24%). The decrease in diagnostic funding reflected cyclical funding from the Gates Foundation to FIND.

Table 9. Kinetoplastid R&D funding 2016 (US$ millions)

Disease	Basic research	Drugs	Vaccines (preventive)	Vaccines (therapeutic)	Diagnostics	Vector control products	Unspecified	Total	%
Leishmaniasis	16	14	4.9	0.3	1.8		4.1	41	31
Sleeping sickness (HAT)	19	14	0.6		1.0	0.7	1.4	37	28
Chagas' disease	12	7.9	0.9	1.7	1.9	0.1	<0.1	25	19
Multiple kinetoplastid diseases	3.4	25	<0.1	-	<0.1	-	0.3	29	22
Total	50	61	6.4	2.0	4.7	0.8	5.9	131	100

- No reported funding
Category not included in G-FINDER

Around three-quarters of kinetoplastid funding went to basic and early stage research ($95m, 73%), with only $19m (15%) going to clinical development and post registration studies. Remaining funding was not allocated to a specific product or R&D stage ($17m, 13%). The focus on basic and early stage research was consistent across each of the kinetoplastid diseases (87% for Chagas' disease, 69% for sleeping sickness and 68% for leishmaniasis), and reflects the state of the R&D pipeline, which has very few candidates in clinical development.

In 2016, the top 12 funders accounted for 87% of total kinetoplastid R&D funding, with just three funders – the US NIH, industry and the Gates Foundation – accounting for more than half ($68m, 52%) of all funding.

Most of the major funding movements among the top funders were related to cyclical funding patterns to PDPs. The Gates Foundation (up $10m 371%, mainly owing to multi-year grants to PDPs) went from being the eighth highest funder in 2015 to the third highest funder in 2016. The Dutch DGIS (up $3.7m, from a low base) became the sixth highest funder due to the start of a new PDP funding round. The German BMBF (down $1.5m, -47%) dropped out of the top 12 in 2016 due to decreased funding to DND*i*. Funding changes not related to PDPs included increased investment from the US NIH (up $4.2m, 12%), which consolidated its position as the top funder of kinetoplastid R&D, and better reporting from the French Institute for Development (IRD), which moved into the top 12 with an investment of $2.6m across the three kinetoplastid diseases.

Table 10. Top kinetoplastid R&D funders 2016

Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
US NIH	33	57	62	66	56	54	47	42	36	40	31
Aggregate industry	4.6	2.9	4.9	11	14	18	17	19	21	15	11
Gates Foundation	53	34	42	23	13	9.3	9.1	19	2.8	13	10
Wellcome Trust	13	11	10	8.1	8.9	11	9.8	13	12	12	9.2
EC	2.6	4.3	9.4	8.3	6.8	5.6	3.7	11	14	12	9.2
Dutch DGIS	-	-	-	1.2	3.7	2.3	4.5	3.7	0.8	4.4	3.4
Brazilian FAPESP			-						2.0	3.4	2.6
Indian ICMR		-	0.1	2.0	3.7	3.3	4.8	4.2	2.9	3.3	2.5
UK MRC	2.4	3.0	2.1	2.4	2.0	1.4	2.1	2.9	2.3	3.1	2.4
US DOD	5.5	4.8	5.3	1.1	1.0	0.5	-	-	3.3	2.8	2.1
French IRD		-								2.6	2.0
Institut Pasteur	-	2.7	2.9	5.4	4.6	2.8	2.4	2.5	2.1	2.5	1.9
Subtotal of top 12^	131	136	158	143	124	128	107	128	103	114	87
Disease total	133	149	173	156	139	141	119	139	114	131	100

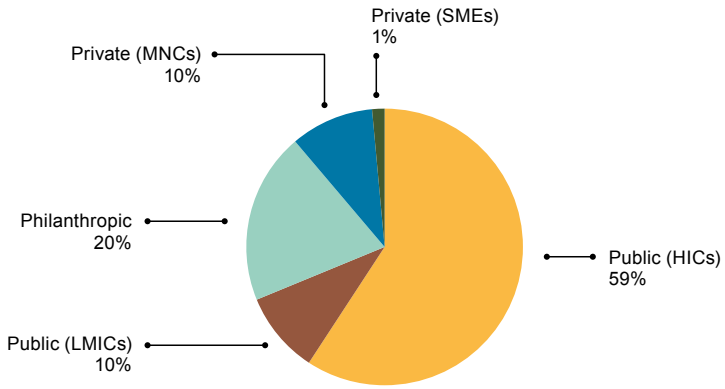
^ Subtotals for 2007-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016

\- No reported funding

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

The public sector accounted for more than two-thirds of funding for kinetoplastids ($90m, 69%), with most of this funding coming from HICs ($78m, 86%). The philanthropic sector contributed a fifth of total funding ($26, 20%), with industry providing the remainder ($15m, 11%). The largest funding increase came from the philanthropic sector (up $10m, 67%), followed by the public sector (up $4.5m, 6.4%), with this latter increase coming from both HICs and LMICs. Industry funding for kinetoplastid R&D decreased in 2016 (down $2.8m, -21%).

Figure 11. Kinetoplastid R&D funding by sector 2016



A decade of investment in kinetoplastid R&D

- Aside from a brief peak from 2008 to 2010, annual global funding for kinetoplastid R&D was essentially steady over the last decade, at around $120m-$140m per year. Leishmaniasis was the best funded of the three diseases (receiving 37% of all kinetoplastid R&D funding over the decade), followed by sleeping sickness (29%) and then Chagas' disease (16%), with the remaining 18% not allocated to a single disease.
- The level of funding going to each of the kinetoplastid diseases has converged over the course of the decade: funding for leishmaniasis peaked in 2009 (driving the increase in overall kinetoplastid R&D funding) but has subsequently fallen, while funding for Chagas' disease has grown, and funding for sleeping sickness has been relatively steady.
- PDPs have been heavily involved in R&D for kinetoplastid diseases, receiving 22% of funding over the past decade. This is the third highest share of any neglected disease, marginally behind malaria and diarrhoeal diseases (both 23%). Like diarrhoeal diseases however, the proportion of all funding for kinetoplastid R&D going to PDPs fell sharply over the decade, from a high of 37% in 2007 to just 16% in 2016.

DENGUE

Dengue, also known as breakbone fever, is a viral infection transmitted to humans by the female *Aedes* mosquito – most often *Aedes aegypti* (common in urban environments) and *Aedes albopictus* (common in rural environments). The dengue virus has four serotypes, each with multiple subtypes. First time infection rarely results in anything more serious than a severe flu-like illness; subsequent infections with a different serotype (or even subtype) can result in severe disease, and are more likely to lead to dengue haemorrhagic fever.[72] For children in affected regions, dengue is a leading cause of serious illness and death. Dengue outbreaks often occur in Asia, Central and South America, and the disease is now present in more than 100 countries, up from nine countries fifty years ago.[73]

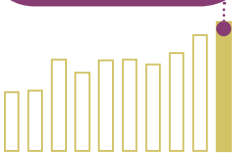
According to the IHME Global Burden of Disease study, dengue was the tenth highest cause of both mortality and morbidity of all the G-FINDER neglected diseases in 2015, resulting in 18,298 deaths and 1.9 million DALYs in developing countries.[2] The WHO Global Health Estimates report an even higher mortality figure, estimating that dengue was responsible for 34,462 deaths in developing countries in 2015.[3]

Dengue's prevalence in several high- and upper-middle-income countries across Asia and Latin America, coupled with demand from travellers and the military, has created a potential commercial market for a dengue vaccine large enough to attract industry investment in vaccine R&D. For this reason, dengue vaccine R&D investment has been excluded from the scope of G-FINDER. The first dengue vaccine – Dengvaxia (CYDTDV) – was registered in December 2015 for use in individuals 9-45 years of age living in endemic areas.

No curative treatment is available for dengue; management is therefore focused on supportive therapy and the control of onward transmission. Despite the need, there is little advanced activity in dengue drug research. Pipeline candidates include celgosivir (an α-glucosidase inhibitor), currently in Phase I trials,[74] and DENV mAb, in pre-clinical development.[75]

There is a pressing need for diagnostics that can detect dengue across the complete spectrum of disease, and distinguish dengue from other causes of fever.[76] The first reverse transcription polymerase chain reaction (RT-PCR) diagnostic test able to detect the presence of all four dengue virus types was approved by the US FDA in 2012 (CDC DENV-1-4), however independent evaluations showed that this product has a lower clinical sensitivity than initially thought.[77] Additionally, real-time RT-PCR tests are less suitable than loop-mediated isothermal amplification (LAMP) -based tests for use in low-resource settings.[78] Several research groups are developing real-time LAMP-based tests, such the DENV RT-LAMP assay currently in development by US Naval Medical Research Center.[78] A number of point-of-care serological tests (based on antigen and/or antibody detection) are available, however these tests cannot distinguish between serotypes, and may lack sensitivity and specificity. A point-of-care test is needed that can diagnose all four serotypes as well as primary and secondary dengue infection.

$113 MILLION



TOTAL SPEND ON DENGUE R&D IN 2016

OF GLOBAL R&D FUNDING

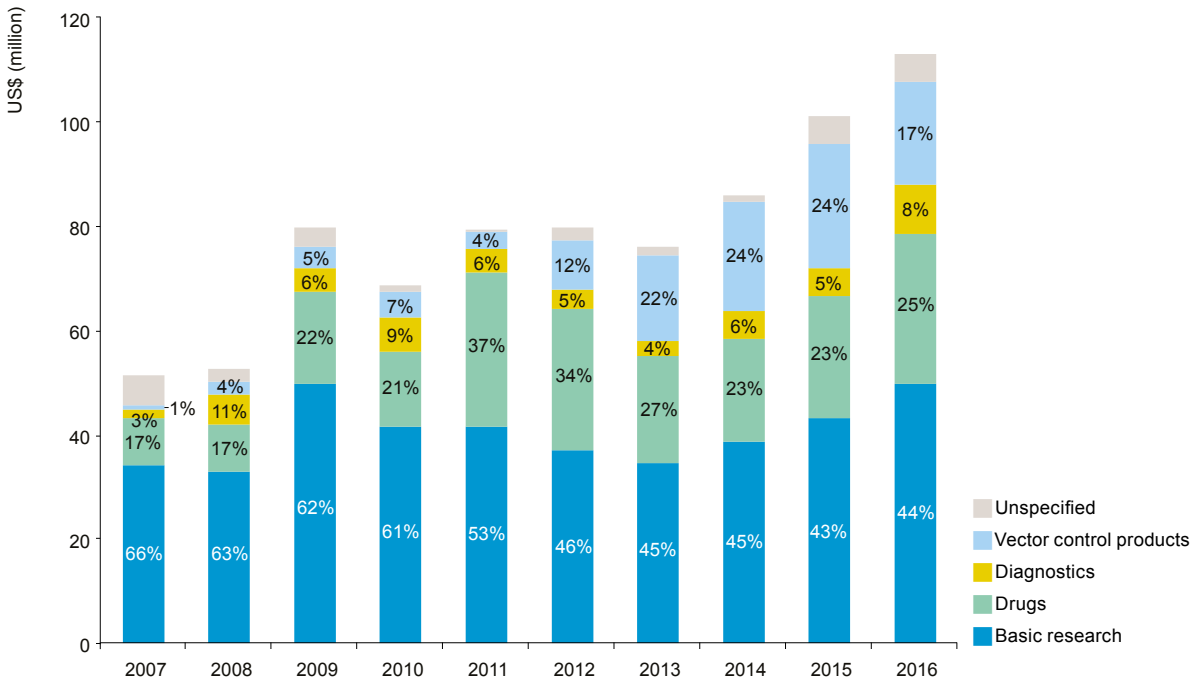
BASIC RESEARCH	IN SCOPE
DRUGS	IN SCOPE
VACCINES (PREVENTIVE)	OUT OF SCOPE
VACCINES (THERAPEUTIC)	OUT OF SCOPE
DIAGNOSTICS	IN SCOPE
VCPs	IN SCOPE

Global funding for dengue R&D in 2016 was $113m. Regular survey participants (YOY funders) increased their investment by $8.4m (up 8.7%) to $106m, with irregular participants providing the remaining $7.1m. This was the third successive year of increasing funding for dengue R&D, at an average of 13% per year; the funding increase in 2016 was primarily driven by the US NIH.

Most dengue R&D funding in 2016 was for basic research ($50m, 44%), followed by drugs ($28m, 25%) and vector control products ($20m, 17%), while diagnostics received less than 10% of total funding ($9.4m, 8.3%). The largest increases were in basic research (up $4.8m, 12%) and drugs (up $4.5m, 19%); funding for diagnostics (up $3.6m, 77%) increased to the highest level ever reported for this area. There was an overall drop in funding for vector control products (down $3.7m, -16%) but this masked opposing changes at the sub-product level. In 2016 funding for vector control products was concentrated in biological control products ($19m, 97%) with pesticides receiving less than $1.0m ($0.6m, 2.8%). This represented a substantial funding drop for pesticide R&D compared to 2015 (down $11m, -95%), reflecting a reduction in the Gates Foundation's funding to IVCC for dengue pesticide R&D (coinciding with a marked increase in its funding to IVCC for malaria pesticide R&D). Investment in biological control products increased (up $7.0m, 58%), due to new funding from the Gates Foundation ($12m) to Monash University's World Mosquito Program, formerly known As Eliminate Dengue.

Three-quarters of all funding for dengue R&D in 2016 was for basic and early stage research ($83m, 74%), with only $3.0m (2.7%) going to clinical or field development. A relatively large amount of funding was not allocated to a specific product or R&D stage ($27m, 24%), although it must be noted that some of this includes funding for biological control products which is currently not allocated to a specific R&D stage category in the G-FINDER survey. Funding for drug development focused on discovery and pre-clinical research ($26m, 91%), reflecting the early stage of the pipeline.

Figure 12. Dengue R&D funding by product type 2007-2016



The top 12 funders in 2016 accounted for almost all (97%) of total dengue R&D funding. The increase in dengue R&D funding in 2016 can essentially be attributed to the US NIH (up $11m, 24%), which also contributed exactly half (50%) of all R&D funding for dengue. Half of the top 12 funders decreased funding, most notably the Gates Foundation (down $2.5m, -14%), Inserm (down $2.1m, -67%) and the US CDC, which dropped out of the top 12 after reporting no funding for dengue in 2016. Two key LMICs public funders reported increased dengue R&D investment – the Brazilian Support Fund for Research in the State of Minas Gerais (FAPEMIG) and the Indian ICMR increased investment by $2.7m and $1.5m (from a low base) respectively.

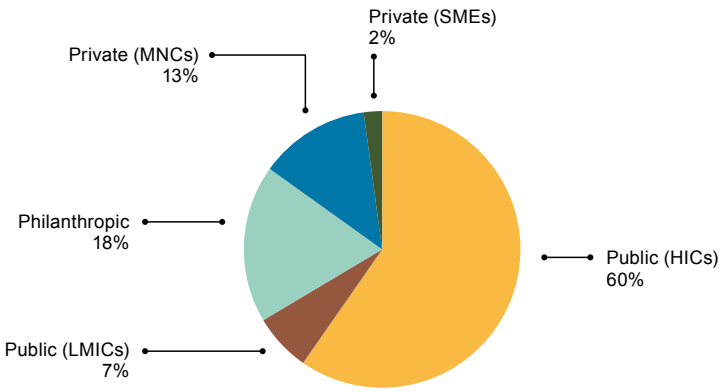
Table 11. Top dengue R&D funders 2016

Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
US NIH	30	25	45	42	49	44	36	41	46	57	50
Aggregate industry	7.4	3.7	5.3	7.4	11	8.6	7.5	7.8	15	17	15
Gates Foundation	1.2	2.1	1.7	1.2	0.1	5.4	17	19	18	15	14
Wellcome Trust	0.9	1.0	1.4	2.0	6.0	4.7	3.4	6.0	5.5	5.4	4.8
Indian ICMR		0.6	1.0	1.4	1.4	1.2	1.8	1.6	1.8	3.3	3.0
Brazilian FAPEMIG			1.5						<0.1	2.8	2.5
EC	1.8	1.6	1.0	0.5	0.4	1.8	2.5	2.3	2.4	2.4	2.1
Institut Pasteur	3.6	2.2	2.0	3.0	2.3	1.8	1.9	1.8	1.9	1.7	1.5
UK MRC	0.2	0.3	0.2	0.1	0.7	0.4	0.5	0.7	1.6	1.5	1.4
US DOD	1.3	2.6	5.0	0.4	1.1	0.4	0.2	0.2	1.0	1.5	1.4
Inserm	-	-	-	-	-	-	-	-	3.2	1.1	1.0
Australian NHMRC	0.7	1.1	1.1	1.3	1.9	2.8	1.6	2.9	0.6	0.7	0.6
Subtotal of top 12^	51	50	73	65	77	77	74	85	97	110	97
Disease total	51	53	80	69	79	80	76	86	101	113	100

^ Subtotals for 2007-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016
- No reported funding
Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

As in previous years, two-thirds of dengue funding came from the public sector ($75m, 66%). Most public sector funding was from HICs ($67m, 90%), and more than three-quarters of HIC funding came from the US NIH ($57m, 85%). The philanthropic sector accounted for just under a fifth ($21m, 18%), and industry for 15% ($17m). Overall public sector funding increased by $9.8m (up 16%), primarily reflecting the US NIH funding increase. Industry investment in dengue R&D also increased slightly (up $1.3m, 9.3%), driven by increased MNC investment (up $1.0m, 7.6%). Philanthropic sector funding fell by $2.7m (-11%).

Figure 13. Dengue R&D funding by sector 2016



A decade of investment in dengue R&D

- Global funding for dengue R&D has more than doubled over the last decade (from $51m in 2007 to $113m in 2016). All product categories benefited from this increase, as did basic research, although the most striking growth was in vector control products, which increased from $0.8m in 2007 to $20m in 2016.
- The increase in dengue R&D funding between 2007 and 2016 came primarily from the public sector (largely the US NIH) and the philanthropic sector (almost entirely from the Gates Foundation), but was also supported by smaller but steady growth in industry investment.
- Just over half (51%) of all dengue R&D funding over the past 10 years was for basic research, with the US NIH providing nearly three-quarters (71%) of this amount. Meanwhile, the Gates Foundation was responsible for nearly two-thirds (62%) of all R&D investment in dengue vector control products over the last decade.

BACTERIAL PNEUMONIA & MENINGITIS

Pneumonia is an infection of the lungs that is transmitted when infected individuals cough or sneeze. Symptoms include coughing, fever, chest pain and shortness of breath, and the illness can be deadly, especially for young children and elderly patients.[79] Although pneumonia can be caused by a range of bacteria and viruses, pneumococcal pneumonia caused by the bacterium *Streptococcus pneumoniae* is by far the most common in developing countries.

Bacterial meningitis is an infection of the fluid that surrounds the brain and spinal cord, most commonly caused by *S. pneumoniae* or *Neisseria meningitidis*. Symptoms of bacterial meningitis can include severe headaches, fever, chills, a stiff neck, nausea and vomiting, sensitivity to light, and an altered mental state.[80] Bacterial meningitis is also often transmitted from person to person through coughing or sneezing. Even with early diagnosis and treatment, 5-10% of infected individuals die within 24-48 hours of showing symptoms.[80]

According to the IHME Global Burden of Disease study, bacterial pneumonia & meningitis was the leading cause of both mortality and morbidity of all the G-FINDER neglected diseases in 2015, resulting in 1.6 million deaths and 75 million DALYs in developing countries.[2]

Pneumococcal conjugate vaccines (PCVs) are highly effective and widely used in high-income countries, but until recently did not offer protection against the most prevalent serotypes in developing countries. The WHO prequalified PCV10 and PCV13 vaccines, which offer broader protection, have been rolled out in a number of developing countries with positive results.[81,82] However PCVs are expensive to make and do not cover all of the 90 plus pneumococcal strains.[81,82] New vaccines are needed that are more affordable, while still providing specific protection for children against serotypes predominant in developing countries, or across all serotypes. Pneumococcal protein vaccines are one potential approach to achieve this, as they offer broad protection while being less expensive to manufacture; several protein vaccine candidates are currently in Phase II clinical trials.[82]

Historically, most epidemic and endemic bacterial meningitis in the meningitis belt of sub-Saharan Africa has been caused by serogroup A meningococci. MenAfriVac, a 50c per dose monovalent conjugate meningitis A vaccine developed by the Meningitis Vaccine Project, has been rolled out in mass vaccination campaigns across the meningitis belt of Africa since 2010, with much success. An infant version of MenAfriVac was prequalified by the WHO in early 2015. But as rates of meningitis A have fallen, other serogroups have become increasingly prominent. Two multivalent meningococcal conjugate vaccines (developed for high-income country needs) are currently available, but are too expensive for widespread use in developing countries, ranging between $12 and $40 per dose.[83] There is an ongoing need for cheaper polyvalent conjugate vaccines, with one candidate in Phase II trials.[84]

TOTAL SPEND ON BACTERIAL PNEUMONIA & MENINGITIS R&D IN 2016

OF GLOBAL R&D FUNDING

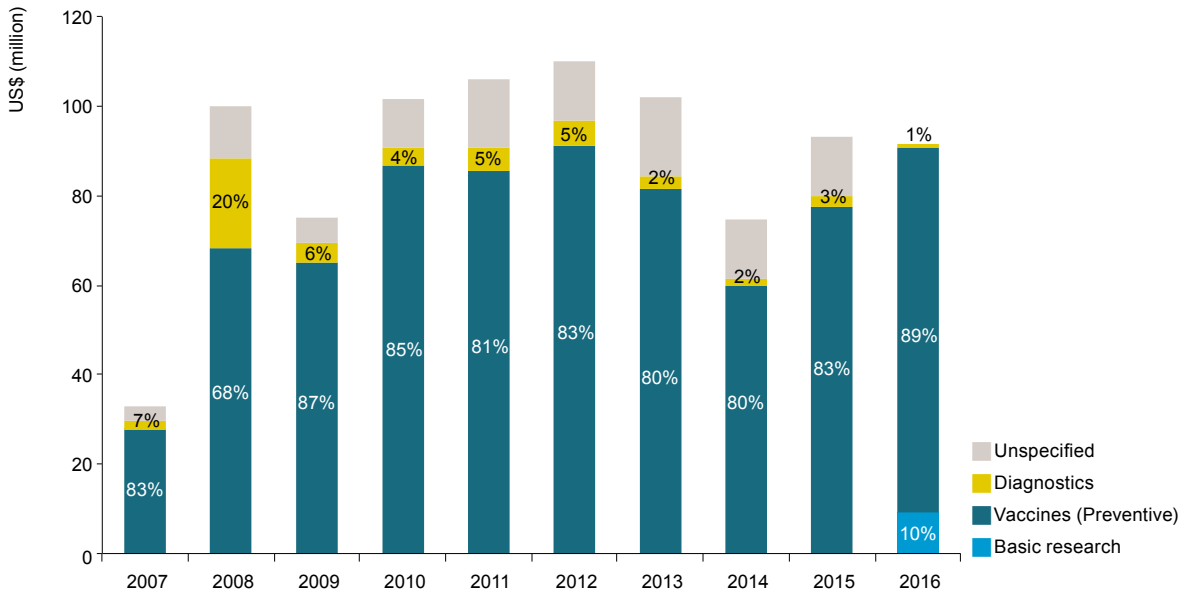
	S. pneumoniae *N. meningitidis*	Both *S. pneumoniae* and *N. meningitidis*
BASIC RESEARCH	RESTRICTED	RESTRICTED
DRUGS	OUT OF SCOPE	OUT OF SCOPE
VACCINES (PREVENTIVE)	RESTRICTED	OUT OF SCOPE
VACCINES (THERAPEUTIC)	OUT OF SCOPE	OUT OF SCOPE
DIAGNOSTICS	IN SCOPE	IN SCOPE
VCPs	OUT OF SCOPE	OUT OF SCOPE

Global funding for bacterial pneumonia & meningitis R&D was $92m in 2016. Regular survey participants (YOY funders) were responsible for $78m of this total, with irregular participants providing the remaining $14m. YOY funding fell slightly (down $3.1m, -3.8%), however there are two caveats to this number: the G-FINDER scope was expanded in 2016 to include developing country-focused basic research, which received $6.9m from YOY funders; and Inserm's investment was adjusted, resulting in a $10m decrease#. Excluding these two changes, YOY funding actually remained stable (up <$0.1m, <0.1%).

S. pneumoniae received the majority of funding ($66m, 72%), despite reduced investment in this area in 2016 (down $9.1m, -14%) related to cyclical funding from the Gates Foundation to PATH. *N. meningitidis* received $25m (27%); this was an increase of $17m (up 371%), due to larger reported industry investment in meningitis vaccine R&D. Just $0.9m (0.9% of total funding) was not allocated to a specific pathogen; this was a decrease of $11m (-93%) compared to 2015, mostly due to the adjustment to Inserm's reporting.

As in previous years, vaccine R&D received the majority of funding with $81m (89%); the newly-included basic research category received $9.3m (10%), and diagnostics just $0.9m (0.9%).

Figure 14. Bacterial pneumonia & meningitis R&D funding by product type 2007-2016



Inserm, the third highest funder in 2015, reported more detailed data for 2016, resulting in a proportion of its reported 2016 investment being considered outside the scope of G-FINDER; it is therefore possible that Inserm's investment in prior years is overstated. Since the majority of Inserm's historical funding is not pathogen- or product-specific, this adjustment affects overall YOY changes but not pathogen or product totals.

Funding for vaccine R&D was relatively stable (up $3.1m, 4.6%), but this hid major changes in pathogen-specific funding. Almost two-thirds of all funding for bacterial pneumonia & meningitis in 2016 went to pneumococcal vaccines ($49m, 63%), however this represented a significant decrease from 2015 (down $14m, -22%), due to cyclical Gates Foundation funding to PATH. Conversely, vaccine funding for meningitis increased more than five times (up $17m, 464%), as a result of the increased industry investment noted earlier. Funding for diagnostics decreased (down $1.8m, -67%).

Funding for bacterial pneumonia & meningitis R&D in 2016 was heavily focused on clinical development and post registration studies ($73m, 80%), followed by basic and early stage research ($15m, 16%). However, this split is influenced by scope restrictions on basic and early stage research in the G-FINDER survey. The remaining investment was not allocated to a specific product or R&D stage ($3.9m, 4.3%).

Funding for bacterial pneumonia & meningitis R&D remained highly concentrated in 2016, with the top two funders – industry and the Gates Foundation – providing the vast majority ($74m, 80%) of total funding. This was even higher than the 75% share these two funders accounted for in 2015, and came despite sharply diverging funding in 2016: aggregate industry remained the top funder, and increased its investment by $16m (52%) after a sharp decrease the previous year. In contrast, Gates Foundation funding was down $15m (-45%) due to cyclical funding to PATH. Other notable changes include the UK DFID moving into the top 12, following the disbursement of $2.9m to PATH (after not having reported any funding in 2015), and the downward adjustment to Inserm's reporting.

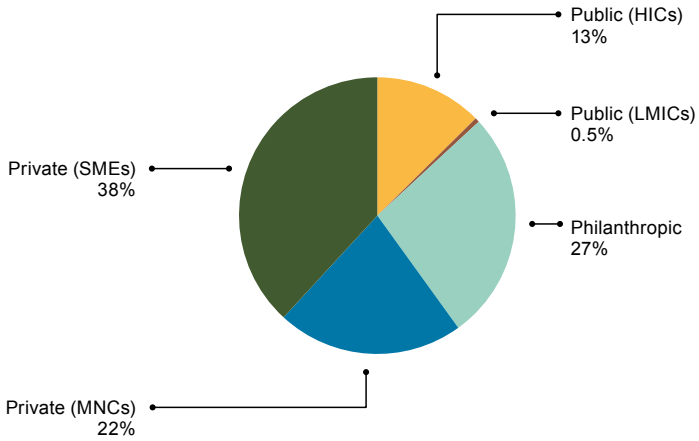
Table 12. Top bacterial pneumonia & meningitis R&D funders 2016

Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
Aggregate industry	14	54	36	32	38	41	49	49	36	55	60
Gates Foundation	6.6	31	25	46	39	44	15	5.5	34	19	20
Gavi				2.5		5.5	11		6.4	4.7	5.1
US NIH	4.9	4.7	4.3	10	16	8.8	6.5	2.2	1.3	3.4	3.7
UK DFID	-	-	-	-	-	0.1	0.8	1.8	-	2.9	3.2
German DFG	-		0.5	0.6	-	0.4	2.5	2.6	1.6	2.2	2.4
UK MRC	1.5	1.7	1.8	0.9	0.6	0.3	0.6	0.5	0.8	1.7	1.9
Wellcome Trust	0.2	0.2	0.1	0.2	0.7	3.2	1.8	1.9	1.1	0.9	1.0
Institut Pasteur	0.4	0.2	0.3	0.3	0.7	0.5	0.3	0.3	0.4	0.6	0.7
French ANR		0.3	-	-	-	-	1.0	-	0.8	0.4	0.4
South African DST	-	-	-	-	-	-	-	-	-	0.3	0.3
Indian ICMR		-	-	-	-	-	-	-	-	0.2	0.2
Subtotal of top 12^	33	99	74	99	106	109	101	75	93	91	99
Disease total	33	100	75	102	106	110	102	75	93	92	100

^ Subtotals for 2007-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016
- No reported funding
Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

Bacterial pneumonia & meningitis had the highest proportion of industry involvement and the lowest proportion of public sector funding for any G-FINDER neglected disease in 2016. Industry was responsible for nearly two-thirds of all funding ($55m, 60%) in 2016. Notably, SMEs invested more than MNCs, accounting for $35m (38%) of all funding for bacterial pneumonia & meningitis R&D; this was also the highest proportion of any of the neglected diseases, and primarily came from Indian firms. The philanthropic sector contributed $25m (27%), and public sector funders just $12m (13%). The increase in industry investment (up $16m, 52%) came from both SMEs† (up $10m, 43%) and MNCs (up $8.1m, 69%). Public sector funding decreased by $4.5m (-32%), due to reduced investment from HICs. Philanthropic funding fell by $15m (-43%), entirely reflecting the cyclical reduction in funding from the Gates Foundation.

Figure 15. Bacterial pneumonia & meningitis R&D funding by sector 2016



A decade of investment in bacterial pneumonia & meningitis R&D

- Since 2008, annual global funding for bacterial pneumonia & meningitis R&D has been relatively steady (albeit within quite a wide range) at between $75m and $110m per year, with peak investment recorded in 2012.
- Industry investment accounted for nearly half (45%) of all global funding for bacterial pneumonia & meningitis R&D over the past decade. Philanthropic funders (primarily the Gates Foundation) provided a further 35%, and the public sector just 20%.
- SME investment in vaccines, particularly for *S. pneumoniae*, has grown strongly in the past four years (from $5.5m in 2012 to $35m in 2016), with much of this investment coming from firms in IDCs. SME investment has exceeded MNC investment for each of the last two years.

† SME increases or decreases refer to organisations that had funding data included in both 2015 and 2016, rather than in every year of the survey, as SME survey participation is inconsistent from year to year

SALMONELLA INFECTIONS

Salmonella infections are a group of diseases caused by the *Salmonella enterica* bacteria, and transmitted through contaminated food or drink. These include typhoid (*Salmonella* Typhi) and paratyphoid fever (*Salmonella* Paratyphi A, B or C), collectively referred to as enteric fever (which affect humans); and thousands of serotypes that are non-typhoidal, referred to as non-typhoidal *Salmonella* (NTS), which affect both humans and animals.[85]

Salmonella infections are more common where there is dirty water and poor sanitation or hygiene. Symptoms can include fever, malaise, headache, constipation or diarrhoea, and an enlarged spleen and liver. Occasionally rose-coloured spots appear on the chest.[86] In the case of typhoid fever, a small percentage of people can recover but still carry and spread the bacteria for as long as a year after infection. Diagnosis of *Salmonella* infections may require a blood, stool or bone marrow sample.

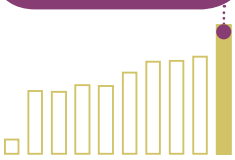
According to the IHME Global Burden of Disease study, *Salmonella* infections were the eighth highest cause of mortality and the sixth highest cause of morbidity of all the G-FINDER neglected diseases in 2015, resulting in 265,947 deaths and 18 million DALYs in developing countries.[2]

Medicines exist to treat enteric fever, however data from endemic regions show antimicrobial resistance is increasing, rendering treatment ineffective.[87] Therefore, there is a need for more efficacious drugs including those suitable for children. There are currently two safe and effective vaccines to prevent typhoid, however more suitable vaccines are required that are appropriate for HIV coinfection or children under the age of two.[88,89] Paratyphoid fever is increasingly causing most enteric fever in Asia, however despite this there are no vaccines that specifically target paratyphoid fever;[90] nor any bivalent vaccines that target both typhoid and paratyphoid fever.[91]

There are some bivalent vaccines in development: the most advanced product is O:2-TT + Vi-TT, however this candidate has not progressed in the past five years. For typhoid, there are several vaccines in the pipeline. The most advanced is a conjugate typhoid vaccine (Typbar TCV) that was licensed in India in 2013 based on immunogenicity data. In October 2017, following a Typbar TCV Phase IIb clinical trial using a controlled human infection model,[92,93] the WHO's Strategic Advisory Group of Experts (SAGE) on Immunization recommended the introduction of typhoid conjugate vaccines for infants and children over six months of age as a single dose in typhoid endemic countries.[94]

For NTS, antibiotics are only recommended for high-risk individuals such as young children, elderly people and immunocompromised patients. There is currently no NTS vaccine available. There are several NTS vaccine candidates in development, although they are all are currently in the pre-clinical stage or earlier.[95]

$91.5 MILLION



TOTAL SPEND ON SALMONELLA R&D IN 2016

OF GLOBAL R&D FUNDING

BASIC RESEARCH	IN SCOPE
DRUGS	IN SCOPE
VACCINES (PREVENTIVE)	IN SCOPE
VACCINES (THERAPEUTIC)	OUT OF SCOPE
DIAGNOSTICS	IN SCOPE
VCPs	OUT OF SCOPE

Global funding for *Salmonella* infections R&D in 2016 was $91m, which was the highest reported level of investment since the start of the G-FINDER survey. After three years of stable funding, investment by regular survey participants (YOY funders) increased considerably in 2016 (up $21m, 32%) to a total of $86m. Irregular survey participants reported the remaining $5.9m.

More than three-quarters of all *Salmonella* R&D funding in 2016 was for typhoid and paratyphoid fever ($71m, 78%), with only $4.7m (5.1%) going to NTS. Most of the overall YOY funding increase was for typhoid and paratyphoid fever (up $16m, 29%) although funding for NTS also increased (up $0.3m, 12%) after investment in this area halved in 2015.

Basic research received half ($45m, 50%) of all *Salmonella* R&D funding in 2016, with vaccine development receiving most of the remainder ($37m, 40%). Almost all of the vaccine funding was for typhoid and paratyphoid fever ($35m, 94% of vaccine funding), with comparatively little investment in NTS vaccine R&D ($0.4m, 1.1% of vaccine funding). As in previous years, only a small proportion of total funding was for diagnostics ($4.2m, 4.6%) and drugs ($3.8m, 4.1%).

YOY funding for *Salmonella* R&D increased across the board, with the largest increase for vaccine development (up $11m, 40%), mainly due to additional SME investment (up $9.5m, 89%). Funding for basic research increased by $7.1m (up 22%), driven by increased investment in basic research by the US NIH (up $6.8m, 32%), which was also the driving force behind the smaller increases in funding for drugs (up $1.3m, 51%) and diagnostics (up $0.7m, 21%).

Table 13. Salmonella R&D funding 2016 (US$ millions)

Disease	Basic research	Drugs	Vaccines (preventive)	Diagnostics	Total	%
Typhoid and paratyphoid fever (S. Typhi, S. Paratyphi A)	31	3.0	35	2.8	71	78
Non-typhoidal *S. enterica* (NTS)	3.0	0.5	0.4	0.8	4.7	5.1
Multiple *Salmonella* infections	11	0.3	1.9	0.6	15	17
Total	45	3.8	37	4.2	91	100

Almost two-thirds of all *Salmonella* R&D funding in 2016 was for basic and early stage research ($58m, 63%), with a further third going to clinical development and post registration studies ($29m, 31%). A relatively small amount of funding was not allocated to a specific product or R&D stage ($5.3m, 5.8%). However, the R&D focus for each product was slightly different, with more than two-thirds of funding for vaccine R&D going to clinical development ($25m, 68%), reflecting the progression of conjugate typhoid vaccine candidates through the pipeline. Conversely, investment in *Salmonella* drug R&D was predominantly focused on the discovery and pre-clinical stages ($3.3m, 87%), and was entirely funded by the US NIH.

The top 12 funders accounted for almost all ($89m, 98%) of total funding for *Salmonella* R&D in 2016, with 82% of total investment ($75m) provided by only three funders – the US NIH, industry and the Gates Foundation. Industry investment ($24m, 26%) was the highest recorded since the start of the G-FINDER survey, reflecting the clinical development of conjugate typhoid vaccine candidates. After small funding decreases in 2015, both industry (up $10m, 71%) and the US NIH (up $9.7m, 33%) increased their investment in *Salmonella* R&D considerably in 2016. Relatively small increases in investment by Inserm (up $1.1m, having not funded *Salmonella* before) and the Swiss National Science Foundation (SNSF, up $0.2m, 36%) meant they entered the top 12 funders. The Chilean National Fund for Scientific and Technological Development (FONDECYT, down $0.1m, -0.2%) and Swedish Research Council (down $0.3m, -78%) dropped out of the top 12. Funding from the Gates Foundation was essentially steady (up $0.3m, 2.2%).

Table 14. Top Salmonella R&D funders 2016

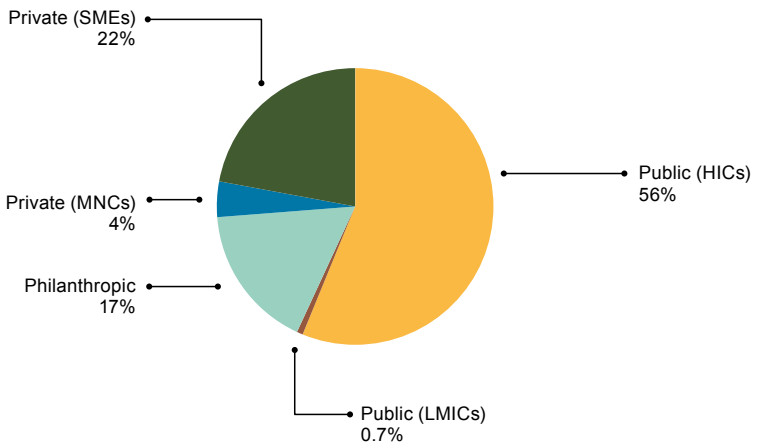
Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
US NIH	9.5	24	30	32	26	35	32	31	29	39	42
Aggregate industry	-	14	3.9	3.3	5.0	4.5	10	16	14	24	26
Gates Foundation	-	-	1.9	3.8	4.5	5.4	9.8	7.0	13	13	14
Wellcome Trust	-	0.9	1.8	2.5	4.3	5.0	4.6	3.7	3.3	2.9	3.2
SFI						0.4	0.4	-	2.1	2.1	2.3
UK MRC	0.8	1.1	0.8	0.6	1.5	1.2	1.3	1.8	2.2	2.0	2.2
Institut Pasteur	-	1.3	1.5	1.4	2.2	1.4	1.6	1.9	1.7	1.9	2.0
German DFG	-		0.5	1.2	1.2	0.9	1.2	1.8	0.4	1.8	1.9
Inserm	-	-	-	-	-	-	-	-	-	1.1	1.2
French ANR		0.5	-	-	-	-	1.6	-	0.6	1.0	1.1
Australian NHMRC	-	0.5	0.5	0.5	0.1	0.3	0.5	0.7	0.3	0.7	0.8
Swiss SNSF				-	0.7	0.7	-	0.8	0.5	0.6	0.7
Subtotal of top 12^	10	44	44	48	47	57	65	65	68	89	98
Disease total	10	45	44	49	48	58	66	66	69	91	100

^ Subtotals for 2007-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016
- No reported funding
Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

As in previous years, public funders accounted for just over half ($52m, 57%) of all *Salmonella* R&D funding in 2016; most of this came from HICs ($51m, 99%), largely from the US NIH ($39m, 76% of HIC funding). Industry invested a further quarter ($24m, 26%) of total funding, with this mainly coming from SMEs ($20m, 84% of industry funding) rather than MNCs ($3.8m, 16%). The philanthropic sector provided the remaining $15m (17% of all funding for *Salmonella* R&D in 2016).

The public sector saw the highest YOY increase in *Salmonella* funding (up $12m, 33%), which was driven by the US NIH. After a halt in industry funding growth in 2015, investment increased once again in 2016 (up $10m, 71%) to a historically high level. As in previous years, this increase was driven by additional investment by Indian SMEs (up $9.5m, 89%). Philanthropic sector funding fell slightly in 2016 (down $0.7m, -4.2%), following an increase the previous year.

Figure 16. Salmonella R&D funding by sector 2016



A decade of investment in *Salmonella* R&D

- Global funding for *Salmonella* R&D has increased markedly over the past decade. From just $10m in 2007, and $45m in 2008 when the category was expanded to also include non-typhoidal *Salmonella enterica*, total investment reached a record high of $91m in 2016. All of this growth was driven by investment in typhoid/paratyphoid, which saw a seven-fold increase over the decade, with funding for NTS actually falling (from $16m in 2008 to just $4.7m in 2016).
- The number of organisations investing in *Salmonella* R&D also increased over the course of the decade, from just three in 2007 to 30 in 2016.
- While public funders have always provided the backbone for *Salmonella* R&D funding, and were the main driver of increased funding over the decade, funding from the philanthropic sector steadily increased over the decade, and SME investment has grown rapidly in the last 2-3 years.

HELMINTH INFECTIONS (WORMS AND FLUKES)

Helminths are parasitic worms and flukes that can cause disease in humans. The most common mode of transmission to humans is through ingesting or coming into contact with contaminated food, water, or soil. Helminth infections transmitted in this manner include ancylostomiasis and necatoriasis (hookworm), ascariasis (roundworm), trichuriasis (whipworm) and strongyloidiasis (intestinal roundworms) – collectively referred to as soil-transmitted helminths – as well as taeniasis/cysticercosis (tapeworm) and schistosomiasis (bilharziasis, also known as snail fever). Other helminth infections are transmitted by bites of blood-sucking arthropods: these include lymphatic filariasis, which is transmitted by mosquitoes, and river blindness (onchocerciasis), which is transmitted by the black fly.

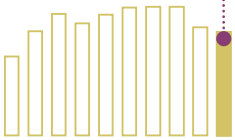
Adult worms can live in the intestines and other organs, causing malnutrition and impaired mental development (hookworms), or progressive damage to the bladder, ureter and kidneys (schistosomiasis). Onchocerciasis is a major cause of blindness in many African and some Latin American countries, while lymphatic filariasis can cause painful, disfiguring swelling of the scrotum (hydrocele) and limbs (elephantiasis).

According to the IHME Global Burden of Disease study, helminth infections were the eleventh highest cause of mortality and the ninth highest cause of morbidity of all the G-FINDER neglected diseases in 2015, resulting in 7,443 deaths and 9.5 million DALYs in developing countries.[2]

There are currently no licensed vaccines for any of the helminth infections. Instead, treatment and prevention relies predominantly on annual or twice-yearly large-scale mass drug administration programmes.[96] The variable efficacy of available drugs and the need to control transmission means that these treatment programmes must continue for many years, increasing the risk of emerging drug resistance.[97] New and more effective drugs are needed for many helminth infections, as are paediatric formulations of some existing drugs. Current diagnostic products for detection of some helminths are outdated or complex; new and effective diagnostics that can measure infection intensity and detect drug resistance are needed.[97]

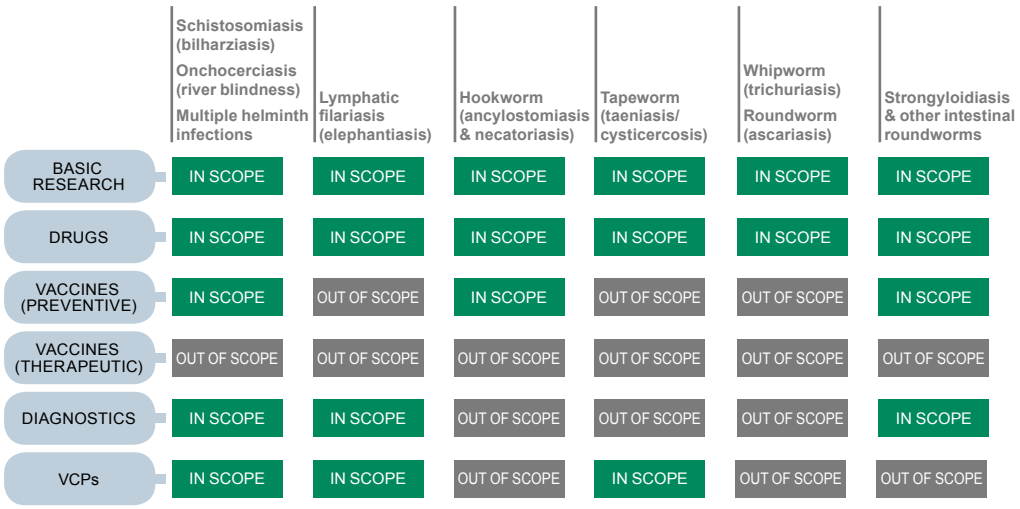
There are several schistosomiasis vaccines in development, the most advanced is Bilhvax in Phase III.[98] Two vaccine candidates against human hookworm infection are in Phase I, and two vaccines against onchocerciasis are in pre-clinical development.[99,100] Three drug candidates for helminth infections have completed or are in Phase III clinical trials: moxidectin for onchocerciasis, Co-Arinate FDC for schistosomiasis and oxantel pamoate for whipworm.[101,102] An orodispersible praziquantel tablet for schistosomiasis for children from three months to six years old is in Phase II trials.[103] There are several diagnostic tests in development for helminth infections, including the Ov16/Wb123 biplex rapid test, a dual detection point-of-care test for onchocerciasis and lymphatic filariasis currently in field evaluation;[104] and the UCP-LF CAA assay to diagnose schistosomiasis in low-prevalence settings is in clinical development.[105]

$74.6 MILLION



TOTAL SPEND ON HELMINTH R&D IN 2016

OF GLOBAL R&D FUNDING



Total funding for helminth infections R&D in 2016 was $75m. Investment by regular survey participants (YOY funders) fell (down $3.9m, -5.5%) for the third year in a row, to $67m. Irregular participants contributed the remaining $7.4m.

A little under two-thirds (60%) of all funding for helminth infection R&D in 2016 was invested in just three diseases: schistosomiasis ($18m, 25%), lymphatic filariasis ($16m, 21%) and onchocerciasis ($10m, 14%), which collectively received $44m. All other helminth infections received less than $4.0m each. The overall YOY decrease for helminths was driven by a drop in funding for onchocerciasis (down $3.4, -28%), which was partly due to reduced diagnostics investment from the Gates Foundation to PATH (down $2.1m, -82%) following the conclusion of evaluation studies for the Ov-16 rapid diagnostic test. Funding for hookworm (down $2.0m, -34%) and schistosomiasis (down $1.3m, -7.2%) also declined. Relatively small funding increases were seen for lymphatic filariasis (up $1.7m, 14%), due to increased investment in basic research by the US NIH and US DOD, tapeworm (up $0.9m, 33%) and whipworm (up $0.5m, 33%).

Table 15. Helminth R&D funding 2016 (US$ millions)

Disease	Basic research	Drugs	Vaccines (preventive)	Diagnostics	Vector control products	Unspecified	Total	%
Schistosomiasis (bilharziasis)	10	2.9	2.2	1.4	0.1	1.6	18	25
Lymphatic filariasis (elephantiasis)	6.6	7.3		0.1	<0.1	1.8	16	21
Onchocerciasis (river blindness)	1.3	7.4	0.4	0.6	<0.1	0.5	10	14
Hookworm (ancylostomiasis & nectoriasis)	0.3	0.8	2.7			<0.1	3.9	5.2
Tapeworm (taeniasis/ cysticercosis)	1.8	1.9			-	-	3.6	4.8
Whipworm (trichuriasis)	0.9	0.9				-	1.8	2.4
Strongyloidiasis & other intestinal roundworms	0.7	0.5	<0.1	0.2		-	1.4	1.9
Roundworm (ascariasis)	0.8	0.4				-	1.3	1.7
Multiple helminth infections	7.0	8.8	2.3	-	-	<0.1	18	24
Total	29	31	7.7	2.5	0.1	3.8	75	100

- No reported funding
Category not included in G-FINDER

Investment for helminth R&D was concentrated on drug development ($31m, 41%) and basic research ($29m, 40%), although it should be noted that these are the only two product areas that are included for *all* helminth infections. All other product areas received 10% of funding or less: preventive vaccines ($7.7m, 10%), diagnostics ($2.5m, 3.3%) and vector control products ($0.1m, 0.1%). Drug R&D (up $0.9m, 3.4%) was the only product area to receive increased funding in 2016, with investment declining in all other product areas. Funding for diagnostics saw the largest YOY drop (down $3.8m, -61%) partly due to for the conclusion of evaluation studies for the onchocerciasis diagnostic test noted earlier. Vaccine investment also declined (down $1.0m, -15%).

More than two-thirds of all R&D funding for helminth infections in 2016 was focused on basic and early stage research ($51m, 69%), while a quarter was for clinical or field development and post registration studies ($19m, 25%). Remaining funding ($4.6m, 6.2%) was not allocated to a specific product or R&D stage. Funding for some helminth infections was more heavily focused on basic and early stage research, particularly schistosomiasis (82%), and tapeworm (77%), while 81% of hookworm funding was for clinical development.

The top 12 funders provided 97% of all funding for helminth R&D in 2016. The top three funders – the US NIH, Gates Foundation and industry – were responsible for over three-quarters ($58m, 77%) of total funding, which was the highest share ever recorded by the G-FINDER survey. Two-thirds of the top 12 funders reduced their investment in 2016, with the largest decreases coming from industry (down $4.1m, -42%) and the EC (down $1.3m, -27%). The Dutch DGIS also fell out of the top 12, with no reported helminths R&D funding in 2016. The top funder of helminth R&D, the US NIH, was responsible for the largest increase in funding (up $2.7m, 9.3%).

Table 16. Top helminth R&D funders 2016

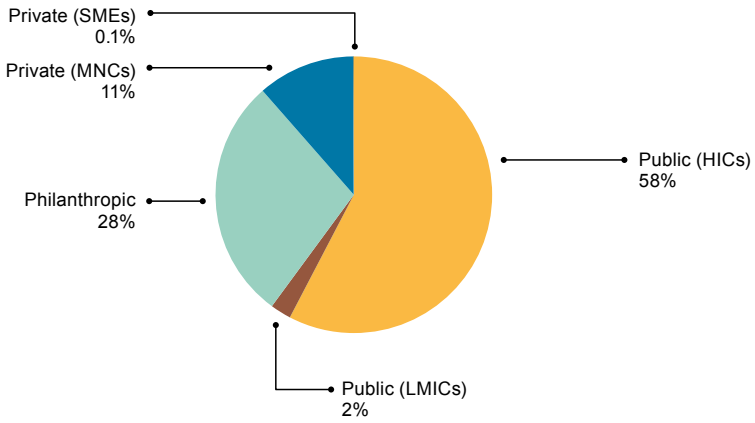
Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
US NIH	33	27	33	35	28	38	30	30	29	31	42
Gates Foundation	8.5	25	19	17	22	20	22	24	18	18	24
Aggregate industry	0.8	5.6	10	6.9	8.0	4.2	8.5	15	12	8.5	11
Wellcome Trust	2.7	3.4	4.4	4.8	7.3	5.6	6.7	4.4	3.6	3.5	4.7
EC	3.9	2.9	2.7	7.3	6.2	7.1	6.8	6.5	4.7	3.4	4.6
Texas Children's Hospital					0.1	0.9	1.3	1.2	1.5	1.5	2.1
German DFG	-		6.3	0.5	0.6	2.5	2.8	-	2.0	1.4	1.8
Indian ICMR		0.4	0.4	1.1	1.2	1.4	1.6	1.4	1.3	1.1	1.5
UK MRC	0.9	1.2	1.0	1.0	3.0	2.0	1.8	2.5	1.3	1.1	1.5
Inserm	0.3	0.5	1.9	<0.1	1.8	1.9	2.2	1.5	1.2	1.0	1.3
Australian NHMRC	1.2	1.8	2.0	2.5	1.3	1.1	0.7	0.8	0.4	0.8	1.1
Swiss SNSF		0.3	0.3	0.1	0.5	0.5	0.3	0.3	0.2	0.7	1.0
Subtotal of top 12^	56	71	83	78	82	87	88	90	76	72	97
Disease total	57	75	87	81	87	92	93	93	78	75	100

^ Subtotals for 2007-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016
- No reported funding
Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

Nearly two-thirds of all funding for helminth R&D in 2016 came from the public sector ($45m, 60%), with the remainder provided by the philanthropic sector ($21m, 28%) and industry ($8.5m, 11%). The vast majority of public funding came from HICs ($43m, 96%). Industry funding was almost entirely provided by MNCs ($8.5m, 99%), with SMEs investing less than $0.1m in 2016.

Industry funding fell significantly in 2016 (down $4.1m, -42%), due to reduced MNC investment in helminth drug R&D, while public (up $1.1m, 2.8%) and philanthropic (down $0.9m, -4.2%) funding remained relatively steady.

Figure 17. Helminth R&D funding by sector 2016



A decade of investment in helminth infections

- Annual global funding for helminth R&D grew steadily over most of the last decade, from $57m in 2007 to a peak of $93m in 2014, but has fallen off slightly since then.
- The US NIH and the Gates Foundation have been the two largest funders of helminth R&D, collectively contributing more than half of total global funding every year, and nearly two-thirds (62%) of all funding over the decade.
- Most of the growth in helminth R&D funding over the decade has been for drug development, which has steadily increased from negligible levels in 2007 to become the highest funded product area in 2016.

Note: The G-FINDER survey does not include loans but would like to acknowledge a particular project which has taken an innovative approach to financing neglected disease R&D. Medicines Development for Global Health (MDGH), an Australian not for profit company, is seeking to register moxidectin, an existing veterinary drug, for the treatment of onchocerciasis. An approval from the FDA could make it eligible for a priority review voucher (PRV). On the basis of the potential sale of the PRV, MDGH has secured a $10m loan from the Global Health Investment Fund for the registration process.

HEPATITIS C

Hepatitis C is an infectious disease caused by the blood-borne hepatitis C virus (HCV), primarily affecting the liver. HCV causes both acute and chronic infection, with symptoms in the acute phase including fever, fatigue and jaundice.[106] However, up to 80% of acute cases are asymptomatic, meaning that many HCV infections will go undetected until chronic disease develops, sometimes decades later. Although 20-40% of acute infections resolve spontaneously without treatment, the remaining 60-80% of people will progress to chronic infection.[106] Without treatment, chronic hepatitis C is a lifelong disease which can lead to serious liver damage (cirrhosis and fibrosis) and hepatocellular carcinoma (liver cancer), both of which can be life threatening.[106]

There are six main genotypes of HCV. Although hepatitis C is a globally-prevalent disease, three genotypes (genotypes 4, 5 and 6) disproportionately affect developing countries, while having a low prevalence in high income countries. As a result, these genotypes are neglected from an R&D perspective. Developing country-specific R&D investment for hepatitis C genotype 4 was included in G-FINDER in 2014, and genotypes 5 and 6 were added in 2015. Genotype 4 is most prevalent in Central Africa and the Middle East, genotype 5 in Southern Africa, and genotype 6 in South-East Asia.[107]

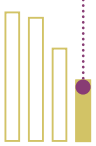
Reliable genotype-specific estimates of morbidity and mortality do not exist. According to the IHME Global Burden of Disease study, hepatitis C (all genotypes) was the sixth highest cause of mortality and the eighth highest cause of morbidity of the thirteen G FINDER neglected disease categories covered by IHME, resulting in 345,600 deaths and 9.6 million DALYs in developing countries in 2015.[2] The WHO Global Health Estimates present a slightly lower mortality figure, estimating that hepatitis C was responsible for 284,946 deaths in developing countries in 2015.[3]

A number of new direct-acting antiviral (DAA) drugs have been approved since 2013. DAA-based regimens are more effective, require a shorter duration of treatment, and have fewer side effects than previous interferon- and ribavirin-based treatments. While appropriate for most patients (including those with HIV co-infection) and covering multiple genotypes, DAA-based regimens are expensive, and access remains limited in developing countries despite discounted pricing. More research is also needed to support the use of DAA-based regimens in developing country populations. There are several multi- or pan-genotypic DAA-based regimens in late stage development, including uprifosbuvir/ruzasvir/grazoprevir; odalasvir/AL-335/SIM; and sofosbuvir/ravidasvir.[108]

There is also a need for hepatitis C diagnostic tests that are affordable, simple to use in developing country contexts,[109] and can differentiate between genotypes. WHO has prequalified six hepatitis C diagnostic tests, including five RDTs and one viral load test, however none of the prequalified RDTs is able to differentiate between genotypes.[110]

There is no vaccine for hepatitis C, although there are some pan-genotypic candidates in early stage development, such as the Burnet Institute's Delta3 candidate.[111]

$22.4 MILLION

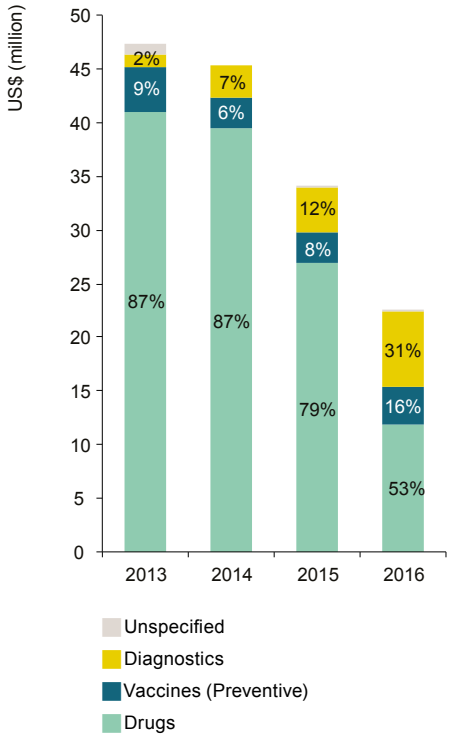


TOTAL SPEND ON HEPATITIS C R&D IN 2016

OF GLOBAL R&D FUNDING

BASIC RESEARCH	OUT OF SCOPE
DRUGS	RESTRICTED
VACCINES (PREVENTIVE)	IN SCOPE
VACCINES (THERAPEUTIC)	OUT OF SCOPE
DIAGNOSTICS	IN SCOPE
VCPs	OUT OF SCOPE

Figure 18. Hepatitis C (genotypes 4, 5 & 6) R&D funding by product type 2013-2016



In order to exclude commercially-driven R&D investment targeting HIC markets, G-FINDER only tracks investment in R&D for hepatitis C that is specifically focused on the genotypes that disproportionately affect developing countries (genotypes 4, 5, 6); or developing country-specific R&D investment in multi- or pan-genotypic technologies.

Global funding for developing country-specific hepatitis C R&D in 2016 was $22m. Almost all of this was reported by regular survey participants (YOY funders), with only $0.7m coming from irregular survey participants. YOY funding dropped significantly for the second year in a row (down $12m, -36%), to the lowest level since hepatitis C was included in the G-FINDER survey in 2013.

More than half of all hepatitis C R&D funding in 2016 was for drug development ($12m, 53%), followed by diagnostics ($7.0m, 31%) and vaccine development ($3.5m, 16%). Funding for hepatitis C drug R&D fell markedly for the second year in a row (down $15m, -56%), entirely due to reduced industry investment (down $15m, -68%) as several late stage clinical trials reached completion. Funding for diagnostics increased (up $2.7m, 67%), on the back of the first reported SME investment in hepatitis C diagnostic development ($3.5m). Funding for vaccine development increased modestly (up $0.3m, 12%).

A little under half ($9.4m, 42%) of all funding for hepatitis C R&D in 2016 was for clinical development and post registration studies, with a further $6.3m (28%) for early stage research. Remaining funding ($6.6m, 30%) was not allocated to a specific product or R&D stage. However, the focus within each product area was slightly different, reflecting the state of the respective R&D pipelines as well the G-FINDER scope. Almost one-fifth ($2.3m, 19%) of investment in drug development was for Phase IV research – the highest proportion of any neglected disease – reflecting the advanced pipeline and the fact that most early stage drug R&D investments are not developing country-specific, and therefore outside the G-FINDER scope. In contrast, investment in vaccine R&D was overwhelmingly focused on the discovery and pre-clinical stages ($2.9m, 82%) reflecting the much less advanced pipeline, and the fact that developing country-specific vaccine R&D investment is largely limited to public sector science and technology agencies or research institutes.

Despite halving its investment, industry remained the top funder of hepatitis C R&D in 2016, accounting for just under half ($10m, 46%) of total funding. Remaining funding came primarily from the French National Agency for Research on AIDS and Viral Hepatitis (ANRS, $4.5m, 20%), the US NIH ($4.2m, 19%) and the EC ($2.1m, 9.3%). The drop in industry investment (down $11m, -52%) was by far the largest funding decrease, with the next largest coming from the EC (down $0.7m, -26%). The largest increase in hepatitis C funding in 2016 came from the French ANRS (up $0.4m, 11%), after a significant drop the previous year.

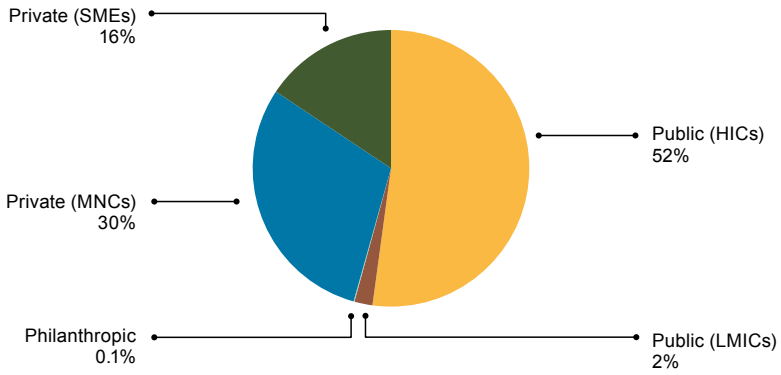
Table 17 . Top hepatitis C (genotypes 4, 5 &6) R&D funders 2016

Funder	US$ (millions) 2013	2014	2015	2016	2016 % of total
Aggregate industry	28	26	21	10	46
French ANRS	1.8	8.6	4.1	4.5	20
US NIH	11	6.6	4.7	4.2	19
EC	0.6	2.8	2.8	2.1	9.3
UK MRC	0.4	0.4	0.4	0.4	1.7
Brazilian FINEP		-	0.2	0.2	1.0
Burnet Institute	0.1	0.1		0.2	1.0
Austrade				0.1	0.7
Australian ACH[2]	<0.1	0.2		0.1	0.6
Thai GPO	0.1	<0.1	0.2	0.1	0.5
Indian DBT	1.1	<0.1	0.4	0.1	0.5
Wellcome Trust	0.1	0.1	<0.1	<0.1	<0.1
Subtotal of top 12^	47	45	34	22	100
Disease total	47	45	34	22	100

^ Subtotals for 2013-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016
- No reported funding
Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

The public sector provided more than half ($12m, 54%) of all funding for hepatitis C R&D in 2016, with industry responsible for almost all of the remainder ($10m, 46%); this was the first time since hepatitis C was included in G-FINDER that the public sector invested more than industry. However, this was not due to an increase in public sector funding – which in fact dropped slightly (down $0.9m, -7.7%) – but rather the substantial decrease in industry funding. This industry drop came entirely from MNCs (down $15m, -68%), with SMEs reporting investment in hepatitis C (totalling $3.5m) for the first time.

Figure 19. Hepatitis C (genotypes 4, 5 & 6) R&D funding by sector 2016



Investment in hepatitis C (genotypes 4, 5 & 6) R&D since 2013

- Global funding for hepatitis C R&D has more than halved, from $47m in 2013 to $22m in 2016, with the decline in funding accelerating in the last two years.
- For most of the past four years, hepatitis C funding was dominated by industry, only to be overtaken by public funding in 2016. Philanthropic funding, on the other hand, was essentially absent.
- Industry, and to a lesser extent the public sector, have decreased their investment in hepatitis C drug R&D over the past four years. As drugs have been the main focus of hepatitis C investment, this decline drove the overall drop in funding. Funding for diagnostics steadily increased over the past decade, but reached a high of only $7.0m in 2016.

LEPROSY

Leprosy, also known as Hansen's disease, is caused by *Mycobacterium leprae* and is transmitted via air droplets from the nose or mouth of infected people. Leprosy mainly affects the skin and nerves and has an incubation period that can be as long as 20 years.[112] The disease is curable with multidrug therapy using a combination of rifampicin, clofazimine and dapsone (for multibacillary leprosy), or rifampicin and dapsone (for paucibacillary leprosy).[112] However, if left untreated, leprosy can cause nerve damage, muscle weakness and permanent impairments.

According to the IHME Global Burden of Disease study, leprosy was the thirteenth highest cause of morbidity of all the G-FINDER neglected diseases, resulting in 30,797 DALYs in developing countries in 2015.[2] IHME estimates do not attribute any mortality to leprosy, but according to the WHO Global Health Estimates, leprosy was responsible for 15,893 deaths in developing countries in 2015.[3]

Diagnosis of leprosy is primarily based on identifying key clinical features of infection, meaning that asymptomatic early-stage cases are often missed or diagnosed late, leading to continued disease transmission. Elimination of leprosy will likely need new and improved diagnostics capable of identifying asymptomatic cases, as well as all symptomatic forms (paucibacillary, borderline tuberculoid, borderline, borderline lepromatous or multibacillary) of the disease.[113] The current drug regimen for leprosy has been standard treatment for 30 years and, although highly effective, it requires 6-24 months of treatment.[114] Further research is needed to improve and simplify drug regimens, and to provide products for nerve function management.[114, 115]

Bedaquiline, an antibiotic approved for the treatment of MDR-TB, has been found to be effective in the treatment of leprosy in animal models,[116] and may hold some promise. The Infectious Disease Research Institute (IDRI) is currently developing rapid diagnostic tests for leprosy.[113, 117]

$11.1 MILLION

TOTAL SPEND ON LEPROSY R&D IN 2016

BASIC RESEARCH	IN SCOPE
DRUGS	IN SCOPE
VACCINES (PREVENTIVE)	OUT OF SCOPE
VACCINES (THERAPEUTIC)	OUT OF SCOPE
DIAGNOSTICS	IN SCOPE
VCPs	OUT OF SCOPE

Global funding for leprosy R&D in 2016 was $11m, meaning that funding levels were essentially unchanged from the preceding year. A little under two-thirds of this funding ($6.6m, 59%) was for basic research, with just $0.6m (5.2%) for product development, reflecting the paucity of the R&D pipeline for leprosy. Diagnostics ($0.4m, 3.5%) received marginally more than drugs ($0.2m, 1.7%). The remaining third ($3.9m, 35%) of all R&D funding for leprosy was for unspecified R&D.

Table 18. Leprosy R&D funding by product type 2007-2016

Product \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
Basic research	4.7	6.1	7.0	5.0	7.3	10	12	7.0	5.5	6.6	59
Diagnostics	0.7	0.6	1.5	1.4	1.3	1.5	0.8	0.2	0.8	0.4	3.5
Drugs	<0.1	0.8	0.9	1.1	0.3	0.8	0.2	<0.1	0.3	0.2	1.7
Unspecified	0.7	3.4	2.5	2.8	-	2.8	0.1	3.5	4.4	3.9	35
Total	6.2	11	12	10	8.9	15	13	11	11	11	100

- No reported funding

Almost two-thirds of leprosy funding went to basic and early stage research ($6.9m, 62%), with a small amount going to clinical development and post registration studies ($0.2m, 1.6%). More than a third of funding was not allocated to a specific product or R&D stage ($4.0m, 36%), however the vast majority of this was core funding given to the Indian National JALMA Institute for Leprosy and Other Mycobacterial Diseases, which typically conducts basic and early stage research, meaning that this type of research actually likely accounted for as much as 95% of all leprosy R&D funding.

As in previous years, the public sector made up the vast majority ($9.4m, 85%) of leprosy R&D funding, all of which came from just two public funders (the US NIH and the Indian ICMR). The philanthropic sector provided $1.3m (12%),## and the remaining $0.4m (3.3%) came from industry (all from MNCs).

Table 19. Top leprosy R&D funders 2016

Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
US NIH	2.3	3.7	6.0	3.8	4.5	11	6.0	5.7	4.3	4.8	44
Indian ICMR		3.3	2.0	3.0	2.4	0.8	3.5	3.5	4.5	3.8	35
LRI									0.5	0.5	4.5
TLMI				0.3	0.4	0.4	0.7	0.6	0.5	0.5	4.3
Aggregate industry	-	-	-	0.1	0.1	-	0.1	0.1	0.7	0.4	3.3
French ANR		-	0.5	-	-	-	-	-	-	0.2	2.1
UK MRC	-	-	-	-	-	-	-	<0.1	0.1	0.2	1.5
DAHW			<0.1	0.1	0.1	0.1	0.1	0.1	<0.1	0.1	1.0
effect:hope										0.1	1.0
CLTRF		-	-		-	-			-	0.1	0.9
Institut Pasteur	0.1	0.2	0.2	0.2	0.1	0.2	0.1	0.1	0.1	0.1	0.9
Swiss SNSF				-	-	-	-	-	-	0.1	0.8
Subtotal of top 12^	6.2	11	12	10	8.9	15	13	11	11	11	99
Disease total	6.2	11	12	10	8.9	15	13	11	11	11	100

^ Subtotals for 2007-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016
- No reported funding
Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

A decade of investment in leprosy R&D

- Although the total quantum of investment remains small, more organisations have provided funding for leprosy R&D over the past decade than for any other 'least funded disease', with a particularly high representation of charitable organisations.
- Since 2007, LMIC government funding for leprosy, as a proportion of public funding, has been far higher than for any other neglected disease. This can largely be credited to India (which has high leprosy prevalence), and Brazil.

The Leprosy Research Initiative (LRI) was established in 2014 and pools funding of its member organisations, including the Netherlands Leprosy Relief (NLR), American Leprosy Missions (ALM), the German Leprosy and Tuberculosis Relief Association (GLRA) and effect:hope (The Leprosy Mission Canada) who may have individually appeared in this report as a top leprosy funder in the past. This does therefore not imply that these individual organisations have decreased their leprosy funding, rather that they are now funding some projects through the LRI ($0.5m in 2016).

CRYPTOCOCCAL MENINGITIS

Cryptococcal meningitis is an opportunistic infection that causes inflammation of the tissue covering the brain and spinal cord. It is caused primarily by *Cryptococcus neoformans*, a microscopic and easily inhaled fungus found in the environment throughout the world. In healthy individuals, inhalation of the fungal spores rarely leads to serious illness; but for people with weakened immune systems, such as those with HIV/AIDS, cryptococcal infection (cryptococcosis) can be both serious and deadly. Cryptococcosis can affect multiple organs, but the primary site of infection is usually the lungs. Cryptococcal meningitis occurs when the infection spreads to the brain and central nervous system, with symptoms including headaches, fever, neck pain, light sensitivity and altered mental state (ranging from confusion to coma).[118] Mortality rates for cryptococcal meningitis can be as high as 70%.[119]

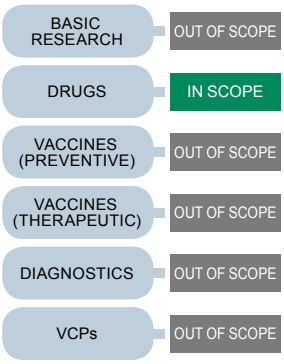
An estimated 181,100 deaths each year are attributed to HIV-associated cryptococcal meningitis infections, predominantly in sub-Saharan African countries that have a high burden of HIV/AIDS.[120] Global mortality estimates have dropped since 2009, when cryptococcal meningitis caused an estimated 624,700 deaths annually.[121] The reduction in deaths was primarily in high income countries, through access to antiretroviral therapy, advances in rapid point-of-care diagnosis[122] and pre-emptive antifungal therapy for people with HIV/AIDS.[120]

Cryptococcal meningitis can be effectively treated with medicines such as amphotericin B (AmB) and flucytosine, but these are poorly suited to developing country use. AmB is both expensive and requires administration at a hospital, and flucytosine requires careful blood monitoring. As a result, in developing countries cryptococcal meningitis is usually treated with fluconazole, which is only partially effective.[123] Affordable, efficacious drugs, adapted for resource poor settings, are needed. A new long-acting azole-like compound (VT-1129) is currently in Phase I and received orphan drug status from the US FDA in 2014.[124] Several oral formulations of AmB are in early stage development.[125]

Accurate rapid diagnostic tests for cryptococcal infection are available and appropriate for use in developing country settings; therefore diagnostics are excluded from the G-FINDER scope.

$5.6 MILLION

TOTAL SPEND ON CRYPTOCOCCAL MENINGITIS R&D IN 2016



Global investment in cryptococcal meningitis R&D in 2016 was $5.6m.

Drug R&D is the only product for cryptococcal meningitis included in the G-FINDER scope. More than two-thirds of all investment ($3.9m, 68%) was for discovery and pre-clinical R&D, with a further $1.1m (19%) for clinical development, and $0.7m (12%) not allocated to a specific R&D stage.

Just five organisations were the source of all reported global investment in cryptococcal meningitis R&D in 2016. Two public HIC organisations, the US NIH and the UK MRC, provided almost all ($5.4m, 96%) of this funding. The French ANRS, another public organisation, reported funding for the first time ($0.2m, 2.8%) making it the only new funder for cryptococcal meningitis R&D since 2013. The remaining investment came from two philanthropic funders: the Wellcome Trust ($0.1m, 1.4%) and the Mérieux Foundation (<$0.1m, 0.2%).

Public HIC organisations accounted for essentially all (98%) cryptococcal meningitis R&D investment for 2016.

Table 20. Cryptococcal meningitis R&D funders 2016

Funder	US$ (millions)				2016 % of total
	2013	2014	2015	2016	
US NIH	1.4	4.2	3.5	4.3	76
UK MRC	1.3	1.2	2.0	1.1	20
French ANRS	-	-	-	0.2	2.8
Wellcome Trust	0.3	<0.1	0.1	0.1	1.4
Mérieux Foundation	<0.1	<0.1	<0.1	<0.1	<0.1
Australian NHMRC	0.1	0.1	-	-	-
Disease total	3.1	5.6	5.6	5.6	100

- No reported funding

Investment in cryptococcal meningitis R&D since 2013

- Since G-FINDER began tracking cryptococcal meningitis R&D in 2013, funding has been essentially stable, with a total of $5.6m contributed each year for the past three years.
- Almost all (98%) of the reported investment in cryptococcal meningitis R&D since its inclusion in G-FINDER has come from the public sector, with philanthropic organisations providing the remainder. There has been no reported investment by industry.

BURULI ULCER

Buruli ulcer, also known as Bairnsdale ulcer, is a chronic disease caused by *Mycobacterium ulcerans*. In developing countries, children under the age of 15 are at greatest risk. While the exact transmission mode is unknown, living around marshy areas with stagnant or slow-moving water can be a risk factor in endemic regions. Buruli ulcer usually appears as a painless lump or nodule that can later develop into an ulcer, usually on the arms or legs. *M. ulcerans* produces a toxin known as mycolactone, which causes tissue damage and can depress the immune response.[126] As a result, co-infection with HIV can make Buruli ulcer more complex to address.[126] If left undiagnosed or untreated, *M. ulcerans* can lead to skin, tissue or bone damage, with amputation or surgery sometimes required.

Buruli ulcer occurs in more than 30 countries, predominantly in sub-Saharan Africa. In 2015, 11 developing countries reported 1,924 new cases to the WHO.[127]

Treatment options including antibiotics and surgery are effective if the disease is diagnosed early, however current diagnostics are both costly and complex.[128] Combination antibiotics (oral and injectable) are effective but cumbersome, as they must be given daily for eight weeks. Treatment failure and resistance are emerging issues, highlighting the need for new drugs that are less complicated to administer or can be given for a shorter period. There are few new drug candidates in development for Buruli ulcer.

The BCG vaccine (designed for TB) provides short-term protection, but this is insufficient. Buruli ulcer vaccine development is in the very early stages of research.[129]

FIND is developing several Buruli ulcer diagnostics in collaboration with the WHO and other partners. These include an instrument-free point-of-care test, and tools that can be used at peripheral health centers.[130]

$2.8 MILLION

TOTAL SPEND ON BURULI ULCER R&D IN 2016

BASIC RESEARCH	IN SCOPE
DRUGS	IN SCOPE
VACCINES (PREVENTIVE)	IN SCOPE
VACCINES (THERAPEUTIC)	OUT OF SCOPE
DIAGNOSTICS	IN SCOPE
VCPs	OUT OF SCOPE

Global investment in Buruli ulcer R&D in 2016 was $2.8m. The bulk of this funding was relatively evenly split between drug R&D ($1.2m, 43%) and basic research ($1.0m, 38%), while diagnostics received $0.5m (18%). No funding has been reported for vaccine R&D since 2013.

Table 21. Buruli ulcer R&D funding by product type 2007-2016

Product \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
Drugs	-	0.2	0.3	0.7	0.7	0.7	0.8	0.2	0.2	1.2	43
Basic research	1.0	1.4	1.0	1.3	0.9	1.7	3.4	1.5	0.9	1.0	38
Diagnostics	<0.1	0.1	0.3	0.7	0.3	1.0	0.7	1.2	0.4	0.5	18
Vaccines (preventive)	-	<0.1	0.2	2.0	1.9	1.9	0.8	-	-	-	-
Unspecified	1.4	0.2	0.1	0.7	2.0	0.8	0.7	0.8	0.4	0.1	1.8
Total	2.4	1.9	1.9	5.5	5.7	6.0	6.4	3.7	1.9	2.8	100

- No reported funding

The vast majority of all R&D funding for Buruli ulcer in 2016 was for basic and early stage research ($2.4m, 85%), with no reported investment in clinical development. Remaining funding was not allocated to a specific product or R&D stage ($0.4m, 15%).

All reported funding for Buruli ulcer R&D globally in 2016 came from just 11 organisations, although this was an increase from the nine organisations who provided funding in 2015. The US NIH ($1.1m, 38% of total funding) invested in Buruli ulcer R&D for the first time since 2013, and was both the largest funder and the only organisation with an investment over $1.0m. Funding from two new funders was captured for the first time; the Flemish Department of Economics, Science and Innovation (EWI) and Inserm, who contributed $0.2m and $0.1m respectively.

The majority of funding for Buruli ulcer R&D was provided by the public sector ($2.2m, 80%), with the philanthropic sector providing the remainder ($0.6m, 20%).

Table 22. Buruli ulcer R&D funders 2016

Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
US NIH	0.8	0.5	0.9	1.2	1.3	1.1	1.0	-	-	1.1	38
Institut Pasteur	0.6	0.3	0.3	0.4	0.2	0.4	0.3	0.4	0.4	0.5	18
UBS Optimus Foundation		0.1	0.1	1.0	1.8	2.0	1.5	2.2	0.4	0.4	15
Flemish EWI										0.2	8.5
French ANR		-	-	-	-	0.1	-	-	0.3	0.2	8.4
Medicor Foundation				0.4	0.1	0.2	0.2	0.2	0.4	0.1	4.4
UK MRC	-	-	-	-	-	-	0.1	0.1	0.1	0.1	3.7
Inserm	-	-	-	-	-	-	-	-	-	0.1	1.8
Australian NHMRC	0.2	0.1	0.1	0.1	0.1	0.1	-	0.1	0.1	<0.1	1.5
DAHW				-	-	<0.1	<0.1	-	-	<0.1	0.6
Wellcome Trust	-	<0.1	<0.1	<0.1	0.3	0.3	0.3	0.2	<0.1	<0.1	0.1
Volkswagen-Stiftung					0.1	<0.1	<0.1	<0.1	0.1		
Disease total	2.4	1.9	1.9	5.5	5.7	6.0	6.4	3.7	1.9	2.8	100

- No reported funding

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

A decade of investment in Buruli ulcer R&D

- Annual global investment in Buruli ulcer has more than halved since its peak in 2013, when there were a number of relatively large concurrent projects, including funding from the UBS Optimus Foundation for the Stop Buruli project and funding for basic research from the German Research Foundation (DFG).
- In 2007 there were only six funders for Buruli ulcer. The base has expanded to 11 in 2016, but the field of funders remains highly concentrated. UBS Optimus Foundation has been the most consistent funder of Buruli ulcer R&D since 2008, having invested $9.5m over the past ten years. The majority of this ($7.8m, 81%) was invested in the Stop Buruli consortium.

LEPTOSPIROSIS

Leptospirosis is an infection caused by bacteria of the genus *Leptospira*, affecting both humans and animals. The infection is transmitted to humans through contact with the urine or blood of infected animals, either directly or via contaminated water, food or soil. People who live in tropical climates, who work in flooded areas such as rice paddies and sugar cane plantations, or who work with animals are most at risk.[131] The bacteria can survive for several weeks in water or soil, and outbreaks often occur after flooding.

Diagnosis of leptospirosis can be challenging due to the non-specific symptoms of early infection, which are shared with a number of other diseases, as well as the fact that some infected individuals may remain asymptomatic. Without treatment, the infection can progress to a more severe second phase, causing meningitis, kidney and liver failure, respiratory distress, and sometimes death.

Available estimates suggest that leptospirosis is responsible for an estimated 58,900 deaths and 2.9 million DALYs globally each year, the majority of which occur in developing countries.[132] Although not directly comparable to the IHME Global Burden of Disease data (because of major differences in methodology), these estimates would rank leptospirosis as the tenth highest cause of both mortality and morbidity of all the G-FINDER neglected diseases in 2015, ahead of kinetoplastids and dengue, respectively.

Effective, appropriate drugs exist for leptospirosis, and therefore infection can be successfully treated if it is diagnosed. However accurate diagnosis of leptospirosis during the acute phase of the disease is currently only possible with sophisticated laboratory tests, which are unsuitable for remote settings. New, easy to use tests are needed that can quickly and accurately diagnose acute infection in the field. A rapid point-of-care test using chromatographic immunoassay technology is currently in development, demonstrating a sensitivity of 85% and specificity of 90% in early studies.[133]

$2.3 MILLION

TOTAL SPEND ON LEPTOSPIROSIS R&D IN 2016

BASIC RESEARCH	OUT OF SCOPE
DRUGS	OUT OF SCOPE
VACCINES (PREVENTIVE)	OUT OF SCOPE
VACCINES (THERAPEUTIC)	OUT OF SCOPE
DIAGNOSTICS	RESTRICTED
VCPs	OUT OF SCOPE

Global funding for leptospirosis R&D in 2016 was $2.3m. This was nearly double the amount invested in this disease in 2015, and the most it has ever received since it was included in the G-FINDER survey. Diagnostics are the only product area for leptospirosis included within the scope of G-FINDER.

No reported funding for leptospirosis R&D in 2016 was allocated to a specific R&D stage.

The largest funder of leptospirosis R&D in 2016 was the Indian ICMR, who reported leptospirosis R&D investment for the first time, and provided nearly half of all funding ($1.1m, 48%). The remainder was provided by two French organisations: Institut Pasteur ($1.0m, 45%); and Inserm ($0.2m, 6.9%), who also reported funding leptospirosis R&D for the first time. The US NIH, which usually provides funding for leptospirosis R&D, did not report any investment in 2016.

All funding was provided by the public sector in 2016, with HICs ($1.2m, 52%) only providing marginally more than LMICs ($1.1m, 48%).

Table 23. Leptospirosis R&D funders 2016

Funder	US$ (millions) 2013	2014	2015	2016	2016 % of total
Indian ICMR	-	-	-	1.1	48
Institut Pasteur	0.4	0.9	0.9	1.0	45
Inserm	-	-	-	0.2	6.9
US NIH	-	0.3	0.3	-	-
Colombian Colciencias		0.1	-	-	-
Disease total	0.4	1.3	1.3	2.3	100

- No reported funding

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

Investment in leptospirosis R&D since 2013

- R&D investment for leptospirosis has only been tracked by G-FINDER since 2013; during this time, global funding has grown from $0.4m to $2.3m per year.
- R&D for leptospirosis has almost exclusively been funded by the public sector, with only one small grant contributed by the philanthropic sector. Institut Pasteur has been the most consistent funder, having provided over 45% of all funding each year, and 62% of all funding for leptospirosis R&D over the last four years.

TRACHOMA

Trachoma is an infectious eye disease caused by the bacterium *Chlamydia trachomatis*. The infection can be spread by contact with infected eyes or nose discharge, including by contact from flies and shared use of clothing and towels.[134] Trachoma is common among children and in areas where there is unclean water and poor sanitation.[135] After repeat infection and without medical treatment, the eyelid can turn inwards, causing the eyelashes to rub against the eyeball, resulting in scarring, visual impairment or irreversible blindness.[135]

Trachoma is not a fatal condition but it is the leading infectious cause of blindness. According to IHME Global Burden of Disease 2015 estimates, trachoma was responsible for 278,190 DALYs in developing countries,[2] the twelfth highest cause of morbidity of G-FINDER neglected diseases.

WHO recommends a combination of interventions known as the SAFE strategy[135] for the elimination of trachoma, which is an acronym for *surgery* (which has low acceptance and high recurrence rates); *antibiotics* (including treatment with azithromycin, however over-reliance on a single drug therapy can increase the risk of drug resistance); *facial cleanliness*; and *environmental improvement* to reduce transmission.

Because of the challenges associated with successful implementation (and sustainability) of the SAFE strategy, a vaccine is needed. There are several trachoma vaccines in development, mostly in the early (pre-clinical and discovery) stages.

Clinical diagnosis of trachoma is not always reliable, and current diagnostic tests are expensive and complex.[136] Studies have shown that an antibody-based multiplex assay could be used to diagnose trachoma in low prevalence settings.[137]

$2.2 MILLION

TOTAL SPEND ON TRACHOMA R&D IN 2016

BASIC RESEARCH	OUT OF SCOPE
DRUGS	OUT OF SCOPE
VACCINES (PREVENTIVE)	IN SCOPE
VACCINES (THERAPEUTIC)	OUT OF SCOPE
DIAGNOSTICS	IN SCOPE
VCPs	OUT OF SCOPE

Note that historical figures for trachoma R&D investment by the US NIH have been amended following a review and refinement of the search terms applied to data mine NIH databases. The G-FINDER figures now exclude investment made in R&D for Chlamydia trachomatis if that work was conducted specifically to progress research into chlamydia (the sexually transmitted infection), rather than trachoma (ocular infection). Historical US NIH and global funding for trachoma R&D is therefore lower than previously reported.

In 2016, funding for trachoma R&D was $2.2m. Vaccines and diagnostics are the only two product areas for trachoma that are included in the G-FINDER scope: more than half ($1.2m, 55%) of all reported funding was for vaccine R&D, while diagnostics received just $0.2m (10%). The remaining $0.8m (35%) of funding was not allocated to a specific product area.

Table 24. Trachoma R&D funding by product type 2007-2016

Product \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
Vaccines (preventive)	-	0.8	0.8	0.8	0.7	1.0	1.1	1.0	1.2	1.2	55
Diagnostics	0.8	<0.1	0.5	2.6	5.1	0.6	0.6	0.2	-	0.2	10
Unspecified	0.6	1.0	0.1	-	-	0.4	0.5	0.1	-	0.8	35
Total	1.4	1.8	1.3	3.5	5.9	2.1	2.2	1.4	1.2	2.2	100

- No reported funding

More than half of all funding for trachoma R&D in 2016 was for clinical development ($1.1m, 52%), with very little funding reported for basic and early stage research ($0.2m, 10%). The remaining funding was not allocated to a specific product or R&D stage ($0.8m, 37%). This split was very different between product areas: funding for vaccine R&D was almost exclusively for clinical development ($1.1m, 96%) – entirely because of a US NIH grant to support planning for a Phase I trial of a live attenuated vaccine – while funding for diagnostic R&D was solely for discovery and pre-clinical research.

In 2016 the funder base for trachoma R&D expanded to four organisations, up from only two in 2015. The US NIH was the top funder, providing nearly two-thirds ($1.4m, 63%) of total investment. The German DFG provided just under a third ($0.7m, 30%), having been absent since 2013, while the Institut Pasteur and the Wellcome Trust accounted for 5.3% ($0.1m) and 1.8% (<$0.1m) of total funding respectively.

Trachoma was almost exclusively funded by the public sector ($2.1m, 98%).

Table 25. Trachoma R&D funders 2016

Funder / US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
US NIH	-	0.8	1.2	1.2	1.1	1.5	1.5	0.9	1.0	1.4	63
German DFG	-		-	-	-	-	0.2	-	-	0.7	30
Institut Pasteur	-	<0.1	-	<0.1	<0.1	-	0.1	0.1	-	0.1	5.3
Wellcome Trust	1.2	-	-	-	-	0.5	0.4	0.3	0.2	<0.1	1.8
US CDC	-	-	-	-	-	-	-	0.1	-	-	-
Aggregate industry	0.1	0.1	-	2.2	4.6	-	-	-	-	-	-
Lygature					0.1						
Swedish Research Council		<0.1	0.1	-	-	-	-	-	-	-	-
SSI	-	0.7	-	-	-	-	-	-	-	-	-
Brazilian DECIT	-	0.2	-	-	-	-	-	-	-	-	-
All other funders	0.1	-	-	-	-	-	-	-	-	-	-
Disease total	1.4	1.8	1.3	3.5	5.9	2.1	2.2	1.4	1.2	2.2	100

- No reported funding

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

A decade of investment in trachoma R&D

- The US NIH has been the most consistent funder of trachoma R&D over the past decade, having reported funding every year since 2008. The next most consistent funder is the Wellcome Trust, which has provided funding in just 6 of the last 10 years.
- Despite having invested nearly a third ($7.0m, 31%) of the ten year total, participation from industry in trachoma R&D has been intermittent, and absent since 2011.

RHEUMATIC FEVER

Rheumatic fever is a bacterial infection caused by Group A *streptococcus* that most commonly affects children aged 5-14 years. It usually follows untreated bacterial throat infections, and without treatment can lead to complications such as rheumatic heart disease, in which the heart valves are permanently damaged. It may also progress to heart failure and stroke.

According to the IMHE Global Burden of Disease study, rheumatic fever was the seventh highest cause of both mortality and morbidity of all the G-FINDER neglected diseases in 2015, resulting in 278,996 deaths and 10 million DALYs in developing countries.[2]

Acute rheumatic fever can be treated using currently available drugs (although post-infection prophylaxis requires multiple doses of antibiotics); however, treatment of rheumatic heart disease often requires surgery. The main R&D need is therefore the development of a vaccine. Several vaccines are in development, the most advanced is a Group A *streptococcus* vaccine in Phase I.[138]

$1.3 MILLION

TOTAL SPEND ON RHEUMATIC FEVER R&D IN 2016

BASIC RESEARCH	OUT OF SCOPE
DRUGS	OUT OF SCOPE
VACCINES (PREVENTIVE)	IN SCOPE
VACCINES (THERAPEUTIC)	OUT OF SCOPE
DIAGNOSTICS	OUT OF SCOPE
VCPs	OUT OF SCOPE

Global funding for rheumatic fever R&D in 2016 was $1.3m.

Preventive vaccines is the only product area for rheumatic fever included in the G-FINDER scope. All funding in 2016 was for early stage research, as there are no vaccine candidates currently in clinical development.

Table 26. Rheumatic fever R&D funding by product type 2007-2016

Product \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
Vaccines (preventive)	1.7	2.2	3.3	2.0	0.8	0.8	0.9	1.2	2.2	1.2	92
Unspecified	0.3	0.3	0.2	-	0.1	0.1	-	0.1	<0.1	0.1	7.7
Total	1.9	2.5	3.4	2.0	0.9	1.0	0.9	1.3	2.3	1.3	100

- No reported funding

There were just two reported funders for rheumatic fever vaccine R&D in 2016. The US NIH contributed the majority of funding ($0.9m, 73%) and the Health Research Council of New Zealand (New Zealand HRC) provided the remainder ($0.3m, 27%). The Brazilian BNDES, which provided $0.6m in 2015, did not report any funding for 2016.

There was no investment from the philanthropic sector or industry in rheumatic fever R&D in 2016.

Table 27. Rheumatic fever R&D funders 2016

Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
US NIH	1.5	0.7	0.9	0.9	0.4	0.5	0.6	0.5	1.0	0.9	73
New Zealand HRC	-	-	-	-	-	-	-	-	0.6	0.3	27
Brazilian BNDES								-	0.6	-	-
Australian NHMRC	0.4	0.4	0.6	0.8	0.3	0.3	0.3	0.6	-	-	-
Aggregate industry	-	1.1	1.7	-	-	-	-	0.1	-	-	-
Swedish Research Council		<0.1	0.1	-	0.1	0.1	-	-	-	-	-
Australian NHF		0.1	0.1	0.2						-	-
Australia - India SRF				0.1							
Fondazione Cariplo		-	0.1	-							
Australian DIIS		0.1	-	-	-	-	-	-	-	-	-
Anonymous funder		<0.1									
Disease total	1.9	2.5	3.4	2.0	0.9	1.0	0.9	1.3	2.3	1.3	100

- No reported funding

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

A decade of investment in rheumatic fever R&D

- There are very few funders of rheumatic fever R&D; the US NIH and Australian NHMRC have been the only consistent funders over the past decade, and the latter has not reported any funding for rheumatic fever since 2014. Industry provided sizeable contributions in 2008 and 2009, but since then has largely been absent.
- Almost all funding for rheumatic fever vaccine R&D over the last decade has been for discovery and pre-clinical development. Although this reflects the state of the R&D pipeline – with only one candidate in clinical development – the lack of clinic-ready candidates is not helped by the incredibly small annual global investment in rheumatic fever R&D.

NEGLECTED DISEASE FUNDERS

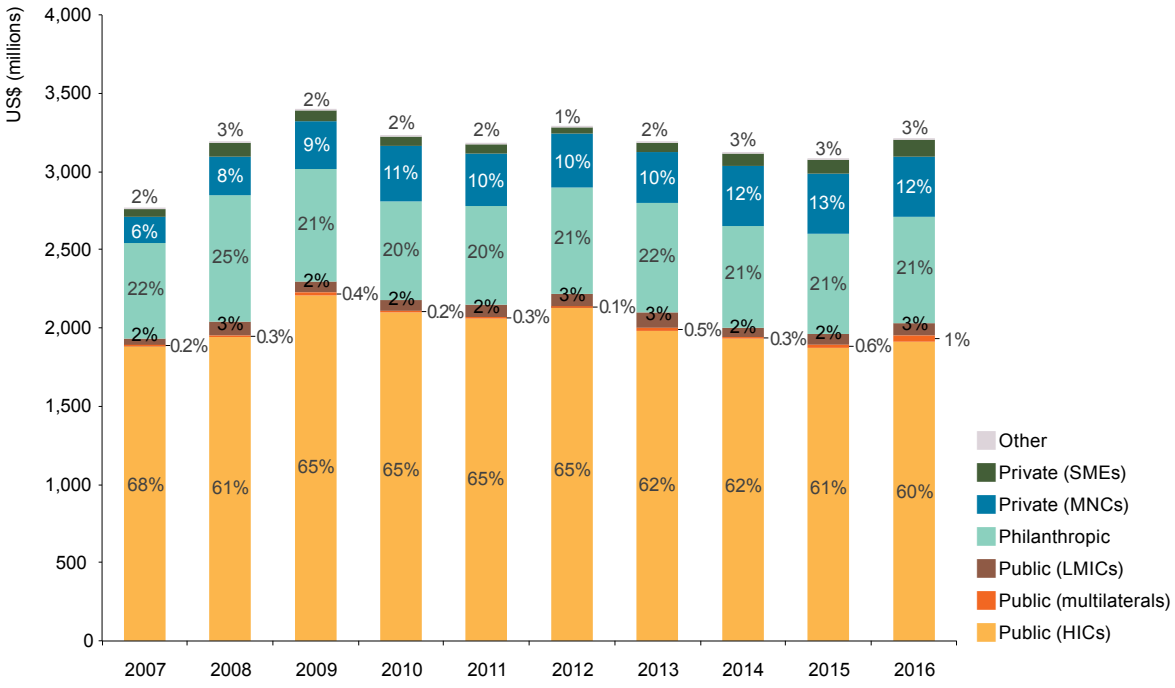
FUNDER OVERVIEW

Funding for neglected disease R&D was higher across all three sectors in 2016, the first time since 2012 that this had occurred. The largest increase came from the public sector (up $49m, 2.6%), with smaller but still significant increases in both philanthropic (up $28m, 4.4%) and industry investment (up $22m, 5.3%). This was the first funding increase in several years from either the public or philanthropic sectors, but marked the fifth consecutive year of increasing industry investment. As a result of the across the board increases in sector funding, the share of total funding coming from each of the public, philanthropic and industry sectors remained unchanged from 2015.

The public sector remained the most significant source of neglected disease R&D funding in 2016, contributing just under two-thirds ($2,034m, 64%) of the global total. As in previous years, most public sector funding came from HIC governments and multilaterals ($1,951m, 96%), with the remainder from LMIC governments. The philanthropic sector provided $671m (21%), and industry $497m (16%); of the industry investment, $391m (79%) came from MNCs, and $106m (21%) from SMEs.

For the first time in the history of the G-FINDER survey, funding increased from every sub-sector – from HIC governments to SMEs – with a notable contribution from organisations in LMICs. While the $49m increase in public sector funding was primarily driven by HIC governments and multilaterals (up $41m, 2.3%), it was supported by strong funding growth from LMIC governments†† (up $18m, 30%). And with only a marginal increase in MNC investment (up $0.8m, 0.2%) in 2016, essentially all of the increase in industry investment came from SMEs†† (up $23m, 30%), primarily from those based in LMICs.

Figure 20. Total R&D funding by sector 2007-2016



†† Reported changes in LMIC public funding and SME investment are based on organisations with funding data in both 2015 and 2016 (rather than in every year of the survey, as is the case in the remainder of the report) as survey participation from these sectors is inconsistent year to year.

PUBLIC FUNDERS

As has been the case in every year of the G-FINDER survey, the top three public funders in 2016 were the US, the UK and the EC. The US is by far the largest funder of these three; it was responsible for nearly three-quarters ($1,490m, 73%) of all global public funding in 2016, with the UK ($101m, 5.0%) and the EC ($77m, 3.8%) collectively contributing less than 10%. And while the UK again became the second largest public funder of neglected disease R&D in 2016 after falling behind the EC the previous year, the gap between the US and the second largest public funder was the largest since 2012.

2016 also saw the first increase in YOY public funding for neglected disease R&D since 2012 (up $49m, 2.6%). The largest increases came from the US government (up $78m, 5.5%), mainly due to increased US NIH investment (up $89m, 7.2%), and two European governments: the Netherlands (up $18m, 447%), who returned to the top 12 after dropping out in 2015, due to a new PDP funding round from the Dutch DGIS; and the UK (up $9.3m, 10%), with increased funding from both the UK MRC and UK DFID. Most of the other notable increases in public funding came from governments outside of North America and Europe. These increases came from Brazil (up $9.0m, 265%), partly due to more accurate reporting by Brazilian FAPEMIG (up $5.1m, from a low base); Sweden (up $6.4m, 78%), Japan (up $5.5m, 50%), which funds neglected disease R&D through the Global Health Innovative Technology (GHIT) Fund, and which made its largest ever investment in 2016; India (up $4.9m, 11%), which overtook France and Germany to become the fourth largest government funder of neglected disease R&D globally in 2016; Germany (up $4.3m, 19%); and South Africa (up $3.3m, 59%). As a result of the increases from Brazil, India and South Africa, public funding from IDCs in 2016 was the highest recorded since 2013 by the G-FINDER survey (up $17m, 32%, to $78m).

All of the notable decreases in public funding for neglected disease R&D in 2016 came from European funders. The most significant reduction came from the EC (down $49m, -39%), although this was linked to reduced funding of EDCTP (down $32m, -80%) as a result of a number of extraordinary payments to EDCTP in 2015 that would otherwise have been made in 2014 and 2016. Reported funding from France decreased (down $16m, -28%), but this was entirely due to more accurate reporting by Inserm (down $20m, -43%). Switzerland was the only other top public funder to invest less in 2016 (down $6.9m, -52%), with lower funding from both the Swiss State Secretariat for Education, Research and Innovation (SERI) and Swiss Agency for Development and Cooperation (SDC). Canada and Ireland both dropped out of the top 12 in 2016.

Table 28. Top public R&D funders 2016

Country \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
United States of America	1,442	1,463	1,687	1,606	1,568	1,668	1,491	1,457	1,415	1,490	73
United Kingdom	88	90	126	138	112	79	107	112	92	101	5.0
EC	113	122	112	87	104	89	106	104	126	77	3.8
India		40	27	40	45	45	53	40	45	50	2.5
France	14	27	45	37	56	50	73	60	60	47	2.3
Germany	12	3.5	32	35	30	51	42	45	51	43	2.1
Netherlands	31	25	25	17	23	14	22	17	4.9	23	1.1
Australia	20	28	25	28	35	44	23	34	20	22	1.1
Brazil	22	24	29	10	11	19	15	8.7	7.4	18	0.9
Switzerland	7.5	4.7	8.5	15	15	17	17	19	21	18	0.9
Japan	4.5	7.3	6.1	9.3	3.4	2.5	11	11	14	17	0.9
Sweden	19	22	28	17	17	16	5.9	6.0	8.3	15	0.7
Subtotal of top 12^	1,827	1,909	2,172	2,045	2,026	2,108	1,979	1,921	1,870	1,922	94
Total public funding	1,932	2,041	2,295	2,176	2,143	2,207	2,095	1,994	1,954	2,034	100

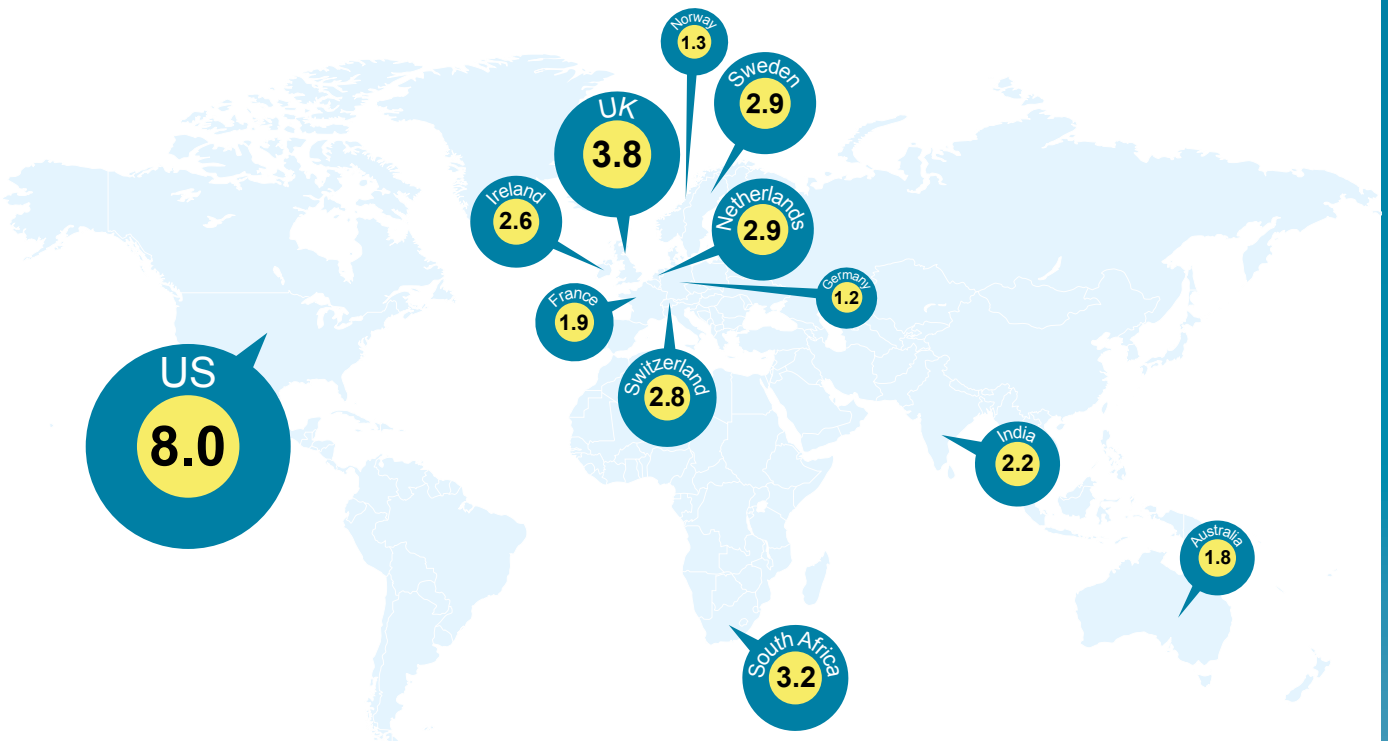
^ Subtotals for 2007-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016
No funding organisations from this country participated in the survey for this year

PUBLIC FUNDING BY GDP

Absolute funding can be a misleading measure of public R&D investment, as it can underplay the relative contributions of smaller countries and LMICs. For this reason, we have also analysed country investments in neglected disease R&D in relation to their gross domestic product (GDP).

When analysed by proportion of GDP rather than absolute funding, a slightly different picture of public funding emerges. Three countries not ranked in the top 12 funders by absolute funding appear in this list when ranked by contribution relative to GDP: South Africa, Ireland and Norway. In contrast, Brazil and Japan drop out of the list when GDP is factored in, as does the EC (which cannot be fairly analysed with this measure). The US, UK, India, France, Germany, Netherlands, Australia, Switzerland and Sweden all ranked in the top 12 using either metrics. South Africa, an IDC, provided the third highest contribution as a percentage of GDP of all countries in 2016, behind only the US and the UK.

Figure 21. Public R&D funding by GDP^ 2016
(A value of 10 is equivalent to an investment of 0.01% of GDP)



^ GDP figures taken from International Monetary Fund (IMF) World Economic Outlook database
Figure provides value of (US$ funding / GDP) * 100,000

HIGH-INCOME COUNTRIES AND MULTILATERALS

HIC governments and multilaterals once again provided almost all ($1,951m, 96%) public funding for neglected disease R&D in 2016. YOY investment increased for the first time since 2012 (up $41m, 2.3%), with a large increase in US funding (up $78m, 5.5%) – also for the first time since 2012. There were also smaller but notable increases from the Netherlands (up $18m, 447%), the UK (up $9.3m, 10%), Sweden (up $6.4m, 78%), Japan (up $5.5m, 50%) and Germany (up $4.3m, 19%). These increases were enough to outweigh decreased funding from a number of other HICs, most notably the EC (down $49m, -39%), France (down $16m, -28%) and Switzerland (down $6.9m, -52%). Funding from the EC fell largely due to a number of extraordinary payments made to EDCTP in 2015 that otherwise would have been made in 2014 and 2016. Reported funding from France dropped to the lowest level since 2010, as a result of Inserm (down $20m, -43%) reporting more detailed data for 2016‡.

Multilaterals invested a total of $42m in 2016, the largest contribution from this sector in G-FINDER history, providing 1.3% of global total funding.

Once again, funding from HIC governments and multilaterals in 2016 was heavily concentrated in just three diseases: HIV/AIDS, TB and malaria, which collectively received over three-quarters ($1,499m, 77%) of total funding. YOY funding increased for HIV/AIDS (up $42m, 5.0%) and malaria (up $6.1m, 2.3%), while funding for TB (down $0.4m, -0.1%) remained essentially steady. The increase in HIV/AIDS was the first since 2012, and was primarily due to increased investment in this disease by the US NIH (up $31m, 4.6%).

‡ Inserm reported more detailed data for 2016, resulting in a proportion of its reported 2016 investment being considered outside the scope of G-FINDER; it is therefore possible that Inserm's investment in prior years is overstated.

The US NIH was also the driving force behind the majority of increases in HIC government and multilateral funding for other neglected diseases in 2016. Strong growth in funding for *Salmonella* infections (up $12m, 33%) and dengue ($9.0m, 16%), both primarily from the US NIH, took these two diseases to historically high levels of investment. The US NIH was also responsible for the more modest increases in HIC government and multilateral funding for kinetoplastids (up $4.1m, 6.4%), assisted by renewed investment in this area from the Dutch DGIS, and helminth infections (up $1.2m, 3.1%).

Table 29. Public (HIC and multilaterals) R&D funding by disease 2007-2016

Disease or R&D area / US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
HIV/AIDS	1,055	1,038	1,084	1,013	977	1,005	927	893	841	873	45
Tuberculosis	238	226	335	307	281	274	271	298	312	341	17
Malaria	232	252	285	307	284	284	283	280	280	285	15
Kinetoplastids	50	86	102	103	93	90	74	79	69	78	4.0
Dengue	40	43	58	51	58	54	45	50	59	67	3.5
Diarrhoeal diseases	50	68	102	84	91	85	87	83	73	56	2.9
Salmonella infections	10	29	37	38	33	41	40	39	38	51	2.6
Helminth infections (worms & flukes)	42	37	51	50	47	59	50	45	42	43	2.2
Hepatitis C (genotypes 4, 5 & 6)							14	19	12	12	0.6
Bacterial pneumonia & meningitis	11	10	13	18	28	16	25	18	16	12	0.6
Cryptococcal meningitis							2.8	5.6	5.5	5.6	0.3
Leprosy	3.9	4.1	7.0	4.0	4.6	11	6.2	5.8	4.5	5.4	0.3
Buruli ulcer	2.3	1.5	1.6	3.7	3.4	3.4	4.0	0.7	0.9	2.2	0.1
Trachoma	-	1.5	1.3	1.2	1.1	1.5	1.8	1.1	1.0	2.1	0.1
Rheumatic fever	1.9	1.3	1.6	1.8	0.9	1.0	0.9	1.2	1.6	1.3	0.1
Leptospirosis							0.4	1.2	1.3	1.2	0.1
Platform technologies	3.1	6.0	7.7	11	11	26	29	11	13	16	0.8
Adjuvants and immunomodulators	<0.1	0.9	3.1	3.9	1.9	19	17	3.4	3.3	11	0.5
General diagnostic platforms	1.2	2.2	2.1	5.7	8.5	7.4	8.5	5.9	9.6	5.5	0.3
Delivery technologies and devices	1.9	2.9	2.6	1.2	0.4	0.4	4.1	1.6	0.6	0.3	<0.1
Core funding of a multi-disease R&D organisation	91	82	62	66	82	66	63	60	75	58	3.0
Unspecified disease	55	65	76	48	69	103	69	45	45	41	2.1
Total public funding (HICs/multilaterals)	**1,885**	**1,950**	**2,225**	**2,105**	**2,064**	**2,121**	**1,993**	**1,935**	**1,891**	**1,951**	**100**

New disease added to G-FINDER in 2013

\- No reported funding

The most notable drops in disease-specific HIC government and multilateral funding were for diarrhoeal diseases (down $16m, -23%) and bacterial pneumonia & meningitis (down $5.0m, -35%), however these were both primarily due to more detailed reporting by Inserm.

Nearly two-thirds (59%) of all HIC government and multilateral funding for neglected disease R&D in 2016 went to basic and early stage research, with only a quarter (27%) going to clinical development and post registration studies. Remaining funding (14%) was not allocated to a specific R&D stage. US NIH funding for the clinical development of HIV/AIDS preventive vaccines accounted for over one-third (37%) of all HIC government and multilateral investment in late stage research. If this funding is excluded, the focus of all remaining HIC government and multilateral funding for neglected disease R&D becomes even more apparent; excluding US NIH funding for HIV/AIDS vaccine clinical trials, just 19% of all other HIC government and multilateral investment is for clinical research and post registration studies, while 66% is for basic and early stage research.

A decade of HIC government and multilateral funding for neglected disease R&D

- HIC governments and multilaterals have provided 96% of all public funding for neglected disease R&D over the last decade. The US, the UK and the EC have consistently been the top three funders, and have contributed more than 85% of all HIC and multilateral funding over this period, with the US government alone accounting for over three-quarters (76%) of this investment.
- Funding from HIC governments and multilaterals was heavily concentrated on HIV/AIDS, TB and malaria, which collectively accounted for three-quarters (76%) of all funding from this group over the past decade.
- HIV/AIDS alone accounted for nearly half (48%) of all funding from HIC governments and multilaterals since 2007, however funding for HIV/AIDS declined over the decade from $1,055m in 2007 to $873m in 2016.

LOW- AND MIDDLE-INCOME COUNTRIES

Public funders in LMICs invested $84m in neglected disease R&D in 2016, representing 4.1% of all global public funding. Inconsistent survey participation by many LMIC organisations makes long-term or multi-year comparisons of neglected disease R&D funding difficult, but investments from LMIC public funders who participated in both 2015 and 2016 grew by $18m (up 30%).[§]

As in previous years, the vast majority of LMIC public funding for neglected disease R&D ($78m, 93%) came from the three IDCs (India, Brazil, and South Africa) all of which increased their funding in 2016. Although nearly two-thirds ($50m, 60%) of all LMIC public funding in 2016 came from Indian organisations, the largest YOY increase came from Brazil (up $9.0m, from a low base), although this was partly a reflection of more accurate reporting by the Brazilian Support Foundation for Research in the State of Minas Gerais (FAPEMIG, up $5.1m, from a low base). Indian government funding for neglected disease R&D increased by $4.9m (up 11%) and South African government funding by $3.3m (up 59%).

[§] As LMIC survey participation is inconsistent from year to year, reported changes in LMIC public funding are based on organisations with funding data in both 2015 and 2016 (rather than in every year of the survey, as is the case in the remainder of the report). This group of funders provided $77m of the $84m in total LMIC public funding for 2016.

LMIC public funding in 2016 remained concentrated on TB, malaria, and kinetoplastids, which collectively received more than half of all funding ($49m, 58%) in 2016. YOY LMIC funding either increased or was steady for each of these diseases in 2016. The largest increase was in TB (up $5.4m, 35%), with record high funding from the Indian ICMR (up $3.9m, 49%) and a large disbursement from the South African MRC (up $2.3m, after not funding TB R&D in 2015). Kinetoplastid R&D funding also increased (up $2.7m, 41%) in 2016, due to large disbursements from three Brazilian organisations: FAPEMIG (up $1.9m, from a low base), the Brazilian State of São Paulo Research Foundation (FAPESP, up $1.4m, 72%) and BNDES (up $0.9m, after not funding kinetoplastid R&D since 2009). Following an increase in 2015, LMIC public funding for malaria R&D was steady (down $0.1m, -0.7%) in 2016. Outside of these three diseases, LMIC public funding also increased for dengue (up $4.1m, 117%) and diarrhoeal diseases (up $2.2m, 38%), both largely due to increased funding from Brazilian public sector organisations.

LMIC public funding for most of the remaining diseases fell in 2016, although all of these drops were relatively small. Funding for HIV/AIDS (down $0.9m, -19%) accounted for the lowest share ($4.0m, 4.7%) of LMIC public funding invested in this disease in G-FINDER history, while funding was also lower for leprosy (down $0.6m, -12%), and hepatitis C (down $0.3m, -39%). Rheumatic fever did not receive any LMIC public funding in 2016, after being funded for the first time (with $0.6m) in 2015.

Inconsistent levels of grant detail provided by LMIC public funders makes any analysis of funding by R&D stage difficult, with most LMIC funding in 2016 not allocated to a specific product or R&D stage ($52m, 62%). Where funding was allocated to a specific R&D stage, it was largely for basic and early stage research ($27m, 32% of total LMIC funding), rather than clinical development and post registration studies ($4.9m, 5.8%).

Table 30. Public (LMIC) R&D funding by disease 2007-2016^

Disease or R&D area	US$ (millions)										2016 % of total
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	
Tuberculosis	3.3	11	9.5	11	17	17	32	14	16	22	26
Malaria	2.9	18	18	9.9	13	20	20	9.1	13	14	17
Kinetoplastids	4.9	7.9	8.1	10	9.0	12	8.2	8.5	8.5	13	15
Diarrhoeal diseases	-	6.0	4.5	7.2	11	4.7	5.4	5.8	5.7	7.9	9.5
Dengue	1.6	3.0	13	5.6	4.0	6.3	3.3	3.2	4.0	7.6	9.1
Leprosy	1.4	5.5	3.8	3.6	2.5	2.1	4.6	3.5	4.7	4.0	4.8
HIV/AIDS	24	26	9.6	17	18	12	18	6.0	5.5	4.0	4.7
Helminth infections (worms & flukes)	2.6	3.0	1.3	1.2	1.9	2.9	1.8	2.7	2.0	1.8	2.2
Leptospirosis							-	0.1	-	1.1	1.3
Salmonella infections	-	0.1	<0.1	0.7	0.5	0.4	0.6	0.6	0.2	0.6	0.8
Bacterial pneumonia & meningitis	-	4.5	0.3	0.3	0.1	0.3	<0.1	0.3	<0.1	0.5	0.6
Hepatitis C (genotypes 4, 5 & 6)							5.5	0.2	0.8	0.5	0.6
Rheumatic fever	-	-	-	-	-	-	-	-	0.6	-	-
Trachoma	-	0.2	-	-	-	-	-	-	-	-	-
Platform technologies	4.3	2.0	-	3.5	0.5	4.5	0.6	0.4	1.3	3.0	3.6
Delivery technologies and devices	-	1.3	-	1.9	<0.1	3.9	0.4	0.3	1.2	2.2	2.6
General diagnostic platforms	1.7	0.5	-	0.9	0.4	0.6	<0.1	0.1	0.1	0.8	1.0
Adjuvants and immunomodulators	2.6	0.2	-	0.6	-	0.1	0.1	<0.1	<0.1	<0.1	<0.1
Core funding of a multi-disease R&D organisation	1.3	4.1	0.7	0.8	0.3	-	0.4	0.3	1.5	1.9	2.3
Unspecified disease	0.1	0.6	0.1	-	0.4	3.7	2.3	3.9	0.2	2.2	2.6
Total public funding (LMICs)	46	92	70	71	79	86	102	59	64	84	100

^ Please note that no funding organisations from India participated in the survey in 2007

New disease added to G-FINDER in 2013

- No reported funding

A decade of LMIC government funding for neglected disease R&D

- The Indian government has steadily increased its investment in neglected disease R&D over the last decade. It has been the top LMIC government funder in every year since 2010, and became the fourth largest government funder globally in 2016.
- The next largest LMIC public funder was the Brazilian government, which has had far more variable levels of investment, ranging from a high of $29m in 2009 to a low of $7.4m in 2015.
- In 2007, LMIC governments invested more in HIV/AIDS than in any other neglected disease, just like HIC governments and multilaterals. By 2016 however, TB had become the highest funded disease by LMIC governments, and HIV had dropped to seventh place.

PHILANTHROPIC FUNDERS

The philanthropic sector provided $671m for neglected disease R&D in 2016, representing 21% of total global funding. As in previous years, the Gates Foundation and the Wellcome Trust collectively provided the vast majority ($642m, 96%) of all philanthropic funding.

YOY philanthropic funding for neglected disease R&D increased in 2016 (up $28m, 4.4%), after two consecutive years of decreasing investment. The largest increase came from the Wellcome Trust (up $17m, 21%) – the result of large core funding disbursements to its international research programmes in Kenya, Thailand, Vietnam and Malawi – followed by the Gates Foundation (up $12m, 2.3%) and MSF (up $4.5m, 77%).

Table 31. Top philanthropic R&D funders 2016

Funder / US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
Gates Foundation	530	707	641	528	525	520	538	532	530	542	81
Wellcome Trust	50	53	58	68	80	124	114	107	83	101	15
MSF	6.6	6.7	4.2	4.3	4.8	5.4	5.5	4.4	5.8	10	1.5
Gavi	12	17		2.5		9.8	19		10	5.8	0.9
Fundació La Caixa		0.3		0.3	3.2	2.6	3.0		3.4	3.3	0.5
Funds raised from the general public	2.3	1.4	0.5	0.4	0.5	0.4	0.7	0.9	1.2	1.1	0.2
UBS Optimus Foundation	0.5	1.1	1.1	6.7	5.0	3.1	2.5	3.4	1.4	0.8	0.1
Kleberg Foundation									0.2	0.6	0.1
Sidaction		0.2						0.4	0.7	0.5	0.1
LRI									0.5	0.5	0.1
ExxonMobil Foundation	2.2	2.1	1.6	0.8	0.3	0.5		0.5	0.5	0.5	0.1
All other philanthropic organisations	6.4	14	18	18	15	20	13	6.4	12	4.9	0.7
Total philanthropic funding	611	803	724	630	634	687	696	655	648	671	100

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

As has been the case in every year of the G-FINDER survey, the three diseases to receive the most philanthropic R&D funding were HIV/AIDS, malaria and TB, which collectively received more than half of all funding ($391m, 58%) in 2016. TB was the only one of these three to see a reduction in YOY philanthropic funding in 2016 (down $33m, -24%), with a drop in Gates Foundation funding to TB Alliance associated with the start of a new project cycle. Philanthropic funding for HIV/AIDS grew by $14m (up 11%), also entirely due to the Gates Foundation, whose increased funding for preventive vaccine development (up $23m, 32%) and $7.1m in funding for therapeutic vaccines more than offset its reduced investment in other product areas. Philanthropic funding for malaria R&D increased by $12m (up 9.6%), due to an almost tripling of Gates Foundation funding for vector control products (up $30m, 193%) which offset decreases in its funding for malaria drugs (down $13m, -24%) and vaccines (down $6.5m, -35%).

Philanthropic funding also increased for kinetoplastids (up $10m, 67%), driven by a grant cycle-related boost from the Gates Foundation to DND*i*, and diarrhoeal diseases (up $4.0m, 8.8%), with MSF funding a Phase III trial of a pentavalent rotavirus vaccine candidate. The only other notable decrease in philanthropic funding in 2016 was for bacterial pneumonia & meningitis (down $15m, -43%), however, as with the previous year's increase, this was due to cyclical funding from the Gates Foundation to PATH.

A third of all philanthropic funding for neglected disease R&D in 2016 was for basic and early stage research ($229m, 34%), most of which was for discovery and pre-clinical R&D ($133m, 20% of total philanthropic funding). Clinical or field development and post registration studies accounted for 26% ($172m) of philanthropic funding in 2016. Most remaining funding was also for product development (rather than basic research) but not allocated to a specific R&D stage, mainly for PDP portfolio projects, biological control products and platform technologies ($172m, 26%), or as core funding to multi-disease R&D organisations ($64m, 9.6%). A relatively small amount was not allocated to a specific disease or product ($34m, 5.0%).

Table 32. Philanthropic R&D funding by disease 2007-2016

Disease or R&D area	US$ (millions)										2016 % of total
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	
HIV/AIDS	118	202	153	154	152	160	149	136	129	141	21
Malaria	173	230	242	136	200	167	152	169	129	140	21
Tuberculosis	138	161	124	136	117	122	145	150	143	110	16
Diarrhoeal diseases	65	49	55	53	37	49	63	47	50	51	7.6
Kinetoplastids	73	52	58	32	23	21	20	33	16	26	3.9
Bacterial pneumonia & meningitis	7.0	31	27	51	40	52	28	7.4	41	25	3.7
Helminth infections (worms & flukes)	12	30	25	22	30	26	33	29	22	21	3.2
Dengue	2.1	3.2	3.1	4.3	6.3	10	21	25	24	21	3.1
Salmonella infections	0.1	0.9	3.7	7.1	9.3	12	15	11	16	15	2.3
Leprosy	0.8	1.1	1.1	2.7	1.7	2.2	2.0	1.2	1.1	1.3	0.2
Buruli ulcer	-	0.2	0.3	1.8	2.3	2.6	2.4	3.0	1.0	0.6	0.1
Cryptococcal meningitis							0.3	<0.1	0.1	0.1	<0.1
Trachoma	1.2	-	-	-	0.1	0.5	0.4	0.3	0.2	<0.1	<0.1
Hepatitis C (genotypes 4, 5 & 6)							0.1	0.1	<0.1	<0.1	<0.1
Rheumatic fever	-	0.1	0.2	0.2	-	-	-	-	-	-	-
Leptospirosis							<0.1	-	-	-	-
Platform technologies	2.4	9.6	17	15	7.0	20	15	11	19	33	4.9
Delivery technologies and devices	0.1	4.8	6.4	5.1	1.5	0.7	1.7	2.4	5.8	14	2.1
General diagnostic platforms	2.3	3.2	7.8	4.0	1.6	9.3	8.4	3.9	4.1	12	1.8
Adjuvants and immunomodulators	-	1.6	2.6	5.7	3.9	9.5	5.0	5.1	8.7	6.9	1.0
Core funding of a multi-disease R&D organisation	15	12	6.4	5.9	4.8	39	40	20	30	64	9.6
Unspecified disease	3.8	20	8.7	7.5	3.3	2.4	11	11	28	22	3.2
Total philanthropic funding	611	803	724	630	634	687	696	655	648	671	100

New disease added to G-FINDER in 2013
- No reported funding

A decade of philanthropic funding for neglected disease R&D

- As the second largest funder of neglected disease R&D globally, the Gates Foundation has been the dominant philanthropic funder over the past decade, providing 83% of all philanthropic funding. Along with the next largest philanthropic funder (the Wellcome Trust, with 12%), these two organisations accounted for 95% of philanthropic funding for neglected disease R&D over the past ten years.
- While the Wellcome Trust doubled its investment between 2007 and 2016 (from $50m to $101m), Gates Foundation funding peaked at $707m in 2008, and since 2010 has been essentially steady at an average of around $530m per year.
- Philanthropic funding has also been heavily concentrated on malaria, HIV/AIDS, and TB over the past ten years, with these three diseases accounting for 68% of all philanthropic funding.

PRIVATE SECTOR FUNDERS

The private sector invested $497m in neglected disease R&D in 2016, accounting for 16% of total global funding. For the third year in a row, this represented both the largest ever industry investment and the largest industry share of total funding in the history of the G-FINDER survey. Although the majority of industry investment in neglected disease R&D once again came from MNCs ($391m, 79%), SME investment in 2016 ($106m, 21%) was the highest ever recorded, and the largest share of total industry investment since 2008.

For the fifth year in a row, YOY industry investment increased (up $22m, 5.3%) in 2016. This also marked the second consecutive year in which the growth in industry investment in neglected disease R&D came from regular SME survey participants (up $23m, 30%), while MNC investment remained steady (up $0.8m, 0.2%).

MULTINATIONAL PHARMACEUTICAL COMPANIES

Just over three-quarters ($296m, 76%) of all MNC investment in neglected disease R&D in 2016 went to malaria, TB and HIV/AIDS, up from 72% in 2015. HIV/AIDS was the only one of these three diseases to see an increase in MNC investment (up $30m, 62%) in 2016. Coming as a result of record high MNC investment in HIV/AIDS preventive vaccine R&D (up $26m, 65%) in 2016, this increase resulted in the largest investment in HIV/AIDS R&D by MNCs in the history of the G-FINDER survey. MNC investment in TB R&D fell in 2016 (down $10m, -11%), continuing the sustained decline seen since 2010, and there was also a slight drop in malaria R&D investment (down $3.8m, -2.9%), although this followed two consecutive years of large funding increases.

Other than HIV/AIDS, the only other notable increase in MNC R&D investment was for bacterial pneumonia & meningitis (up $8.1m, 69%), with a sharp increase in reported investment in meningococcal vaccine development (up $11m, 609%). In contrast, MNC investment in hepatitis C decreased (down $15m, -68%) to its lowest level since G-FINDER started tracking hepatitis C R&D funding, likely associated with the conclusion of late stage clinical trials and the regulatory approval of new DAAs. For the third year in a row, MNC investment in diarrhoeal diseases also decreased (down $6.1m, -31%), in this case driven by reduced investment in rotavirus R&D, likely associated with the conclusion of post registration safety and impact studies for approved rotavirus vaccines.

Almost two-thirds of all MNC investment in neglected disease R&D in 2016 was for clinical development and post registration studies ($239m, 61%), with a further 31% ($121m) going to basic and early stage research, essentially all of which was for discovery and pre-clinical R&D (rather than basic research). Remaining MNC investment ($30m, 7.7%) was not allocated to a specific product or R&D stage.

Table 33. MNC R&D funding by disease 2007-2016

Disease or R&D area (US$ millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
Malaria	72	75	77	104	85	99	70	112	135	132	34
Tuberculosis	54	81	118	151	147	131	111	99	94	87	22
HIV/AIDS	7.5	21	19	17	14	15	9.8	40	48	77	20
Bacterial pneumonia & meningitis	14	32	27	24	32	35	31	31	12	20	5.1
Dengue	4.9	3.4	4.3	6.9	11	8.1	7.2	7.3	14	15	3.7
Diarrhoeal diseases	9.8	24	36	33	23	28	38	31	20	14	3.5
Kinetoplastids	4.6	1.2	3.6	9.4	9.7	17	16	12	16	13	3.3
Helminth infections (worms & flukes)	0.1	4.6	9.5	3.7	2.6	3.5	8.4	6.8	11	8.5	2.2
Hepatitis C (genotypes 4, 5 & 6)							28	26	21	6.7	1.7
Salmonella infections	-	1.3	2.0	3.1	5.0	4.1	4.1	3.8	3.3	3.8	1.0
Leprosy	-	-	-	-	-	-	0.1	0.1	0.7	0.4	0.1
Rheumatic fever	-	1.1	1.7	-	-	-	-	0.1	-	-	-
Trachoma	0.1	0.1	-	-	-	-	-	-	-	-	-
Buruli ulcer	-	0.1	-	-	-	-	-	-	-	-	-
Core funding of a multi-disease R&D organisation	-	-	-	-	-	-	2.2	8.0	8.2	11	2.9
Unspecified disease	-	-	-	-	3.1	1.5	7.7	4.1	2.5	2.5	0.6
Total MNC funding	167	246	297	352	333	343	333	381	385	391	100

New disease added to G-FINDER in 2013
- No reported funding

A decade of MNC investment in neglected disease R&D

- MNC R&D investment grew rapidly between 2007 and 2010, driven by investment in TB and malaria drug development, with a further small increase in 2014, driven by increased investment in malaria drug development, but has otherwise been relatively stable.
- Nearly three-quarters (71%) of all MNC investment in neglected disease R&D over the last decade went to TB, malaria and HIV/AIDS.
- MNC R&D investment in TB has declined considerably since its peak in 2010, driven by falling investments in drug R&D. In contrast, MNC investment in malaria and HIV/AIDS has increased sharply, especially since 2013.

SMALL PHARMACEUTICAL AND BIOTECHNOLOGY FIRMS

SMEs invested $106m in neglected disease R&D in 2016. Not only was this the highest reported investment by SMEs in the history of the G-FINDER survey, it also accounted for the largest share (21%) of total industry investment in neglected disease R&D that this sector has contributed since 2008. More than two-thirds ($73m, 69%) of all SME investment in neglected disease R&D in 2016 came from firms in innovative developing countries, with firms from developed countries contributing the remainder ($33m, 31%).

Just over two-thirds ($71m, 67%) of all SME funding was invested in three disease groups: bacterial pneumonia & meningitis, *Salmonella* infections and diarrhoeal diseases. SMEs, along with LMIC public funders, are the only sectors that did not have HIV/AIDS, malaria and TB as their top three highest funded diseases.

Irregular survey participation among SMEs makes analysis of funding trends difficult, but investment from regular survey participants[‡] increased significantly in 2016, highlighted by historically high levels of investment in a number of diseases. SME investment in bacterial pneumonia & meningitis R&D (up $10m, 43%) was the highest ever recorded by G-FINDER, reflecting increased investment in the clinical development of new pneumococcal conjugate vaccines. SME investment in *Salmonella* R&D almost doubled in 2016 (up $9.4m, 86%), also to its highest recorded level, reflecting the progression of new vaccine candidates for typhoid fever through the pipeline. SME investment in R&D for diarrhoeal diseases increased (up $2.5m, 18%) for the fourth year in a row, also to historically high levels, while 2016 also saw the first reported SME investment in hepatitis C R&D ($3.5m).

Reductions in SME investment in 2016 – where they did occur – were generally smaller, with the largest drops seen in kinetoplastids (down $2.4m, -56%) and malaria (down $1.6m, -32%), followed by helminth infections (down $0.8m, -92%) and TB (down $0.8m, -7.8%).

Table 34. SME R&D funding by disease 2007-2016

Disease or R&D area	US$ (millions)										2016 % of total
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	
Bacterial pneumonia & meningitis	0.5	22	9.1	7.7	6.0	5.5	18	17	24	35	33
Salmonella infections	-	13	2.0	0.2	0.1	0.3	6.0	12	11	20	19
Diarrhoeal diseases	2.8	1.9	5.4	0.7	5.2	2.7	6.3	8.9	14	16	15
Tuberculosis	17	15	18	18	15	9.3	5.1	8.2	10	9.1	8.6
HIV/AIDS	12	28	19	14	9.6	7.6	6.4	6.4	8.5	6.7	6.3
Malaria	10	9.8	19	11	7.2	7.1	5.8	6.3	6.6	5.2	4.9
Hepatitis C (genotypes 4, 5 & 6)							-	-	-	3.5	3.3
Dengue	2.5	0.2	0.9	0.5	0.5	0.5	0.3	0.5	1.0	2.4	2.3
Kinetoplastids	<0.1	1.7	1.4	1.4	3.8	0.8	0.6	7.0	4.8	1.9	1.8
Helminth infections (worms & flukes)	0.7	1.1	0.4	3.2	5.3	0.8	0.1	8.5	0.9	0.1	0.1
Trachoma	-	-	-	2.2	4.6	-	-	-	-	-	-
Leprosy	-	-	-	0.1	0.1	-	-	-	-	-	-
Buruli ulcer	<0.1	0.2	-	-	-	-	-	-	-	-	-
Core funding of a multi-disease R&D organisation	-	-	-	-	-	-	-	0.2	-	-	-
Unspecified disease	0.7	-	-	-	-	<0.1	1.9	5.5	3.6	5.9	5.6
Total SME funding	47	93	76	61	58	35	51	81	84	106	100

New disease added to G-FINDER in 2013
- No reported funding

‡ SME increases or decreases refer to organisations that had funding data included for both 2015 and 2016, rather than in every year of the survey, as SME survey participation is inconsistent from year to year

More than three-quarters of all SME investment in neglected disease R&D in 2016 was in clinical or field development and post registration studies ($82m, 78%), with most of the remainder invested in basic and early stage research ($16m, 15%), the vast majority of which was for discovery and pre-clinical R&D, rather than basic research. Remaining investment was not allocated to a specific product or R&D stage ($7.9m, 7.5%).

A decade of SME investment in neglected disease R&D

- Annual global SME investment in neglected disease R&D first peaked at $93m in 2008, before declining to a low of $35m in 2012. Since then, SME investment has grown rapidly, to reach a record high of $106m in 2016.
- The largest increases in SME investment since 2012 have been for bacterial pneumonia & meningitis (up $29m, from $5.5m), *Salmonella* infections (up $20m, from $0.3m) and diarrhoeal diseases (up $13m, from $2.7m).
- Firms from India and the US have contributed more than two-thirds (68%) of all SME investment in neglected diseases since 2007. In 2016, SMEs from India alone accounted for 66% of all SME investment in neglected diseases.

IN-KIND CONTRIBUTIONS

In addition to their direct R&D spend, companies conducting neglected disease R&D incur a range of other costs, such as infrastructure costs and costs of capital. These costs are not included in G-FINDER, due to the difficulty of accurately quantifying or allocating them to neglected disease programmes. G-FINDER also does not include the cost of companies' non-R&D contributions to combating neglected diseases, such as drug donations for mass drug administration programmes.

Companies also provide in-kind contributions that are specifically targeted to neglected disease R&D, but cannot easily be captured in monetary terms. Although difficult to quantify, these inputs are of substantial value to their recipients, and may represent a significant cost to companies.

We note that while some companies have nominated areas where they provide such contributions, others wished to remain anonymous.

Table 35. Typical industry in-kind contributions 2016

In-kind contribution	Examples	Some company donors^
Transfer of technology and technical expertise to develop, manufacture, register and distribute neglected disease products	• Identifying scientific obstacles • Sharing best practices and developing systems for clinical, technical and regulatory support • Developing capacity for pharmacovigilance • Donating equipment	Eisai GSK Johnson and Johnson MSD Novartis Sanofi Otsuka
Provision of expertise	• Supporting clinical trials • Collaboration of scientists, sharing trial results and facilitating parallel, concurrent testing • Participation on scientific advisory or management boards of external organisations conducting neglected disease R&D • Providing expertise in toxicology/ADME and medicinal chemistry • Evaluating new compounds proposed by external partners • Allowing senior staff to take sabbaticals to work with neglected disease groups	Abbvie Eisai GSK Johnson and Johnson MSD Novartis Pfizer Sanofi Otsuka
Teaching and training	• In-house attachments offered to Developing Country trainees in medicinal chemistry, clinical trial training etc • Providing training courses for Developing Country researchers at academic institutions globally • Organising health care provider training in Developing Country for pharmacovigilance of new treatments • Organising conferences and symposia on neglected disease-specific topics	Abbvie GSK Johnson and Johnson MSD Novartis Sanofi Otsuka
Intellectual property	• Access to proprietary research tools and databases • Sharing compound libraries with WHO or with researchers who can test and screen them for possible treatments • Providing public and non-for-profit groups with information on proprietary compounds they are seeking to develop for a neglected disease indication • Forgoing license or providing royalty-free license on co-developed products	Abbvie GSK Johnson and Johnson MSD Novartis Pfizer Sanofi
Regulatory assistance	• Allowing right of reference to confidential dossiers and product registration files to facilitate approval of generic combination products • Covering the cost of regulatory filings • Providing regulatory expertise to explore optimal registration options for compounds in development	GSK Johnson and Johnson Novartis Sanofi

^ Company donors listed do not necessarily engage in all activities listed as examples of in-kind contributions

FUNDING BY ORGANISATION

Neglected disease R&D funding remained highly concentrated in 2016, with the top 12 funders (including aggregate industry) providing 91% ($2,908m) of all global funding. The US NIH, Gates Foundation and aggregate industry collectively contributed almost three-quarters of total investment ($2,373m, 74%), up from 73% in 2015, and 72% in 2014.

Nine of the 11 individual organisations in the top 12 (i.e. excluding aggregate industry) increased their investment in 2016, compared to just five in 2015. The largest increase came from the largest global funder of neglected disease R&D, the US NIH (up $89m, 7.2%), following three consecutive years of diminishing funding. Unitaid, which gave a $28m grant to Partners In Health for the endTB project, entered the top 12 funders for the first time (up $24m, 150%). The Wellcome Trust also increased its funding in 2016 (up $17m, 21%), following a big drop the preceding year, with the increase due to large core funding disbursements to its international research programmes in Kenya, Thailand, Vietnam and Malawi. The next largest increase came from the Gates Foundation (up $12m, 2.3%), followed by the Indian ICMR (up $7.2m, 22%), UK MRC (up $6.2m, 17%), US DOD (up $5.5m, 7.5%), German BMBF (up $4.3m, 19%) and UK DFID (up $3.1m, 5.8%).

Only two of the top 12 funders in 2016 reduced their investment: the EC and USAID. Funding from the EC decreased significantly (down $49m, -39%), however this was largely due to a number of extraordinary payments made to EDCTP in 2015 that otherwise have been made in 2014 and 2016. The smaller drop in USAID funding (down $9.8m, -12%) reflected the conclusion of a multi-year grant to IPM for the development of the dapivirine ring for HIV/AIDS.

Table 36. Top neglected disease R&D funders 2016

Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
US NIH	1,238	1,258	1,455	1,407	1,371	1,478	1,298	1,259	1,245	1,335	42
Gates Foundation	530	707	641	528	525	520	538	532	530	542	17
Aggregate industry	214	339	373	413	391	377	384	462	469	497	16
Wellcome Trust	50	53	58	68	80	124	114	107	83	101	3.1
US DOD	86	79	108	76	85	83	97	98	73	79	2.5
EC	113	122	112	87	104	89	106	104	126	77	2.4
USAID	95	98	99	101	95	96	83	78	82	72	2.3
UK DFID	40	38	75	82	64	38	62	67	53	56	1.8
UK MRC	44	46	46	52	45	40	42	42	36	42	1.3
Indian ICMR		24	19	23	22	23	36	33	33	41	1.3
Unitaid			6.9			0.4	11	10	16	40	1.2
German BMBF	4.8	1.0	6.5	8.9	8.1	16	14	17	23	28	0.9
Subtotal of top 12^	2,492	2,813	3,042	2,899	2,853	2,940	2,835	2,847	2,801	2,908	91
Total R&D funding	2,771	3,185	3,393	3,219	3,168	3,277	3,177	3,112	3,073	3,203	100

^ Subtotals for 2007-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

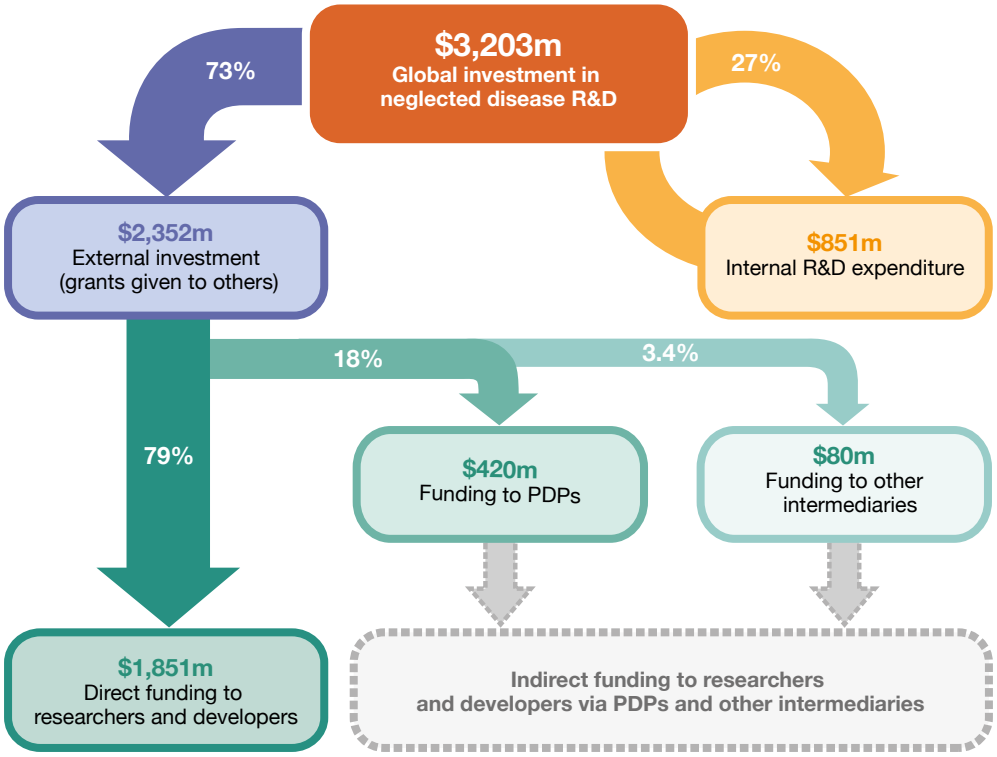
Top funders of neglected disease R&D over the last decade

- In every year of the G-FINDER survey, the top three funders have been the US NIH (always by far the largest contributor); the Gates Foundation and the aggregate pharmaceutical industry.
- The top 12 funders have consistently contributed over 85% of total funding each year.
- There has been very little variation in the top 12 funding organisations over the last decade, with eight individual organisations consistently making it into the top 12 funders list each year – the US NIH, Gates Foundation, EC, USAID, US DOD, Wellcome Trust, UK DFID and UK MRC – along with the aggregate pharmaceutical industry.

FUNDING FLOWS

Organisations can invest in neglected disease R&D in two main ways: by funding their own in-house research (internal investment, also referred to as intramural or self-funding); or by giving grants to others (external investment). This external investment can either be given directly to researchers and developers, or it can be provided via PDPs**and other intermediaries. Some organisations invest only internally (for example, most pharmaceutical companies); others, such as the Wellcome Trust, only invest externally (i.e. they do not conduct R&D themselves). Other organisations, such as the US NIH and the Indian ICMR, use a mixed model, providing external grants to others in addition to funding their own research programmes.

Figure 22. R&D funding flows 2016



A key point to note when analysing external investment flows is that different types of funders generally invest in different types of recipients. Science and technology (S&T) agencies, for example, mainly provide funding directly to researchers and developers (usually providing around three-quarters of their funding). Philanthropic and aid agency funders are the source of the vast majority of PDP funding (approximately 90%). In contrast, non-PDP intermediary organisations generally have a broad funding base, supported by both S&T and development agencies, as well as philanthropic funders.

As a result, changes in S&T agency funding are more likely to affect researchers and developers; changes in philanthropic or aid agency funding are more likely to affect PDPs; and non-PDP intermediary organisations are least vulnerable to changes from one donor funding stream.

** Although there is no single universally-accepted definition of PDPs, they are typically public health driven, not-for-profit intermediary organisations that use private sector management practices to drive product development in conjunction with external partners. Some PDPs focus on a single disease or product type, while others work across multiple diseases and products, but all share a common goal to develop products that are suitable for developing country use in areas of market failure. While their primary aim is the advancement of public health rather than commercial gain, PDPs generally use industry practices in their R&D activities, for instance portfolio management and industrial project management. Additionally, many PDPs conduct global advocacy to raise awareness of their targeted neglected diseases.

FUNDING FLOW TRENDS

Nearly three-quarters ($2,352m, 73%) of all funding for neglected disease R&D in 2016 was given externally in the form of grants (or contracts), with internal investments ($851m, 27%) making up the remainder. External funding increased in 2016 (up $95m, 4.4%) for the first time since 2012, driven by the US NIH. Self-funding was essentially flat (up $4.7m, 0.6%), with ongoing growth in industry investment (up $20m, 4.6%), particularly from SMEs, offset by a decrease in internal investment by government agencies (down $19m, -5.1%).

Almost four-fifths ($1,851m, 79%) of all external funding disbursed in 2016 was given directly to researchers and developers. In line with overall external investment, YOY funding to researchers and developers also increased for the first time since 2012 (up $147m, 9.1%), driven by both S&T agencies and philanthropic organisations. The increase in S&T agency funding to researchers and developers (up $80m, 6.4%) was almost entirely due to increased external grant funding from the US NIH (up $77m, 9.7%). Philanthropic funding given directly to researchers and developers increased by $62m (up 18%) due to increased funding from the Gates Foundation (up $43m, 16%) and the Wellcome Trust (up $19m, 24%).

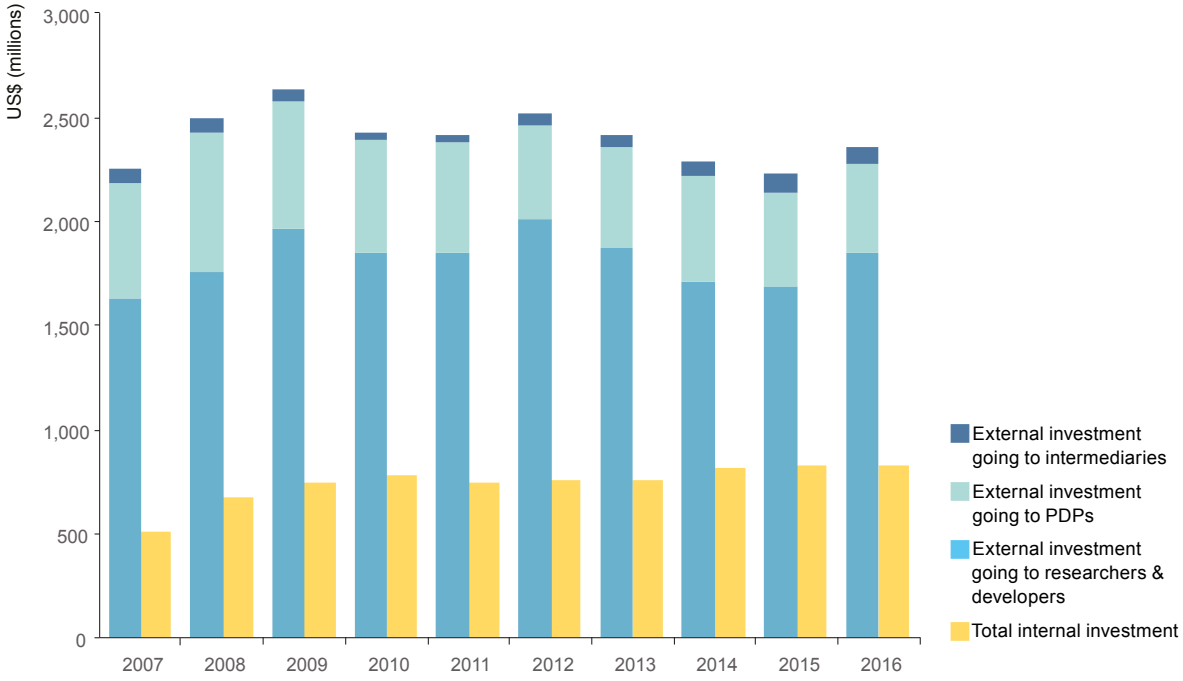
As noted earlier, not all external grant funding for neglected disease R&D is given directly to researchers and developers. Approximately one-fifth ($501m, 21%) of all external funding disbursed in 2016 was given to fund managers (PDPs and other intermediaries), who then either pass this funding on to researchers and developers or invest it in their own internal R&D activities. This was a marked reduction in funding given to fund managers compared to 2015 (down $52m, -10%), with this drop affecting both PDPs and other intermediaries.

A total of $420m (18% of all external investment) was channelled through PDPs in 2016. This was the lowest level of PDP funding recorded in the history of the G-FINDER survey, although this should be interpreted with caution given the highly cyclical nature of funding to PDPs and other intermediaries, especially from the Gates Foundation. Funding to PDPs decreased by $29m in 2016 (-6.8%), as disbursements from the top three funders of PDPs – the Gates Foundation, USAID and the UK DFID – collectively decreased by $42m (-11%). The only notable increase in funding to PDPs came from the Dutch DGIS (up $18m, 447%), which started a new PDP funding round, with funding from all other sources either down or flat.

Other intermediaries received $80m (3.4% of all external investment) in 2016, a decrease of $23m (-25%). This drop was the result of sharply lower funding from the EC to EDCTP (down $32m, -80%) – reflecting a number of extraordinary payments from the EC to the EDCTP in 2015 that would otherwise have been made in 2014 and 2016 – which more than offset slightly increased member state funding to EDCTP, and smaller increases in funding to the International Union Against Tuberculosis and Lung Disease (The Union) and the GHIT Fund.

A more in-depth analysis of funding for PDPs and other intermediaries is presented from page 97 onwards.

Figure 23. R&D funding flow trends 2007-2016



FUNDING FLOWS BY R&D STAGE

Nearly half of all funding for neglected disease R&D in 2016 was allocated to basic and early stage research (48%), followed by clinical or field development and post registration studies (32%), with the remaining funding comprising of core funding (4.2%), platform technologies (1.6%) and other R&D (14%).

Exactly half (50%) of all self-funding in 2016 was allocated to clinical or field development and post registration studies, with 37% allocated to basic and early stage research. The remaining 14% was not allocated to a specific disease or product area. However, this overall pattern obscures the very focus of industry investments compared to non-industry self-funding. Industry investment accounted for 57% of all self-funding; two-thirds (66%) of this industry investment was for clinical or field development and post registration studies, and less than one-third (28%) for basic and early stage research (all of which was for discovery and pre-clinical R&D, rather than basic research). In contrast, non-industry self-funding – primarily from government S&T agencies, and in particular the US NIH – was focused more on basic and early stage research (49%) than on clinical or field development and post registration studies (27%). The true extent of the upstream focus of non-industry self-funding is likely even higher, given that much of the remaining 24% of funding that was not allocated to a specific product or R&D stage is in fact highly likely to be for basic research.

Reflecting the fact that this funding stream is also dominated by S&T agencies (and especially the US NIH), almost two-thirds (62%) of all funding given directly to researchers and developers went to basic and early stage research, with just 22% for clinical or field development and post registration studies; the remaining 16% was not allocated to a specific product or R&D stage.

The very different pattern of funding given to PDPs reflects their product-development focus. More than two-fifths (42%) of all funding to PDPs was for clinical or field development and post registration studies, more than double the amount (19%) that was for basic and early stage research (essentially all of which was for discovery and pre-clinical R&D, rather than basic research). The remaining 38% of funding given to PDPs was not allocated to a specific R&D stage, but instead used to support the development of a portfolio of products from discovery through to post registration.

The small number of other intermediaries and the specific focus of each organisation results in different patterns of funding by R&D stage. For example, almost all (96%) of TB funding that went to other intermediaries was for The Union, all of which was allocated to clinical development and post registration studies for drugs. On the other hand, 88% of HIV/AIDS funding to other intermediaries went to the Aaron Diamond AIDS Research Center, with the vast majority (93%) of this allocated to basic and early stage research for vaccines. The EDCTP and the GHIT Fund received 88% of all non-disease-specific funding for other intermediaries, none of which was product- or R&D stage-specific.

FUNDING FOR PRODUCT DEVELOPMENT PARTNERSHIPS

PDPs received $420m in 2016, accounting for 13% of all neglected disease R&D funding and 18% of all external investment. This was the lowest level of PDP funding recorded in the history of the G-FINDER survey, corresponding to the lowest funding from the Gates Foundation to PDPs recorded by G-FINDER. Annual changes in funding to PDPs should be interpreted with caution given the highly cyclical nature of this funding, especially from the Gates Foundation.

It is important to note that the central role of PDPs is somewhat obscured by the 'NIH factor'. The US NIH was by far the largest funder of neglected disease R&D, but allocated only a small portion of its funding to PDPs ($8.8m or 0.7% of its total investment). If the US NIH is excluded, the role of PDPs in product development for neglected diseases becomes clearer, with PDPs collectively managing 34% of all non-NIH external grant funding for neglected disease R&D.

Although the cyclical pattern of funding to PDPs from philanthropic organisations and government aid agencies – the main funders of PDPs – means that their identities change, the three highest funded PDPs in any given year consistently account for between 40% and 50% of annual PDP funding. In 2016, these three PDPs were IAVI, MMV and PATH, who collectively received just under half ($196m, 47%) of all PDP funding.

There were some large shifts in funding to PDPs in 2016, including decreases to the TB Alliance (down $32m, -49%), PATH (down $27m, -37%) and MMV (down $14m, -20%); and increases to IAVI (up $22m, 34%) and DND*i* (up $15m, 54%) – with these changes mostly attributable to cyclical funding from the Gates Foundation. The increased funding to DND*i* was also due to the start of a new PDP funding round for the Dutch DGIS. The conclusion of Phase III trials of the dapivirine ring in 2016 led to a $5.8m (-22%) reduction in funding to IPM, with USAID's contribution dropping by $10m (-77%).

Most funding to PDPs in 2016 ($315m, 75%) was invested in three diseases that received the most funding overall: of this amount, $121m was for HIV/AIDS, $113m was for malaria, and $81m was for TB.

Table 37. Funds received by PDPs 2007-2016

PDPs \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of total
IAVI	85	93	75	70	64	63	61	41	66	88	21
MMV	85	50	45	73	76	52	67	74	77	60	14
PATH	45	130	145	77	102	87	84	122	76	47	11
DND*i*	28	22	32	33	36	30	33	53	31	47	11
TB Alliance	44	38	39	52	38	46	52	56	71	38	8.9
IVCC	-	11	16	17	<0.1	11	22	9.9	29	33	7.7
Aeras	45	74	59	43	44	40	41	55	32	31	7.3
FIND	26	35	23	27	23	22	23	24	15	22	5.3
IPM	46	65	34	32	14	23	30	26	26	20	4.8
CONRAD	18	17	24	19	26	32	27	18	3.9	9.2	2.2
IDRI	9.5	17	19	13	24	11	6.1	14	6.3	8.2	2.0
IVI	15	2.3	13	9.9	5.7	8.4	9.8	6.5	7.1	6.5	1.5
Sabin Vaccine Institute	8.9	17	10	4.3	8.9	6.5	6.6	5.5	3.1	5.0	1.2
EVI	7.1	4.0	3.5	4.8	7.1	2.0	6.0	2.8	3.4	1.8	0.4
FHI360	15	20	19	20	12	6.0	4.6	0.2	-	1.3	0.3
TBVI[A]	-	-	0.1	3.8	3.5	4.9	5.3	1.3	1.5	1.3	0.3
WHO/TDR[B]	34	38	35	28	31	-	-	2.2	2.5	1.0	0.2
OWH[C]	32	33	17	23	11	7.3	-	-	-	-	-
Total funding to PDPs	544	667	609	550	526	452	478	512	452	420	100

[A] The totals attributed to TBVI in 2014-2016 do not include funds from the EC that were paid directly to researchers under the auspices of TBVI's PDP activities. The totals only include EC's financial support for TBVI's services, as well as funding from other organisations

[B] TDR's mission extends beyond product development, but it operated as a de facto PDP from the 1970s until 2012, when it decided to focus on implementation research and research capacity strengthening. Funds received in 2014-2016 are related to the pooled fund demonstration projects

[C] As of 2013, OWH funding is included under PATH

- No reported funding

FUNDERS OF PDPs

Philanthropic organisations provided over half of all funding to PDPs ($239m, 57%). Almost all remaining funding came from HIC governments ($164m, 39%), mostly via their aid agencies ($142m, 87% of HIC funding to PDPs).

Funding from almost all the top PDP funders was either lower or flat in 2016, with an overall decrease of $29m (-6.8%). The largest decrease came from the Gates Foundation (down $30m, -12%). Although it remained the largest funder of PDPs, with a contribution of $229m (54% of all funding to PDPs), this represents the lowest investment in PDPs by the Gates Foundation recorded in the history of the G-FINDER survey. Funding from USAID to PDPs also declined (down $12m, -21%), reflecting reduced funding to IPM (down $10m, -77%) associated with the conclusion of its dapivirine ring Phase III clinical trials. The largest increase was the result of the Dutch DGIS opening a new funding round for PDPs (up $18m, 447%). Three of the top 12 funders of PDPs – Dutch DGIS, Australian Department of Foreign Affairs and Trade (DFAT) and Irish Aid – once again allocated 100% of their funding for R&D to PDPs.

Public sector multilateral organisations gave $14m to PDPs in 2016 (3.4% of all PDP funding). Almost all multilateral funding came from Unitaid ($12m, 84% of all multilateral PDP funding), though Unitaid's funding to PDPs decreased (down $3.9m, -25%) after a peak in 2015.

Table 38. Top funders of PDPs 2016

Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2016 % of org's funds given to PDPs	2016 % of total PDP funding
Gates Foundation	273	399	334	297	266	252	244	301	260	229	42	54
UK DFID	28	24	69	82	64	38	62	67	50	51	90	12
USAID	79	79	81	80	78	77	64	58	59	47	65	11
Dutch DGIS	29	18	18	15	19	11	21	17	4.1	22	100	5.3
Unitaid			6.9			0.4	8.6	10	16	12	30	2.8
US NIH	4.9	3.9	8.8	3.0	21	8.2	12	9.5	4.7	8.8	0.7	2.1
German BMBF			-	-	1.2	5.7	4.8	6.6	8.2	7.6	27	1.8
Australian DFAT						8.0	-	7.6	7.5	7.4	100	1.8
Swiss SDC	2.3	2.3	2.5	4.6	3.6	3.3	4.4	6.6	7.8	5.7	97	1.4
Irish Aid	22	6.3	4.8	6.0	5.8	5.7	7.8	2.2	5.6	4.8	100	1.1
MSF	6.6	6.7	4.2	4.3	4.6	5.4	5.5	4.4	4.4	4.4	43	1.1
Aggregate industry	1.1	6.6	2.1	2.2	1.7	1.7	1.5	1.8	1.4	3.2	0.7	0.8
Subtotal of top 12 funders of PDPs^	498	611	561	518	486	423	445	494	430	403		
Total PDP funding	544	667	609	550	526	452	478	512	452	420		
% of total PDP funding (top 12)	92	92	92	94	93	94	93	97	95	96		

^ Subtotals for 2007-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016
- No reported funding
Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

A decade of neglected disease R&D funding for PDPs

- PDPs are highly dependent on the Gates Foundation and government aid agencies, which have collectively provided almost 90% of all PDP funding over the last decade. The Gates Foundation alone has accounted for more than half (55%) of all funding for PDPs over this period.
- Global funding of PDPs and Gates Foundation funding of PDPs both fell to record lows in 2016. Although a number of the year-to-year drops can be explained by funding cycles, total funding to PDPs in 2016 is down a quarter of a billion dollars ($246m, -37%) from its 2008 peak.
- PATH has been the largest recipient of all PDP funding over the last decade, and has been the top funded PDP in seven of the last ten years, with the others to hold this spot being IAVI (twice) and MMV.

FUNDING FOR OTHER INTERMEDIARIES

'Other' intermediary organisations (i.e. those that are not PDPs) also aim to accelerate neglected disease product development, but do so without managing a product portfolio of their own. Instead, they generally act as coordinating agencies, receiving funding from multiple sources and passing this on to researchers and developers (either directly or via PDPs). They may also perform research themselves (often operational research or research into existing treatment regimens) or be involved in clinical trials of novel products being developed by other organisations.

Non-PDP intermediaries collectively received $80m in 2016, representing 2.5% of all neglected disease funding, and 3.4% of all external funding. The organisations that received the most funding were the GHIT Fund ($32m, 39%), EDCTP ($23m, 29%), The Union ($12m, 15%) and the Barcelona Institute for Global Health (ISGlobal, $9.2m, 11%).

The $23m decrease in funding to other intermediaries (-25%) was a reflection of a number of extraordinary payments from the EC to the EDCTP in 2015 that would otherwise have been made in 2014 and 2016, rather than a structural shift away from funding for these organisations. YOY funding for EDCTP decreased (down $26m, -53%), while funding for most other non-PDP intermediaries increased – led by The Union (up $3.2m, 37%) and the GHIT Fund (up $1.7m, 5.9%).

Most funding for intermediaries ($63m, 78%) was not earmarked for a specific disease by the funder. Of the $18m (22%) of funding given to non-PDP intermediaries that was disease-specific, $12m was for TB, $3.2m was for HIV/AIDS, $1.9m was for malaria and $0.4m was for kinetoplastid diseases.

FUNDERS OF OTHER INTERMEDIARIES

Non-PDP intermediary organisations receive funding from a relatively diverse range of sources, with less reliance on a single 'type' of funding organisation than either PDPs or researchers and developers. The majority of funding for other intermediaries comes from government agencies, with S&T agencies usually providing approximately half of all funding to other intermediaries, and aid agencies around one-fifth.

In 2016, funding for other intermediaries was uncharacteristic, with a marked decrease in the share of funding from S&T agencies (to 22% of all funding for other intermediaries) and an increase in funding from the Japanese government (up to 23% of all funding for other intermediaries). However, these irregularities were due to the EC's extraordinary payments to the EDCTP in 2015 and an increase in Japanese government investments in the GHIT Fund.

The EC is usually the largest funder of non-PDP intermediaries, due to its support for EDCTP. The large drop in EC funding to EDCTP in 2016 (down $32m, -79%) meant that it fell to third place in the list of top funders of intermediaries, behind the Japanese government, which increased its investment in the GHIT Fund (up $5.5m, 50%), and USAID, which increased its funding to The Union (up $3.2m, 37%). The drop in EC funding to EDCTP (which was due to extraordinary payments made in 2015), meant that European Union member state contributions to EDCTP in 2016 exceeded the EC's for only the second time. These included the UK DFID ($5.4m), the Swedish International Development Agency (SIDA, $4.4m), the UK MRC ($2.7m), the German BMBF ($2.3m), the Portuguese Foundation for Science and Technology ($0.2m) and the Dutch Organisation for Scientific Research ($0.2m).

Funding to other intermediaries is geographically driven. Of the top 12 funders, essentially all funding to intermediaries from the EC, the UK DFID, the Swedish SIDA and the German BMBF went to the EDCTP; Japanese government and industry investment went to the GHIT Fund; and Spanish public sector organisations funded ISGlobal. Few funders – beyond the EC, the US NIH and the Gates Foundation – support more than one non-PDP intermediary organisation.

Table 39. Top funders of intermediaries 2016

Funder	US$ (millions)										2016 % of org's funds given to intermediaries	2016 % of total intermediary funding
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016		
Japanese government							10	10	11	17	100	21
USAID	<0.1	4.3	5.4	5.9	5.8	5.6	5.1	9.4	8.7	12	16	15
EC	39	36	18	2.0	23	24	24	22	41	8.7	11	11
Aggregate industry	-	1.4	3.2	-	-	-	3.8	8.3	5.5	7.7	1.6	9.6
Gates Foundation	11	8.4	14	6.0	5.3	4.2	6.9	7.6	7.6	7.5	1.4	9.3
UK DFID	12	13	6.1	-	-	-	-	-	3.1	5.4	9.7	6.8
Swedish SIDA	4.0	1.9	2.1	1.9	<0.1	-	0.6	-	3.0	4.4	79	5.5
Fundació La Caixa					1.0	1.0	1.0		1.8	3.3	100	4.1
Catalan Department of Health					-	1.0	0.7			3.2	100	3.9
US NIH	-	1.1	3.5	3.2	1.3	2.1	1.8	3.6	3.3	2.8	0.2	3.5
UK MRC	-	-	-	4.4	-	<0.1	-	-	2.7	2.7	6.4	3.4
German BMBF			-	1.1	0.2	<0.1	0.1	0.1	0.1	2.7	9.8	3.4
Subtotal of top 12 funders of intermediaries^	70	76	55	31	41	53	56	64	97	77		
Total funding to intermediaries	70	76	55	32	41	54	57	64	98	80		
% of total intermediary funding (top 12)	100	100	99	97	100	98	99	100	99	96		

^ Subtotals for 2007-2015 top 12 reflect the top funders for those respective years, not the top 12 for 2016
- No reported funding
Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

A decade of neglected disease R&D funding for other intermediaries

- The EC has been the largest contributor of funding to other intermediaries for neglected disease R&D. It has provided 38% of all funding to other intermediaries over the last decade, primarily to EDCTP.
- The US government has been the next largest funder (providing 14% of all funding to other intermediaries over the last decade), followed by the Gates Foundation (12%), both of whom have supported a wider range of recipient organisations. The Japanese government has also become a notable funder, averaging $12m per year to the GHIT Fund since its creation in 2013.
- The two largest recipients of funding of all the other intermediaries are the EDCTP (which received 48% of all funding to other intermediaries over the last decade) and the GHIT Fund (17% of all funding, despite only having been established in 2013).

DISCUSSION

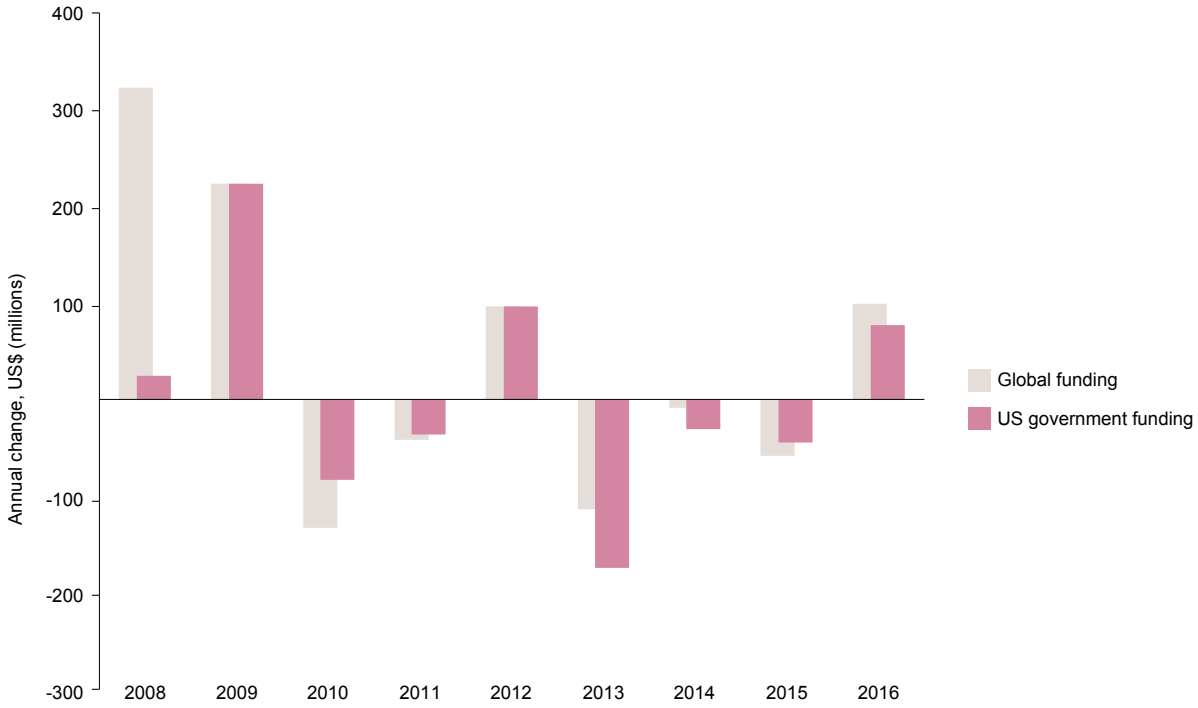
Global funding for neglected disease R&D increased for the first time since 2012, driven by an increase in funding from the US government

Global funding for neglected disease R&D increased (up $99m, 3.4%) to $3,203m in 2016. This was the first increase in global funding since 2012, and came on the back of an increase in neglected disease R&D investment by the US government (up $78m, 5.5%), also for the first time since 2012. This in turn was due to increased investment in neglected disease R&D by the US NIH (up $89m, 7.2%) – again, for the first time since 2012.

The US government was not alone in increasing funding for neglected disease R&D in 2016. The philanthropic sector (up $28m, 4.4%) and the pharmaceutical industry (up $22m, 5.3%) both increased their investment, with the latter driven by increased SME investment. There were also notable increases from the Dutch and UK governments, as a well as from a host of governments outside of North America and Europe – Brazil, Japan and India in particular – which helped to offset reduced funding from the EC and a number of other European governments.

The US government is just one funder among many making critical contributions to neglected disease R&D. But as the largest funder of all, changes in total global investment are closely aligned to changes in US government funding: every increase or decrease in US government investment in neglected disease R&D over the last decade has been accompanied by a corresponding change in total global funding.

Figure 24. The US government's influence on changes in annual funding for neglected disease R&D



An overreliance on US government funding is defining the shape of R&D for neglected diseases

In 2016, the US government was the source of 47% of global funding for neglected disease R&D, and 73% of all public sector funding. Its investment of $1,490m was triple the combined investment of the rest of the world's governments, and fifteen times larger than that of the next biggest government funder (the UK, with $101m).

The fact that the US government contributes such a large share of global funding means that not only are changes in US government funding the main driver of changes in total global funding for neglected disease R&D, but that the nature of neglected disease R&D is being defined by the focus of US government funding.

US government funding for neglected disease R&D is overwhelmingly focused on HIV/AIDS, TB and malaria, which received 82% of all US government funding for neglected disease R&D in 2016 (and 81% of its funding over the last decade). Despite the rest of the world (across all funding sectors) only directing 60% of their collective investment to these three diseases, they account for a full 70% of global funding.

US government funding for neglected disease R&D is also overwhelmingly focused on basic and early stage research. Two-thirds (67%) of all US government funding for neglected disease R&D in 2016 was for basic and early stage research, compared to just 28% for clinical or field development and post registration studies, with the remaining 5% not allocated to a specific R&D stage. But this headline figure doesn't quite tell the whole story, due to the US government's massive investment in clinical trials for HIV/AIDS vaccines, which totalled a quarter of a billion dollars ($245m) in 2016.

If US government funding for HIV vaccine clinical trials is excluded, 80% of all US government funding for neglected disease R&D – and 70% of all funding from HIC governments – was for basic and early stage research, compared to just 14% for clinical or field development and post registration studies.

The sustained growth in industry investment in neglected disease R&D – lately driven by SMEs – continues to be a good news story

After a brief dip in 2011, industry investment in neglected disease R&D has increased in every one of the last five years, and reached new record highs in each of the last three years. In 2016, total industry investment was $497m, accounting for 16% of all global funding for neglected disease R&D. Since 2008, reported industry investment in neglected disease R&D has increased by nearly 50%, while funding from both the public and philanthropic sectors has fallen over the same period.

The vast bulk of industry investment (79% in 2016) comes from MNCs, who have also been responsible for much of the growth in industry investment in neglected disease R&D over the last decade – driven by increased activity in malaria and HIV/AIDS especially. Since 2014 however, MNC investment has essentially plateaued, with annual increases of less than 1% in both 2015 and 2016.

Increased investment by SMEs since 2012, particularly from those in India, has helped to sustain the growth of overall industry investment. SME investment in neglected disease R&D tripled between 2012 and 2016 (from $35m to $106m); this was driven by Indian SMEs, whose investment increased from $9.3m to $70m over the same period, and now exceeds that of the Indian government. The $22m increase in industry investment in 2016 came entirely from SMEs (up $23m, 30%), who also provided their highest ever recorded investment, and the largest share of total industry investment (21%) since 2008. Importantly, much of this investment growth has also been in new areas: while 76% of MNC investment in 2016 was for malaria, TB and HIV/AIDS, none of these three diseases was in the top three diseases invested in by SMEs. Instead, 67% of SME investment in 2016 was for bacterial pneumonia & meningitis, *Salmonella* infections and diarrhoeal diseases.

In addition to SMEs, a number of other funders have been making a small but growing contribution in areas of need

As well as SMEs, a number of other traditionally smaller funders have been noticeably increasing their investment in neglected disease R&D: key global health initiatives (Unitaid, MSF and Gavi, the Vaccine Alliance), the Japanese government, and governments in LMICs.

Unitaid, MSF and Gavi have each expanded their focus to include support for neglected disease R&D, particularly for clinical or field development and post registration studies. Unitaid has expanded its focus from affordability, procurement and pricing to also include support for drug and diagnostic R&D for TB, malaria and HIV/AIDS. The first reported R&D funding from Unitaid was to FIND ($6.9m in 2009), and the organisation has increased funding in four of the last five years. Unitaid invested $40m in neglected disease R&D in 2016, providing more funding than all but six governments globally. This included $28m for clinical development and post registration studies to the endTB partnership, which is focused on the development of new treatments for MDR-TB.

MSF supports R&D across multiple diseases and product areas. It helped found the product development partnership DND*i*, and support to DND*i* represents the vast majority ($51m, 87%) of MSF's funding for neglected disease R&D over the last decade. But in recent years MSF has also become increasingly involved in direct collaborations with other R&D organisations – such as the recent Phase III trial of Serum Institute of India's BRV-PV rotavirus vaccine candidate in Niger – with non-DND*i* funding accounting for over half of MSF's $10m investment in neglected disease R&D in 2016.

Gavi has made a similar adjustment to Unitaid, expanding its focus from vaccine financing and supply to include support for clinical development and post registration studies of new vaccines for bacterial pneumonia & meningitis, diarrhoeal diseases and *Salmonella* infections. Gavi was the only one of the three global health initiatives to reduce its funding in 2016 (providing $5.8m, down from a peak of $19m in 2013), but it has the second highest contribution of the three over the last decade, with $76m.

The Japanese government – along with Japanese pharmaceutical companies – is increasingly investing in neglected disease product development following the establishment of the GHIT Fund in 2013. Between 2007 and 2012, the Japanese government invested an average of $5.5m per year in neglected disease R&D; since then, its annual investment has never been lower than $10m, and reached a record high of $17m in 2016. And, reflecting the focus of the GHIT Fund, this increased investment has been directed towards product development (both early and late stage), rather than basic research.

Finally, funding from LMIC governments increased strongly in 2016, to $84m. More than 90% of this funding ($78m, 93%) came from the three IDCs (India, Brazil, and South Africa) – all of whom increased their investment in 2016 – with India becoming the fourth largest government funder of neglected disease R&D, ahead of both France and Germany. And unlike HIC governments, which directed nearly half of all their funding for neglected disease R&D in 2016 to HIV/AIDS, LMIC governments invested more in each of TB, malaria, kinetoplastids, diarrhoeal diseases, dengue and leprosy in 2016 than they did in HIV/AIDS.

Conclusion

The US government's contribution to neglected disease R&D funding is unparalleled. But an overreliance on US government funding is reflected in the heavy concentration of global funding on HIV/AIDS, malaria and TB, and the overwhelming focus of HIC government funding on basic and early stage research. The growth of non-traditional funders is promising, but their collective contribution is still just a fraction of overall global funding. And while Gates Foundation investment in product development has consistently been relied on to balance the public sector focus on basic research – it has provided 55% of all funding to PDPs and 47% of all funding for platform technologies over the last decade – this is again a reflection of overreliance on a single funder. The world can ill afford to keep relying on the US government and the Gates Foundation to provide two-thirds of all global funding for neglected disease R&D over the next ten years, as they have done for the last decade.

ANNEXE 1

Advisory Committee members & additional experts

ADVISORY COMMITTEE MEMBER	ORGANISATION	TITLE
Dr Ripley Ballou	GlaxoSmithKline Biologicals	Vice President and Head, Global Vaccines US R&D Center
Dr Graeme Bilbe	Drugs for Neglected Diseases initiative (DND*i*)	Research & Development Director
Dr François Bompart	Sanofi	Vice President, Access to Medicines
Dr Wanderley de Souza	Financiadora de Estudos e Projetos (FINEP)	Former President
Professor Alan Fenwick	Imperial College London	Professor of Tropical Parasitology
Dr Arnaud Fontanet	Institut Pasteur	Head of the Emerging Diseases Epidemiology Unit
Dr Sue Kinn	UK Department for International Development (DFID)	Team Leader and Research Manager
Dr Line Matthiessen	European Commission (EC)	Head of Infectious Diseases and Public Health Unit, Directorate-General for Research and Innovation
Dr Carl Mendel	TB Alliance	Senior Vice President, Research and Development
Dr Firdausi Qadri	International Centre for Diarrhoeal Disease and Research (icddr,b)	Emeritus Scientist and Acting Senior Director, Infectious Diseases Division
Dr John Reeder	World Health Organization: Special Programme for Research and Training in Tropical Diseases (WHO/TDR)	Director
Professor Nelson Sewankambo	Makerere University College of Health Sciences	Principal (Head)
Dr Soumya Swaminathan	Indian Council of Medical Research (ICMR)	Director General
Wendy Taylor	United States Agency for International Development (USAID)	Former Director, Center for Accelerating Innovation and Impact
Dr Tim Wells	Medicines for Malaria Venture (MMV)	Chief Scientific Officer

ADDITIONAL EXPERT	ORGANISATION	TITLE
Dr Judith Mueller	Institut Pasteur	Research affiliate, Institut Pasteur and Professor in epidemiology at EHESP French School of Public Health
Dr Rashmi Arora	Indian Council of Medical Research (ICMR)	Senior Deputy Director General and Head, Division of Epidemiology and Communicable Diseases

ANNEXE 2

Survey respondent list

- AbbVie
- Aeras
- Aidsfonds*
- American Leprosy Missions (ALM)
- amfAR, The Foundation for AIDS Research*
- Apopo
- Argentinian Ministry of Science, Technology and Productive Innovation (MINCYT)
- Argentinian National Council for Scientific and Technical Research (CONICET)
- Arisan Therapeutics
- Atomo Diagnostics
- Austrade
- Australian Commonwealth Scientific and Industrial Research Organisation (CSIRO)
- Australian Department of Foreign Affairs and Trade (DFAT)
- Australian Department of Industry, Innovation and Science (DIIS)
- Australian National Health and Medical Research Council (NHMRC)
- Australian National Heart Foundation
- Australian Research Council (ARC)
- Austrian Leprosy Relief Association (ALRA)
- Barcelona Institute for Global Health (ISGlobal) including Clinic Foundation for Biomedical Research (FCRB), Barcelona Centre for International Health Research (CRESIB), and Centre for Research in Environmental Epidemiology (CREAL)
- BASF
- Baylor College of Medicine
- Becton, Dickinson and Company (BD)
- Belgian Ministry of Foreign Affairs, Foreign Trade and Development Cooperation (DGDC)
- Bernhard Nocht Institute for Tropical Medicine (BNI)
- Bill & Melinda Gates Foundation
- Biological E
- Biotechnology Industry Research Assistance Council (BIRAC)
- Brazilian Development Bank (BNDES)
- Brazilian Innovation Agency (FINEP)
- Brazilian Ministry of Health: Department of Science and Technology (DECIT)
- Brazilian Ministry of Health: National STD and AIDS Programme
- Brazilian Research Support Foundation of the State of Bahia (FAPESB)
- Brazilian Research Support Foundation of the State of Minas Gerais (FAPEMIG)
- Brazilian Support Foundation for Research and Innovation in the State of Santa Catarina (FAPESC)
- Brazilian Support Foundation for Research in the State of São Paolo (FAPESP)
- Burnet Institute
- Cairo University
- Campbell Foundation*
- Canadian Institutes of Health Research (CIHR)
- Carlos III Health Institute
- Cebu Leprosy and Tuberculosis Research Foundation (CLTRF)
- Cepheid
- Chilean National Commission for Scientific and Technological Research (CONICYT)
- Chilean National Fund for Scientific and Technological Development (FONDECYT)
- Coalition for Epidemic Preparedness Innovations (CEPI)
- Colombian Department for Science, Technology and Innovation (Colciencias)
- CONRAD*
- Daiichi-Sankyo
- Damien Foundation (DFB)
- Danish Ministry of Foreign Affairs and the Danish International Development Agency (DANIDA)

* Denotes organisations where funding data was only received via the HIV Vaccines and Microbicides Resource Tracking Working Group

- DesignMedix
- Drugs for Neglected Diseases initiative (DND*i*)
- Dutch Ministry of Foreign Affairs - Directorate General of Development Cooperation (DGIS)
- Dutch Organisation for Scientific Research (NWO)
- effect:hope (The Leprosy Mission Canada)
- Eisai
- European & Developing Countries Clinical Trials Partnership (EDCTP)
- European Commission including the Directorate General for Research and Innovation
- European Vaccine Initiative (EVI)
- FAIRMED
- FHI 360
- Finnish Funding Agency for Technology and Innovation (TEKES)
- Fio
- FK Biotec
- Fontilles
- Foundation for Innovative New Diagnostics (FIND)
- French National Agency for Research on AIDS and Viral Hepatitis (ANRS)
- French National Institute of Health and Medical Research (Inserm)
- French National Research Agency (ANR)
- French Research Institute for Development (IRD)
- Gavi, The Vaccine Alliance
- GeoVax
- German Federal Ministry for Economic Cooperation and Development (BMZ)
- German Federal Ministry of Education and Research (BMBF)
- German Federal Ministry of Health (BMG)
- German Leprosy and TB Relief Association (DAHW)
- German Research Foundation (DFG)
- GlaxoSmithKline (GSK)
- Global Affairs Canada
- Global Health Innovative Technology Fund (GHIT Fund)
- GSK Bio
- Hawaii Biotech
- Health Research Council of New Zealand (HRC)
- Hebron
- Indian Council of Medical Research (ICMR)
- Indian Council of Scientific and Industrial Research (CSIR)
- Indian Department of Biotechnology, Ministry of Science and Technology (DBT)
- Indian Department of Health Research, Union Ministry of Health and Family Welfare
- Indian Department of Science and Technology (DST)
- Innovative Medicines Initiative (IMI)[#]
- Innovative Vector Control Consortium (IVCC)
- Inovio
- InPheno
- Institut Pasteur
- Institute of Tropical Medicine Antwerp (ITM)
- Integral Molecular
- International AIDS Vaccine Initiative (IAVI)
- International Centre for Genetic Engineering and Biotechnology (ICGEB)
- International Partnership for Microbicides (IPM)*
- International Union Against Tuberculosis and Lung Disease
- International Vaccine Institute (IVI)
- Irish Aid
- Japanese National Institute of Infectious Diseases (NIID)*
- Jarvis Laboratory
- Johnson & Johnson
- KNCV Tuberculosis Foundation
- Korean Institute of Tuberculosis
- Leadiant Biosciences (previously Sigma-Tau)
- Lepra India - Blue Peter Public Health & Research

* Denotes organisations where funding data was only received via the HIV Vaccines and Microbicides Resource Tracking Working Group
[#] Denotes organisations where funding data was taken from publicly available sources

Centre (BPHRC)
- Leprosy Relief Canada (SLC)
- Leprosy Research Initiative (LRI)
- Lilly
- Liverpool School of Tropical Medicine (LSTM)
- Mapp Biopharmaceutical
- Max Planck Institute for Infection Biology (MPIIB)
- Médecins Sans Frontières (MSF)
- Medicines for Malaria Venture (MMV)
- Meningitis Research Foundation (MRF)
- Mérieux Foundation
- Mexican National Council of Science and Technology (CONACYT)
- Mexican National Institute of Public Health (INSP)
- MSD / Merck
- Mymetics
- Netherlands Leprosy Relief (NLR)
- Noguchi Memorial Institute for Medical Research
- Norwegian Institute of Public Health
- Novartis
- Ontario HIV Treatment Network*
- Osel*
- Otsuka
- Ouro Fino
- Partners in Health
- PATH including the Malaria Vaccine Initiative (MVI)
- Pfizer
- Pharmaceutical Laboratory of the State of Pernambuco (LAFEPE)
- ProtoPharma
- Public Health Agency of Canada (PHAC)*
- Public Health England (PHE)
- Research Centre Borstel
- Research Council of Norway
- Royal Norwegian Ministry of Foreign Affairs and the Norwegian Agency for Development Cooperation (NORAD)
- Royal Society of New Zealand (RSNZ)
- Sabin Vaccine Institute
- San Raffaele Scientific Institute (IRCCS)*
- Sanofi
- Science Foundation Ireland (SFI)
- Serum Institute of India
- Shionogi
- Sidaction*
- South Africa Medical Research Council (MRC)
- South African Department of Science and Technology (DST)
- South African Technology Innovation Agency (TIA)
- Statens Serum Institute (SSI)
- Sumagen*
- Swedish International Development Agency (SIDA)
- Swedish Research Council
- Swiss Agency for Development and Cooperation (SDC)
- Swiss National Science Foundation (SNSF)
- Swiss State Secretariat for Education, Research and Innovation (SERI)
- Swiss Tropical & Public Health Institute (Swiss TPH)
- Syngenta
- Synstar Japan
- Sysmex
- Takeda Pharmaceutical Company
- TB Alliance
- Thai Government Pharmaceutical Organisation (GPO)
- Thai Red Cross AIDS Research Center (TRC-ARC)*
- Thailand National Science and Technology Development Agency (NSTDA)
- The Leprosy Mission International (TLMI)
- The Wellcome Trust
- TuBerculosis Vaccine Initiative (TBVI)
- Turing Foundation
- UBS Optimus Foundation
- UK Department for International Development (DFID)

* Denotes organisations where funding data was only received via the HIV Vaccines and Microbicides Resource Tracking Working Group

- UK Medical Research Council (MRC)
- University of Georgia
- University of Lagos
- University of Nebraska Medical Center
- University of Pittsburgh
- US Agency for International Development (USAID)
- US Centers for Disease Control and Prevention (CDC) including the CDC Foundation
- US Department of Defense (DOD) including Defense Advanced Research Projects Agency (DARPA), US Army Medical Research Institute of Infectious Diseases (USAMRIID), the US Naval Medical Research Center (NMRC), Defense Threat Reduction Agency (DTRA) and the Walter Reed Army Institute of Research (WRAIR)
- US National Institutes of Health (NIH) including the US National Institute of Allergy and Infectious Disease (NIAID)
- Vestergaard
- World Bank
- World Health Organization: Special Programme for Research and Training in Tropical Diseases (WHO/TDR)

* Denotes organisations where funding data was only received via the HIV Vaccines and Microbicides Resource Tracking Working Group

ANNEXE 3

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