G-FINDER | 2016

POLICY CURES RESEARCH.

NEGLECTED DISEASE RESEARCH AND DEVELOPMENT: A PIVOTAL MOMENT FOR GLOBAL HEALTH

POLICY CURES RESEARCH

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ACKNOWLEDGEMENTS

This is the ninth in a series of annual reports published as part of the G-FINDER project. Initially hosted within the George Institute for International Health, the G-FINDER team – then led by Dr Mary Moran – established Policy Cures in 2010. In 2016, Policy Cures separated into two organisations; moving forward, the G-FINDER project will be delivered by Policy Cures Research, a new, independent, not-for-profit research group established by the research and policy team from Policy Cures. The Policy Cures Research team would like to thank Dr Moran for her commitment and contribution to G-FINDER over the past decade.

We are also very grateful to all of the survey participants who have contributed to this effort. With their commitment, we have been able to continue to provide accurate, up-to-date financial information in the field of research and development (R&D) for neglected diseases. The patience and engagement of the participating government and multilateral agencies, academic and research institutions, product development partnerships (PDPs), philanthropic institutions and pharmaceutical and biotechnology companies have made this project possible.

We would like to extend our gratitude to our Advisory Committee and other experts for their invaluable advice on the design and scope of our study. A particularly warm thank you goes to the HIV Vaccines and Microbicides Resource Tracking Working Group for coordinating their initiative with ours where possible.

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EXECUTIVE SUMMARY

The survey

The ninth G-FINDER survey reports on 2015 global investment into research and development (R&D) of new products for neglected diseases, and identifies trends and patterns across the nine years of global G-FINDER data. In all, 185 organisations completed the survey for FY2015, which covered:

- 39 neglected diseases
- 160 product areas for these diseases, including drugs, vaccines, diagnostics, microbicides and vector control products
- Platform technologies (adjuvants, delivery technologies, diagnostic platforms)
- All types of product-related R&D, including basic research, discovery and preclinical, clinical development, Phase IV and pharmacovigilance studies, and baseline epidemiological studies.

In 2015, following a review by our Advisory Committee, the survey introduced the new grouped disease category of African viral haemorrhagic fevers (VHFs). In addition to Ebola, which was already part of the survey, this new category allowed respondents to report R&D funding for Marburg and Other and/or multiple African VHFs. The scope for *Streptococcus pneumoniae* vaccines was also revised to better reflect current approaches to developing pneumococcal vaccines for low-resource settings.

Findings

In 2015, a reported $3,041m was invested in neglected disease R&D, consisting of $2,906m from repeat survey participants (called year-on-year – YOY – funders) and $135m from irregular survey participants. Total YOY funding for neglected disease R&D decreased by $68m (-2.3%). This marked the third consecutive year of declining funding, which has also fallen in every year but one since 2009.

FUNDING BY DISEASE

As in previous years, the 'top tier' diseases – HIV/AIDS, tuberculosis (TB) and malaria – collectively received the vast majority of global neglected disease R&D funding ($2,144m, 71%). Overall funding to the top tier fell by $71m (-3.3%). This was driven by decreased investment in both HIV/AIDS (down $56m, -5.4%) and malaria (down $17m, -3.0%), although this followed a sharp increase in malaria funding in 2014. TB funding remained essentially flat (up $2.4m, 0.5%).

'Second tier' diseases include diarrhoeal diseases, kinetoplastids, dengue, bacterial pneumonia & meningitis, helminths, salmonella infections and hepatitis C (genotypes 4, 5 & 6). Funding for this tier fell by $38m (-5.9%), with lower funding for kinetoplastids (down $21m, -18%), diarrhoeal diseases (down $18m, -11%), hepatitis C (down $11m, -25%) and helminths (down $10m, -13%) partially offset by smaller increases for dengue (up $12m, 14%), bacterial pneumonia & meningitis (up $8.7m, 12%) and salmonella infections (up $2.0m, 3.2%). As in previous years, the 'third tier' diseases – leprosy, cryptococcal meningitis, trachoma, rheumatic fever, Buruli ulcer and leptospirosis – each received less than 0.5% of global R&D funding.

Global funding for neglected disease R&D continued to fall in 2015

Industry investment in neglected disease R&D in 2015 was the highest ever recorded in the G-FINDER survey

Non-disease-specific investment increased to $228m in 2015, with YOY funding increasing by $43m (up 25%), following a sharp drop in 2014. Most of this increase was due to a jump in core funding – non-earmarked funds given to organisations working on multiple neglected diseases – which grew by $32m (up 38%) to $118m, the highest level recorded since the start of the survey. Funding for platform technologies increased by $11m (up 51%), which was essentially a return towards normal levels after a large drop in 2014.

FUNDERS

Public sector funding for neglected disease R&D fell once again in 2015 – extending the decline seen since 2012 – while industry investment edged slightly higher, following a significant increase in 2014. Coupled with a small drop in philanthropic funding, these changes resulted in both the lowest public sector funding share and the highest industry funding share ever recorded in the history of the G-FINDER survey.

Nevertheless, the public sector continued to play a key role in neglected disease R&D, providing close to two-thirds of funding ($1,925m, 63%), almost all of which came from high-income country (HIC) governments and multilaterals ($1,866m, 97%). The philanthropic sector provided 21% of global funding ($645m), and industry contributed the remaining 15% ($471m).

In line with previous years, the top three public funders in 2015 were the US, the European Union (EU) and the UK, with the US contributing over two-thirds of total public R&D investment ($1,378m, 72%). Of the top three funders, only the EU (up $21m, 20%) significantly increased funding in 2015, reflecting its expanded contributions under the second phase of the European and Developing Countries Clinical Trials Partnership (EDCTP). Funding was lower from both the US (down $44m, -3.0%) and the UK (down $22m, -18%). Other notable drops in public funding came from Australia (down $16m, -47%) and the Netherlands (down $13m, -76%), the latter due to the Dutch Ministry of Foreign Affairs' (DGIS) transition between product development partnership (PDP) funding rounds.

Private sector investment in neglected disease R&D in 2015 – in both absolute terms, and as a proportion of global funding – was the highest ever recorded in the history of the G-FINDER survey. YOY industry funding increased marginally (up $7.1m, 1.7%), driven by a $4.7m increase in investment by small pharmaceutical and biotechnology firms (SMEs, up 9.9%), which was mostly for bacterial pneumonia & meningitis and diarrhoeal diseases. Philanthropic funding decreased slightly (down $22m, -3.5%) mainly due to reduced funding from the Wellcome Trust (down $27m, -22%). Funding from the Bill & Melinda Gates Foundation (the Gates Foundation) was steady (down $2.3m, -0.4%).

FUNDING FLOWS

Almost three-quarters of all neglected disease R&D funding in 2015 was external investment in the form of grants ($2,202m, 72%). Three-quarters of this funding went directly to researchers and developers ($1,656, 75% of external investment), $450m (20%) went to PDPs, and the remaining $96m (4.3%) was channelled through other intermediary organisations.

This meant that direct YOY funding to researchers and developers decreased slightly (down $38m, -2.3%). Funding to PDPs also fell (down $65m, -13%) after two years of increased investment, reflecting the highly cyclical nature of grant funding to PDPs, especially from the Gates Foundation. Funding to other intermediary organisations increased substantially (up $31m, 50%), primarily driven by increased funding from S&T agencies (up $22m, 83%) to EDCTP2.

Internal investment continued its slow and steady growth (up $3.8m, 0.5%), largely reflecting the ongoing increase in industry investment in neglected disease R&D.

Ebola and other African VHFs

In light of the unprecedented nature of the global response to the Ebola threat – and its distorting effect on investments in 'traditional' neglected disease R&D – funding for Ebola and other African VHFs (for both 2014 and 2015) has been analysed separately in this year's G-FINDER report. Because only Ebola was included in both the FY2014 and FY2015 surveys, analysis of YOY funding changes has been restricted to Ebola-specific investment.

A total of $631m was invested in R&D for Ebola and other African VHFs in 2015, of which the vast majority was Ebola-specific ($574m, 91%). YOY funding for Ebola R&D more than tripled (up $411m, 258%) – an unprecedented increase compared to any of the neglected diseases traditionally tracked by G-FINDER. Ebola vaccines received the majority of this funding ($370m, 65%) and also saw the highest YOY increase (up $301m, 436%), driven by industry investment.

Although nearly two-thirds ($383m, 61%) of total reported funding for Ebola and other African VHFs came from the public sector, a remarkable 36% ($226m) was contributed by industry, essentially all of which was MNC investment in Ebola vaccine development. This was a major increase in industry funding share compared to 2014, as a near-tripling of YOY Ebola investment by the public sector (up $210m, 182%) was matched by a seven-fold increase by industry (up $194m, 614%).

US Government agencies were responsible for more than three-quarters ($298m, 78%) of all public funding for Ebola and other African VHFs in 2015, and were the primary driver behind the overall increase in public investment in Ebola, with the largest increases coming from the US Biomedical Advanced Research and Development Authority (BARDA, up $78m, 297%) and the US Department of Defense (DOD, up $46m, 423%), followed by the US National Institutes of Health (NIH, up $20m, 32%). However, there was also a more than five-fold increase in European public funding for Ebola (up $63m, 452%), primarily driven by increases from the European Union (EU, up $40m, 900%) and the UK Medical Research Council (MRC, up $18m from zero in 2014). Philanthropic funding for Ebola and other African VHFs was relatively low ($22m, 3.4%).

Due to the high level of industry involvement, internal R&D investments represented a much larger share of total funding for Ebola and other African VHFs (54%) than was the case for other neglected diseases (28%). Almost all external (grant or contract) funding was given directly to researchers and developers (including industry), rather than being channelled through intermediary organisations; PDPs received a single grant, and there was no funding to other intermediaries specifically earmarked for Ebola and other African VHFs.

DISCUSSION

The scale and nature of the global R&D funding response to the West African Ebola outbreak is now truly apparent

- In 2015, a total of $631m was invested in R&D for Ebola and other African VHFs – more than in any neglected disease except for HIV/AIDS.
- The US Government provided 78% of all public funding Ebola and other African VHFs, despite a more than five-fold increase in Ebola R&D investment by European public funders.
- Industry invested $226m in R&D for Ebola and other African VHFs in 2015, far more than they did in any single neglected disease, and more than their combined investment in all neglected diseases other than malaria and TB.

Global funding for neglected disease R&D reached historic lows in 2015, driven by declining public sector investment

- In contrast to Ebola and other African VHFs, funding for neglected disease R&D in 2015 fell to its lowest level since 2007, with YOY global funding now $180m below its 2012 peak.
- Public sector funding for neglected disease R&D also fell to its lowest level since 2007, driven by another drop in US Government funding (down $44m, -3.0%), which fell to the lowest level ever recorded in the history of the G-FINDER survey.
- Increased funding from the EU (up $21m, 20%) made it the second-largest public funder of neglected disease R&D globally in 2015, moving ahead of the UK (down $22m, -18%).

In sharp contrast to the public sector, industry investment in neglected disease R&D reached historical highs

- 2015 was the fourth year in a row that industry has increased its investment in neglected disease R&D – the only sector to have recorded year-on-year growth for such a stretch.
- Industry's share of global funding is now comparable to that of the Gates Foundation, although this level of investment in neglected disease R&D by industry may be put at risk if public funding continues to fall.
- Industry funding was focused on a subset of neglected diseases, with malaria and TB alone accounting for more than half of all industry investment in neglected disease R&D in 2015.

The highly concentrated nature of neglected disease R&D funding remains an area of concern

- Researchers and developers continue to rely upon a small number of large funders, particularly the US Government (the US NIH especially) and the Gates Foundation.
- 40% of all neglected disease R&D funding goes to organisations that receive more than 80% of their funding from the US Government, which has reduced its funding for neglected disease R&D by a quarter of a billion dollars since 2012.
- PDPs remain highly reliant on the Gates Foundation; in 2015, nearly half of all PDPs received more than half their funding from the Gates Foundation.

Conclusion

- The findings of this year's report show that there are significant additional financial resources available – including from the pharmaceutical industry – for R&D into infectious diseases that largely exist only in the developing world.
- When funding for Ebola and other African VHFs is added to that for neglected diseases, global investment in R&D increased by $396m (up 13%) in 2015 – the largest single year increase ever recorded by G-FINDER – with public funding growing by $210m (up 10%) and investment by industry nearly doubling (up $201m, 44%).
- There is an opportunity to capitalise on the lessons learned from the global response to the Ebola epidemic – not only to ensure that we are better prepared for the next emerging infectious disease outbreak, but also to secure adequate and sustainable R&D funding to address the existing and much larger challenge posed by neglected diseases.

INTRODUCTION

Background to the G-FINDER survey

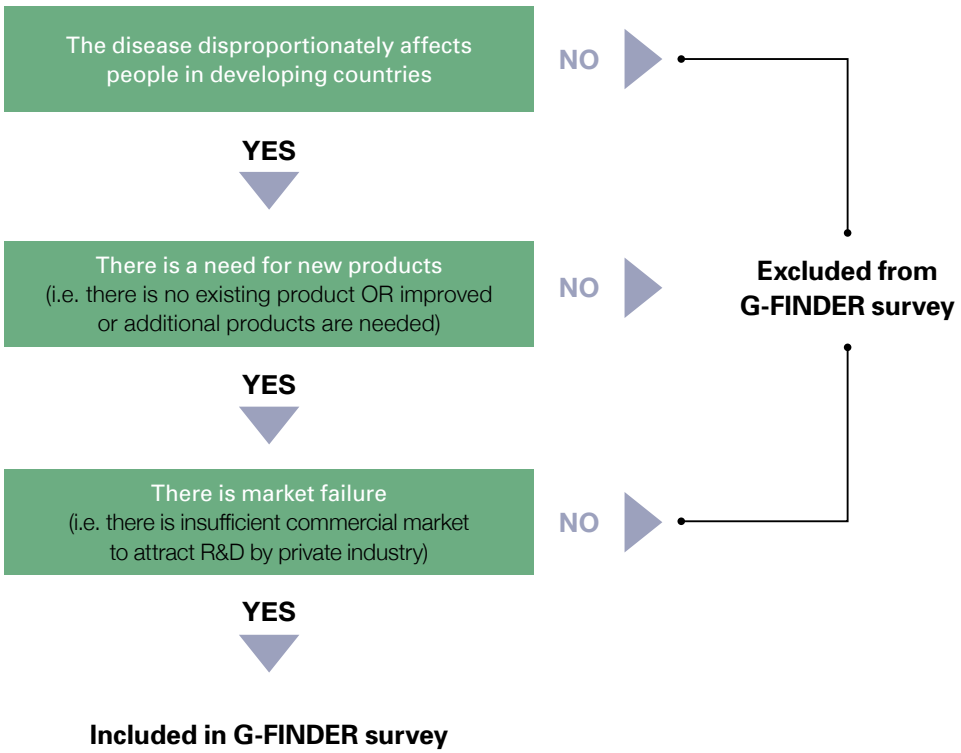
The first eight G-FINDER reports shed light on global investment into research and development (R&D) of new products to prevent, diagnose, manage or cure neglected diseases of the developing world each year since 2007. The ninth G-FINDER survey reports on 2015 investments.

The survey

WHICH DISEASES AND PRODUCTS ARE INCLUDED?

The scope of the G-FINDER survey is determined by applying three criteria (see Figure 1). Application of these criteria results in 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



Ebola and other African viral haemorrhagic fevers analysed separately

All product R&D is covered by the survey, including:

- Drugs
- Vaccines (preventive and therapeutic)
- Diagnostics
- Microbicides
- Vector control products (pesticides, biological control agents and vaccines targeting animal reservoirs)
- Platform technologies (adjuvants, diagnostic platforms and delivery devices). These are technologies that can potentially be applied to a range of neglected diseases and products, but which have not yet been attached to a specific product for a specific disease.

We note that not all product types are needed for all diseases. For example, effective pneumonia management requires new developing-world specific vaccines, but does not need new drugs as therapies are either already available or in commercial development.

Funders were asked to only report investments *specifically* targeted at developing-country R&D needs. This is important to prevent neglected disease data being swamped by funding for activities not directly related to product development (e.g. advocacy and behavioural research); or by 'white noise' from overlapping commercial R&D investments (e.g. HIV/AIDS drugs and pneumonia vaccines targeting Western markets, and investments in platform stechnologies with shared applications for industrialised countries). As an example, G-FINDER defines eligible pneumonia vaccine investments by strain, vaccine type and target age group; while eligible HIV/AIDS drug investments are restricted to developing-country relevant products such as fixed-dose combinations (FDCs) and paediatric formulations.

The initial scope of G-FINDER diseases and eligible R&D areas was determined in the first survey year (2007) in consultation with an international Advisory Committee (AC) of experts in neglected diseases and neglected disease product development. A second round of consultations took place in year two. As a result of this process, for the 2008 survey, the typhoid and paratyphoid fever disease category was broadened to include non-typhoidal *Salmonella enterica* (NTS) and multiple *Salmonella* infections; while diagnostics for lymphatic filariasis were added as a neglected area.

In year seven, following a review by our AC (Annexe 2), the survey was expanded to include three additional diseases: cryptococcal meningitis, hepatitis C genotype 4 and leptospirosis. The AC review also decided that dengue vaccines no longer fit the criteria for inclusion in the G-FINDER survey given the emergence of a significant commercial market, and dengue vaccine R&D (including all previously reported investments) was removed from the scope of the survey. This does not affect other dengue products, which continue to be included.

In response to the 2014 West African Ebola epidemic, the survey scope was expanded again in year eight to capture investments in Ebola R&D for diagnostics, drugs and preventive vaccines, as well as basic research. On the advice of the AC, the scope of the hepatitis C category was also expanded to capture investment into R&D for two additional genotypes that disproportionately affect people in developing countries (genotypes 5 and 6).

After further consultation with the AC, a new grouped disease category was incorporated in this year's survey: African viral haemorrhagic fevers (VHFs). In addition to Ebola, this new category allowed respondents to report R&D funding for Marburg and Other and/or multiple African VHFs. Because of the unique nature of the Ebola threat and global response – evidenced by the significant influx of private sector investment seen in this year's survey – R&D funding for Ebola and other African VHFs has been analysed separately in order not to distort the main neglected disease analysis.

The scope of G-FINDER neglected diseases, products and technologies included in year nine is shown in Table 1.

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

Disease		Basic research	Drugs	Vaccines (Preventive)	Vaccines (Therapeutic)	Microbicides	Vector control products	Diagnostics
HIV/AIDS		R	R	Y		Y		Y
Tuberculosis		Y	Y	Y	Y			Y
Malaria	*P. falciparum*	Y	Y	Y			Y	Y
	P. vivax	Y	Y	Y			Y	Y
	Other and/or unspecified malaria strains	Y	Y	Y			Y	Y
Diarrhoeal diseases	Rotavirus			R				
	Cholera	Y	R	Y				Y
	Shigella	Y	R	Y				Y
	Enterotoxigenic *E. coli* (ETEC)			Y				Y
	Cryptosporidium	Y	R	Y				Y
	Enteroaggregative *E.coli* (EAggEC)			Y				Y
	Giardia							Y
	Multiple diseases	Y	R	Y				Y
Kinetoplastids	Leishmaniasis	Y	Y	Y	Y			Y
	Sleeping sickness	Y	Y	Y			Y	Y
	Chagas' disease	Y	Y	Y	Y		Y	Y
	Multiple diseases	Y	Y	Y	Y		Y	Y
Dengue		Y	Y				Y	Y
Bacterial pneumonia & meningitis	*S. pneumoniae*			R				Y
	N. meningitidis			R				Y
	Both bacteria							Y
Helminth infections	Schistosomiasis (bilharziasis)	Y	Y	Y			Y	Y
	Lymphatic filariasis (elephantiasis)	Y	Y				Y	Y
	Onchocerciasis (river blindness)	Y	Y	Y			Y	Y
	Hookworm (ancylostomiasis & necatoriasis)	Y	Y	Y				
	Tapeworm (cysticercosis/taeniasis)	Y	Y				Y	
	Strongyloidiasis & other intestinal roundworms	Y	Y	Y				Y
	Whipworm (trichuriasis)	Y	Y					
	Roundworm (ascariasis)	Y	Y					
	Multiple diseases	Y	Y	Y			Y	Y
Salmonella infections	Typhoid and paratyphoid fever (*S. typhi, S. paratyphi A*)	Y	Y	Y				Y
	Non-typhoidal *S. enterica (NTS)*	Y	Y	Y				Y
	Multiple *Salmonella* infections	Y	Y	Y				Y
Hepatitis C (genotypes 4, 5 & 6)			R	Y				Y
Leprosy		Y	Y					Y
Cryptococcal meningitis			Y					
Trachoma				Y				Y
Rheumatic fever				Y				
Buruli ulcer		Y	Y	Y				Y
Leptospirosis								R
Platform technologies (non-disease specific)		General diagnostic platforms			Adjuvants and immunomodulators		Delivery technologies and devices	
			R			R		R
African viral haemorrhagic fevers (VHFs)	Ebola	Y	Y	Y				Y
	Marburg	Y	Y	Y				Y
	Other and/or multiple African VHFs	Y	Y	Y			Y	Y

'R' denotes a restricted category where only some investments are eligible, as defined in the neglected disease R&D scope document
'Y' denotes a category where a disease or product is included in the survey

WHAT TYPES OF INVESTMENTS ARE INCLUDED?

G-FINDER quantifies neglected disease investments in the following R&D areas:

- Basic research
- Product discovery and preclinical development
- Product clinical development
- Phase IV/pharmacovigilance studies of new products
- Baseline epidemiology in preparation for product trials

Although we recognise the vital importance of activities such as advocacy, implementation research, community education and general capacity building, these are outside the scope of G-FINDER. We also exclude investment into non-pharmaceutical tools such as bednets or circumcision, and general therapies such as painkillers or nutritional supplements, as these investments cannot be ring-fenced to neglected disease treatment only.

HOW WAS DATA COLLECTED?

Two key principles guided the design of the G-FINDER survey. We sought to provide data in a manner that was consistent and comparable across all funders and diseases, and as close as possible to 'real' investment figures.

G-FINDER was therefore designed as an online survey into which all organisations entered their investment data in the same way according to the same definitions and categories, and with the same inclusion and exclusion criteria. All funders were asked to only include disbursements, as opposed to commitments made but not yet disbursed; and we only accepted primary grant data. The exception was the United States National Institutes of Health (US NIH), for whom data was collected by mining the US NIH's Research Portfolio Online Reporting Tools (RePORTER) and Research, Condition, and Disease Categorization (RCDC) process.

Participating multinational pharmaceutical companies (MNCs) agreed to provide full data on their neglected disease investments. However, as these companies do not operate on a grant basis, the reporting tool was varied. Instead of grants, companies agreed to enter the number of staff working on neglected disease programmes, their salaries, and direct project costs related to these programmes. All investments were allocated by disease, product and research type according to the same guidelines used for online survey recipients. As with other respondents, companies were asked to include only disbursements rather than commitments. They were also asked to exclude 'soft figures' such as in-kind contributions and costs of capital.

The ninth G-FINDER survey was open for a six-week period from June to July 2016, during which intensive follow-up and support for key recipients led to a total of 9,070 entries being recorded in the database for financial year 2015.

With the exception of grants from major key funders, in particular the US NIH, all entries over $0.5m (i.e. any grant over 0.01% of total funding) were verified against the inclusion criteria and crosschecked for accuracy. Cross-checking was conducted through automated reconciliation reports that matched investments reported as disbursed by funders with investments reported as received by intermediaries and product developers. Any discrepancies were resolved by contacting both groups to identify the correct figure. 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). Industry data was aggregated for MNCs and for small pharmaceutical and biotechnology companies (SMEs) in order to protect their confidentiality.

WHO WAS SURVEYED?

A total of 185 organisations participated directly in the G-FINDER survey, reporting data on behalf of a total of 209 organisations. This meant that we received data for more organisations than the previous year, despite targeting our survey follow-up to increase efficiency.

G-FINDER is primarily a survey of funding, and thus of funders. In its ninth year, 143 funders in 29 countries around the world participated in the survey. These included:

- Public, private and philanthropic funders in:
  - High-income countries (HICs) that are part of the Organisation for Economic Co-operation and Development (OECD)
  - European Union (EU) member states and the European Commission (EC)
- Public funders in three Innovative Developing Countries (IDCs) (Brazil, India and South Africa)
- Public funders in an additional three middle-income countries (MICs) (Colombia, Mexico and Thailand)
- Private sector funders in two MICs (Brazil and India)

G-FINDER also surveyed a wide range of funding intermediaries, product development partnerships (PDPs), and researchers and developers who received funding. Data from these groups was used 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.

HOW WERE CHANGES IN PARTICIPATION MANAGED?

It is important when comparing figures between survey years to distinguish between real changes in funding and *apparent* changes due to fluctuating numbers of survey participants. Funding figures have therefore been broken down to distinguish between:

1. Increases or decreases reported by repeat survey participants – called YOY funders – which represent real funding changes
2. Changes associated with irregular survey participants. These include increases reported by new survey participants and decreases due to non-participation by organisations that provided data to G-FINDER in previous years but which were lost to follow-up. These do not represent true changes in neglected disease funding, but rather are related to expansion or contraction of G-FINDER's data capture.

Reading the findings

The ninth G-FINDER survey collected data on financial year 2015 investments. Throughout the text, we refer to survey years as follows: 2007 refers to financial year 2007 (year one of the survey), 2008 refers to financial year 2008 (year two of the survey) and so on up to the current year (financial year 2015, year nine of the survey).

Any changes in funding (increases or decreases) noted in the report refer only to those organisations that participated across all years of the survey, i.e. YOY funders. Any real new funding streams, for example the introduction of the Global Health Innovative Technology Fund (GHIT), are also included in YOY analysis. YOY amounts reported in previous years may not always match the YOY amount reported in year nine due to dropouts (i.e. loss to follow-up).

All funding is reported in constant 2015 US dollars

As in previous G-FINDER reports, all funding data has been adjusted for inflation and converted to US dollars (US$) to eliminate artefactual effects caused by inflation and exchange rate fluctuations, thus allowing accurate comparison of YOY changes. In line with the new approach to financial reporting implemented in year seven, the base year of the survey for inflation adjustment purposes has been updated to the current financial year of the survey, and so all funding data is reported in 2015 US$. As a result of this rebasing, historical G-FINDER data for the years 2007 to 2014 presented in this report will differ from the figures published in previous G-FINDER reports.

Unless noted otherwise, all DALY (disability-adjusted life year) and mortality figures in the report specifically represent low- and middle-income country (LMIC) figures and are taken from the Global Burden of Disease Study 2015 (GBD 2015),[1] which represent the most comprehensive and recent figures available. We note that some of the GBD 2015 methodologies have been updated compared to previous GBD studies,[2] so the figures quoted in this report may not be directly comparable to the figures published in previous G-FINDER reports. Due to the level of detail in GBD 2015, figures for bacterial pneumonia & meningitis reflect only DALYs and mortality related to pathogens that are within G-FINDER scope. In some cases, GBD 2015 estimates are different from those derived using other methods or published by other groups, however they allow the most consistent approach across diseases.

For brevity, we use the terms 'LMICs' and 'developing countries' (DCs) to denote low- and middle income countries and 'HICs' to denote high-income countries as defined by the World Bank.[3] IDCs refers to developing countries with a strong R&D base (Brazil, India and South Africa) who participated in the G-FINDER survey. MNCs are defined as multinational pharmaceutical companies with revenues of over $10bn *per annum*.

Around 1.6% ($53m) 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.

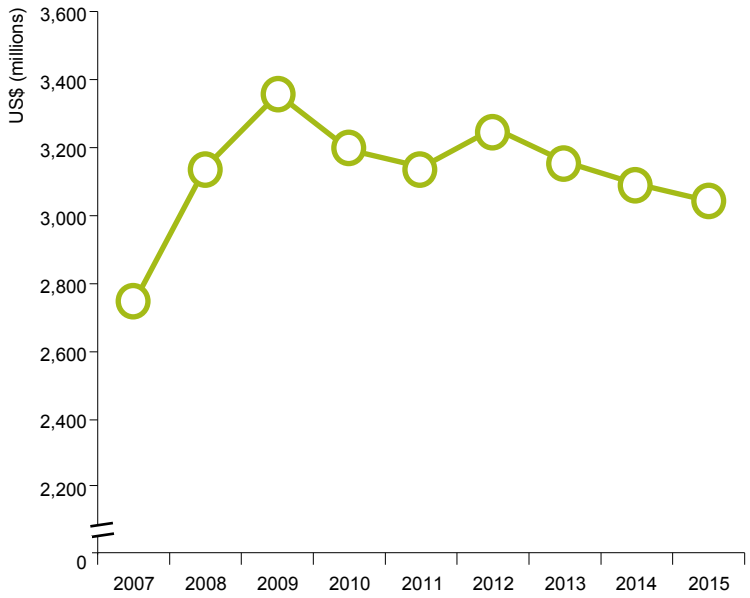
A further 4.1% ($132m) was given as core funding to R&D organisations that work in multiple disease areas, for example, the European and Developing Countries Clinical Trials Partnership (EDCTP) and the Foundation for Innovative New Diagnostics (FIND). As this funding could not be accurately allocated 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.

Finally, readers should be aware that, as with all surveys, there are limitations to the data presented. Survey non-completion by funders will have an impact, as will methodological choices (see Online annexe A for further details).

FUNDING BY DISEASE

Total global investment in R&D for neglected diseases in 2015 was $3,041m. Of this, $2,906m was reported by repeat survey participants (called year-on-year – YOY – funders), and the remaining $135m by irregular survey participants.

Figure 2. Total R&D funding for neglected diseases 2007-2015



Compared to 2014, YOY funding fell by $68m (-2.3%). This marked the third consecutive year of declining funding for neglected disease R&D, which has fallen in every year but one since 2009.

Neglected diseases fall into three distinct funding tiers. The 'top tier' diseases – HIV/AIDS, TB and malaria – collectively received more than two-thirds ($2,144m, 71%) of total global neglected disease R&D funding, with HIV/AIDS receiving 33% and TB and malaria 19% each. Funding fell for both HIV/AIDS (down $56m, -5.4%) and malaria (down $17m, -3.0%) after a sharp increase in investment for the latter in 2014, whilst TB funding remained essentially flat (up $2.4m, 0.5%).

'Second tier' diseases are those that receive between 1% and 6% of total funding. This group includes diarrhoeal diseases, kinetoplastids, dengue, bacterial pneumonia & meningitis, helminths, salmonella infections and hepatitis C (genotypes 4, 5 & 6). Funding for most of these diseases decreased quite significantly: kinetoplastids (down $21m, -18%), diarrhoeal diseases (down $18m, -11%), hepatitis C (down $11m, -25%) and helminths (down $10m, -13%). Investment for dengue (up $12m, 14%) and bacterial pneumonia & meningitis (up $8.7m, 12%) increased, while funding for salmonella infections remained fairly stable (up $2.0m, 3.2%).

Table 2. R&D funding by disease 2007-2015^

Disease or R&D area	US$ (millions)									2015 % of total
	2007	2008	2009	2010	2011	2012	2013	2014	2015	
HIV/AIDS	1,204	1,294	1,265	1,195	1,150	1,187	1,091	1,063	1,012	33.3
Tuberculosis	444	486	596	614	568	545	559	562	567	18.6
Malaria	493	584	639	573	594	579	533	581	565	18.6
Diarrhoeal diseases	126	147	200	175	165	167	197	174	160	5.3
Kinetoplastids	134	149	173	156	140	142	119	140	112	3.7
Dengue	50.6	52.0	78.2	67.8	78.9	79.1	75.1	85.1	99.7	3.3
Bacterial pneumonia & meningitis	32.9	98.4	74.2	100	104	108	101	74.5	92.1	3.0
Helminths (worms & flukes)	56.1	74.4	86.4	80.0	86.6	91.5	92.2	91.8	76.8	2.5
Salmonella infections	10.2	43.9	43.7	48.3	48.2	57.8	65.1	65.7	67.9	2.2
Hepatitis C (genotypes 4, 5 & 6)							46.4	44.7	33.5	1.1
Leprosy	5.9	10.7	11.7	10.1	8.8	14.7	12.6	10.5	10.8	0.4
Cryptococcal meningitis							3.2	5.7	5.8	0.2
Trachoma	1.6	2.2	2.0	5.2	10.9	9.9	6.0	6.8	4.8	0.2
Rheumatic fever	1.9	2.5	3.4	2.0	0.9	0.9	0.9	1.3	2.2	0.1
Buruli ulcer	2.4	1.9	1.8	5.5	5.7	6.0	6.4	3.6	1.8	0.1
Leptospirosis							0.4	1.2	1.2	<0.1
Platform technologies	9.6	17.7	24.8	30.3	18.2	49.8	43.8	22.3	33.1	1.1
General diagnostic platforms	5.1	5.8	9.7	10.4	10.7	17.1	16.6	9.6	13.7	0.4
Adjuvants and immunomodulators	2.5	2.5	6.2	10.1	5.7	27.7	21.2	8.4	11.9	0.4
Delivery technologies and devices	2.0	9.3	8.8	9.8	1.9	4.9	6.1	4.3	7.4	0.2
Core funding of a multi-disease R&D organisation	108	96.9	71.6	74.2	88.2	108	111	92.4	118	3.9
Unspecified disease	58.1	83.5	83.0	53.7	73.1	109	89.9	68.8	76.9	2.5
Disease total	2,738	3,144	3,354	3,190	3,140	3,254	3,153	3,094	3,041	100

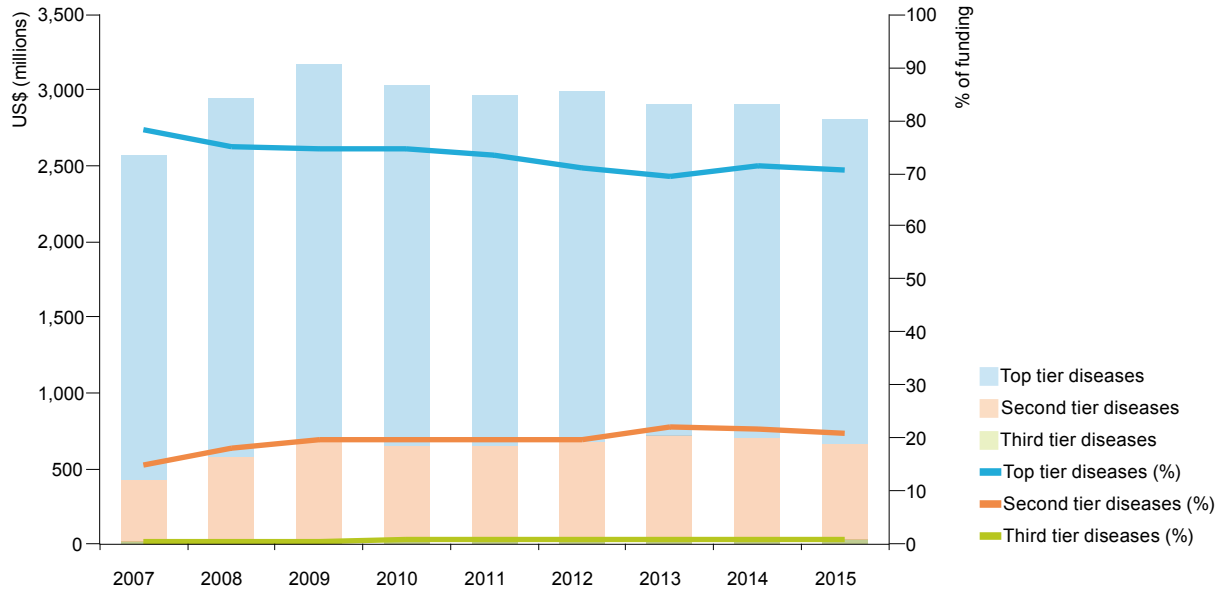
^ Please note that some of the diseases listed are actually groups of diseases, such as the diarrhoeal illnesses and helminth infections. This reflects common practice and also the shared nature of research in some areas. For example, *Streptococcus pneumoniae* R&D is often targeted at both pneumonia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

New disease added to G-FINDER in 2013

'Third tier' diseases each receive less than 0.5% of global funding, making them the most poorly funded of the neglected diseases covered in this report. These include leprosy, cryptococcal meningitis, trachoma, rheumatic fever, Buruli ulcer and leptospirosis. Because of the small numbers of funders and grants these diseases receive in any given year it is not possible to meaningfully comment on YOY funding trends.

YOY funding was lower for both the top and second tiers in 2015 (top tier down $71m, -3.3%; second tier down $38m, -5.9%). The share of funding for each tier remained stable, with top tier diseases accounting for 71% (unchanged from last year), second tier 21% (down slightly from 22%) and third tier diseases 0.9% (unchanged from last year).

Figure 3. Funding distribution 2007-2015^



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

Non-disease-specific investment increased to $228m in 2015, with YOY funding up by $43m (up 25%), following a sharp drop in 2014. Most of this increase was due to a jump in core funding – investment given to an organisation that researches and develops products for multiple neglected diseases and not earmarked for a specific disease – which grew by $32m (up 38%) to $118m, the highest level recorded since the start of the survey. This was almost entirely due to increased core funding from the European Union[i] (EU) to the European and Developing Countries Clinical Trials Partnership (EDCTP, up $19m, 86%), reflecting the expanded budget of EDCTP2, and a grant cycle-related increase from the Bill & Melinda Gates Foundation (Gates Foundation, up $17m, from $0.5m in 2014).

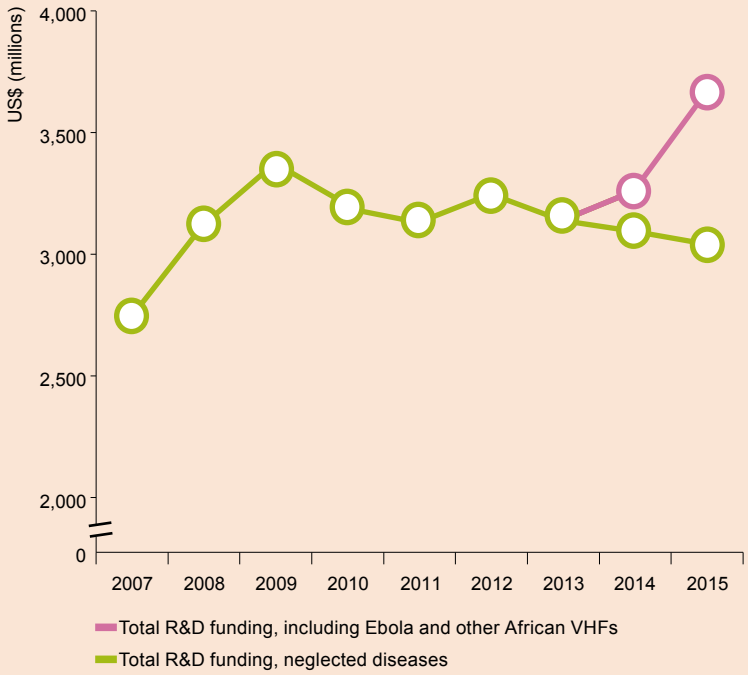
Platform technologies – tools that can potentially be applied to a range of areas, but which are not yet focused on a specific product or disease – received $33m. YOY funding grew by $11m (up 51%); this was essentially a return towards normal levels, after a large drop in 2014. The increase was evenly shared between diagnostic platforms (up $3.9m, 43%), adjuvants and immunomodulators (up $3.5m, 43%) and delivery technologies and devices (up $3.4m, 85%). The Gates Foundation accounted for the majority of the funding increase for both adjuvants and immunomodulators (up $3.5m, 70%) and delivery technologies and devices (up $3.3m, 137%), while the increase for diagnostic platforms came primarily from the German Federal Ministry of Education and Research (BMBF, up $3.5m, from a very low base).

[i] The term 'European Union' is used here and throughout the report to refer 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 and Developing Countries Clinical Trials Partnership and the Innovative Medicines Initiative)

Ebola and other African VHFs

In response to the 2014 West African Ebola epidemic, last year's G-FINDER survey tracked funding for Ebola R&D for the first time (capturing FY2014 investments). This year, the survey scope was expanded to also include R&D funding for African viral haemorrhagic fevers (VHFs) other than Ebola, and funding that was directed at multiple African VHFs.

Figure 4. Total R&D funding with Ebola and other African VHFs 2007-2015



In the 2015 survey, the true scale of the global response to the Ebola outbreak became apparent. Total investment in R&D for Ebola and other African VHFs was $631m; investment in Ebola and other African VHFs went up significantly by $464m (up 288%), with the majority of the increase being for Ebola specifically (up $411m, 258%).

If this funding is included in the analysis of the 'traditional' G-FINDER neglected diseases, the funding picture is changed significantly. Had Ebola and other African VHFs been included in the 2015 totals, YOY funding for neglected disease R&D would have increased by $396m, (up 13%) to a total of $3,627m, and Ebola and other African VHFs would have been the second-highest funded of all the neglected diseases – receiving significantly more than both malaria and TB – accounting for 17% of total funding.

This increase would have been enough to make Ebola and other African VHFs a 'top tier' disease – meaning that total funding for the top tier diseases increased by $393m (up 17%) to $2,775m, accounting for more than three-quarters (76%) of total funding. Consequently, funding share of the second and third tier diseases would have fallen to 17% and 0.7%, respectively.

Because of the unprecedented nature of the global response to the Ebola threat – and its distorting effect on existing investments in neglected disease R&D – funding for Ebola and other African VHFs has been analysed separately. Where relevant, a comparison has been made between funding for neglected diseases with and without Ebola and other African VHFs. This is a departure from last year's approach, when Ebola investment was included in all neglected disease analysis.

HIV/AIDS

The Acquired Immune Deficiency Syndrome (AIDS) is caused by the Human Immunodeficiency Virus (HIV). This virus infects cells of the human immune system, destroying or impairing their function. As the immune system becomes progressively weaker, the patient becomes more susceptible to other diseases, often dying from TB or other opportunistic infections.

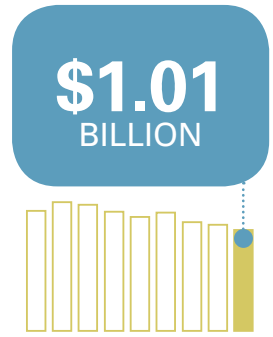
HIV/AIDS was responsible for 66 million DALYs and 1.2 million deaths in the developing world in 2015, making it the second highest cause of morbidity and the third highest cause of mortality from neglected diseases.

The rapid mutation of the HIV virus has posed a significant challenge for vaccine development, with an efficacious vaccine still many years away. Whilst proving for the first time that a vaccine could prevent HIV infection, Phase III clinical trials of the most advanced vaccine candidate (a prime boost combination) in 2009 demonstrated a modest 31% efficacy.[4] However, a new vaccine regimen based on this combination has recently started Phase IIb/III trials in South Africa (HVTN 702), the first HIV vaccine efficacy study to launch anywhere in seven years. There are several other vaccines in Phase I and II trials, aiming to either block the infection through antibody response or clear the infection via cell-mediated immunity.

Antiretroviral (ARV) drugs are available, but many are not adapted for DC use, and fixed-dose combinations (FDCs) and paediatric formulations are needed. Although the paediatric formulation of LPV/r pellets, currently in late-stage development, has many advantages, its poor taste will be a barrier.[5]

Current methods for early diagnosis and support of HIV treatment are also often unsuitable for DCs, especially for infants, although there has been progress towards robust, simple, rapid point-of-care (POC) diagnostics, with several promising candidates in preclinical and clinical development. The LYNX HIV p24 Antigen Test, the only platform in the pipeline dedicated entirely to early infant diagnosis, is undergoing evaluation in Africa and Asia.[6]

Several microbicide candidates have failed in Phase II/III trials (including PRO 2000®, BufferGel® and VivaGel®) and tenofovir gel's Phase III FACTS 001 trial was unable to replicate promising results from an earlier late-stage trial.[7] Most recently, Phase III results for the long acting dapivirine ring are promising: among women over 21 who appeared to use the monthly ring consistently, HIV risk was cut by at least 56%, a statistically significant finding. The developers plan to apply for regulatory approval by Q1 2017.[8] However, potential resistance to the ARV components of microbicides and its impact on treatment will require monitoring.[9]



TOTAL SPEND ON HIV/AIDS R&D IN 2015

OF GLOBAL R&D FUNDING

R&D needed for HIV/AIDS in DCs includes:

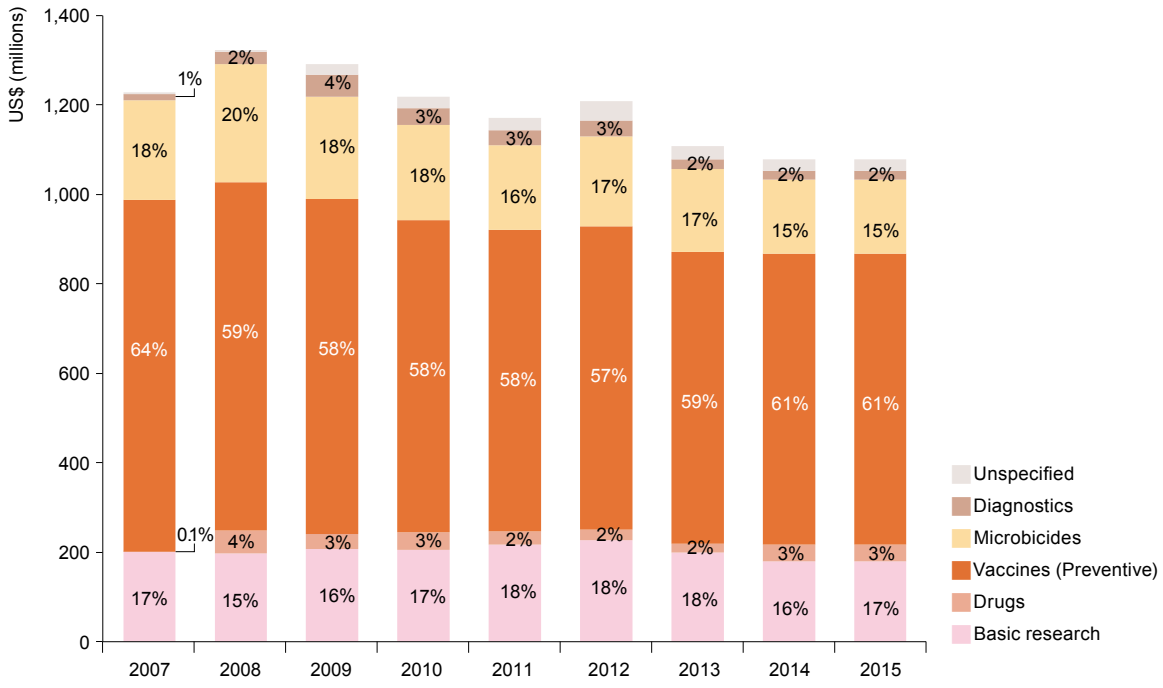
- Basic research
- Drugs specific to DC needs
- Preventive vaccines
- Diagnostics
- Microbicides

HIV/AIDS received $1,012m in R&D funding in 2015; $991m of this came from regular survey participants (YOY funders), with the remaining $21m reported by irregular participants. Although HIV/AIDS once again received around one-third (33%) of all neglected disease R&D investment, YOY funding was down by $56m (-5.4%). Proportionally this was not a major drop, but it marked the sixth year in the last seven in which funding for HIV/AIDS R&D has fallen.

Over half of all HIV/AIDS funding in 2015 was for vaccine development ($619m, 61%), and most of the remainder went towards basic research and microbicides, which received $175m (17%) and $147m (15%) respectively. Developing world-focused R&D in drugs ($26m, 2.6%) and diagnostics ($19m, 1.9%) both received very little funding by comparison.

YOY funding fell for all product types in 2015. The largest decrease was in vaccines (down $29m, -4.5%), mainly due to reduced funding from the US Department of Defense (DOD, down $27m, -49%), although this may partly reflect more accurate reporting for 2015. Microbicide investment was down by $18m (-11%), reflecting the conclusion of major product trials conducted by the International Partnership for Microbicides (IPM), and funding for drug development fell by a third (down $11m, -32%), driven by reduced funding from the Gates Foundation (down $7.8m, -56%). Funding for basic research (down $1.9m -1.1%) and diagnostics (down $0.9m, -4.7%) was relatively stable.

Figure 5. HIV/AIDS R&D funding by product type 2007-2015



The top 12 funders provided 96% of total HIV/AIDS R&D funding in 2015. The US National Institutes of Health (NIH) remained by far the largest funder, contributing two-thirds ($664m, 66%) of total investment. Almost all of the major HIV/AIDS funders dropped their funding in 2015, with the most dramatic cut coming from the US DOD (down $34m, -54%), which halved its funding for HIV/AIDS

R&D. As mentioned previously, this may partly reflect more accurate reporting by the US DOD in 2015; notably, however, this was this organisation's lowest recorded investment in R&D for HIV/AIDS since 2008. Smaller reductions came from the Wellcome Trust (down $4.9m, -21%), the Gates Foundation (down $4.5m, -4.1%) and the US NIH (down $2.8m, -0.4%). Several other funders who featured in the top 12 HIV/AIDS funders in last year's report dropped their funding considerably, including the UK Department for International Development (DFID, related to the conclusion of IPM's microbicide trials, down $9.6m, -86%) and the Dutch Ministry of Foreign Affairs (DGIS, down $4.7m, -79%).

After quadrupling its investment in 2014, industry further increased its investment in R&D for HIV/AIDS in 2015 with $9.2m (up 22%), mainly for clinical development. The only other increase of over $1.0m came from the German BMBF (up $1.8m, 98%, albeit from a low base).

Table 3. Top HIV/AIDS R&D funders 2015

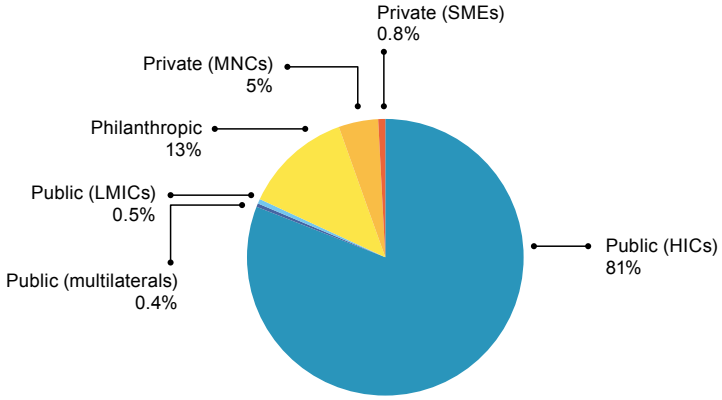
Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total	2007-2015 trend
US NIH	778	738	790	754	723	744	677	667	664	66	
Gates Foundation	105	184	137	136	127	125	122	111	107	11	
USAID	77	78	78	78	74	73	66	59	58	5.7	
Aggregate industry	19	49	37	31	24	22	16	46	55	5.5	
US DOD	32	28	39	36	48	53	56	62	28	2.8	
Wellcome Trust	6.5	9.1	9.2	11	16	26	21	23	18	1.8	
EU	23	24	25	17	17	13	16	13	11	1.1	
Inserm	0.3	1.1	12	13	13	12	12	11	11	1.1	
Canadian CIHR	3.3	1.9	5.2	8.2	7.7	7.4	7.7	7.9	6.3	0.6	
UK MRC	12	11	12	11	6.3	4.9	6.0	7.0	5.3	0.5	
French ANRS	9.6	14	11	10	8.9	9.6	11	4.2	4.2	0.4	
German BMBF			-	2.4	0.9	1.6	2.1	1.9	3.7	0.4	
Subtotal of top 12^	1,134	1,201	1,195	1,126	1,082	1,112	1,019	1,023	972	96	
Disease total	1,204	1,294	1,265	1,195	1,150	1,187	1,091	1,063	1,012	100	

^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015
- 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

Public funders continued to provide the vast majority of HIV/AIDS R&D funding in 2015, investing $829m (82%). Virtually all public funding (99%) came from HICs, which in turn primarily came from the US NIH (81%). Philanthropic funders remained the second highest contributors, investing $128m (13%). The pharmaceutical industry invested $55m (5.5%) in DC-specific HIV/AIDS R&D. Of this, the majority ($47m, 85%) came from multinational pharmaceutical companies (MNCs) and the rest ($8.3m, 15%) from small pharmaceutical and biotechnology firms (SMEs).

Industry was the only sector to increase its HIV/AIDS R&D investments in 2015 (up $7.5m, 22%), mostly from MNCs, with funding lower from both the public (down $56m, -6.4%) and philanthropic (down $9.6m, -7.1%) sectors.

Figure 6. HIV/AIDS R&D funding by sector 2015



TUBERCULOSIS

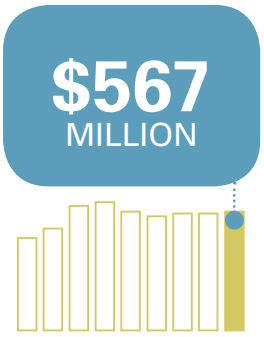
Tuberculosis (TB) is a bacterial disease that usually affects the lungs, and is spread by air droplets. After infection, TB may remain latent with no symptoms. However, if it progresses to active disease, it causes coughing, night sweats, fever and weight loss. TB is a leading cause of death among people with HIV/AIDS. In 2015, TB was responsible for 40 million DALYs and 1.1 million deaths in the developing world. It was the fifth highest cause of morbidity and fourth highest cause of mortality from neglected diseases.

The only available TB vaccine is the BCG vaccine, an 80 year-old vaccine that is highly effective against disseminated TB in children, but not against primary infection or reactivation.[10] A new vaccine is needed that is more effective than, and as safe as, BCG. Current TB drug regimens are complex and last 6-24 months, leading to poor compliance and fuelling drug resistance, treatment failure and death. New drugs are needed that act more rapidly, are effective against multidrug-resistant and extensively drug-resistant TB (MDR-TB and XDR-TB), and are safe to use with HIV treatments. Whilst the introduction of Cepheid's Xpert® MTB/RIF diagnostic platform was a major advance, its cost remains a barrier to access despite the significant discounts offered to DCs.[11] There is a need for more effective and accessible POC tests,[12] tests that can diagnose TB in children, and tests for drug susceptibility.[13]

There are several vaccine candidates in clinical development, mostly targeting the same antigens.[12] VPM1002, which is based on the BCG vaccine and specifically developed for infants in endemic areas, started a Phase II trial in HIV exposed newborns in mid-2015.[14] A Phase IIb trial for M72+AS01E in adults is underway, while Phase II results of this candidate in infants are currently being analysed.[15] Another promising candidate being developed in a BCG prime-boost regimen (H4/AERAS-404 + IC31) started Phase II trials in 2014.[16] However, there have been some setbacks, with trials being downscaled[17] and products showing inadequate efficacy in infants.[18]

Despite being given conditional approval for MDR-TB in recent years, access to two novel drugs (delamanid and bedaquiline) is minimal.[12] A bedaquiline donation programme announced in 2014 may improve access.[19] While delanamid remains in Phase III trials to finalise its approval status, bedaquiline was registered in late 2015. Bedaquiline is also in development in several combinations, the most advanced being in Phase III trials for MDR- and XDR-TB.[20] Another novel drug (pretomanid) is also being tested in different combinations, with the most advanced being the PaMZ regimen for TB and MDR-TB in Phase III.[21]

The development of new diagnostics has been slow, with the World Health Organization (WHO) unable to recommend the use of Eiken's TB-LAMP and Hain Lifescience's MTB DRsl tests in 2013 due to insufficient evidence.[22,23] Cepheid's GeneXpert® Omni, a POC molecular test for TB diagnosis, is expected to be available in emerging markets by Q3 2017.[24]



TOTAL SPEND ON TB R&D IN 2015

OF GLOBAL R&D FUNDING

R&D needs for TB include:

- Basic research
- Drugs
- Diagnostics
- Preventive vaccines
- Therapeutic vaccines

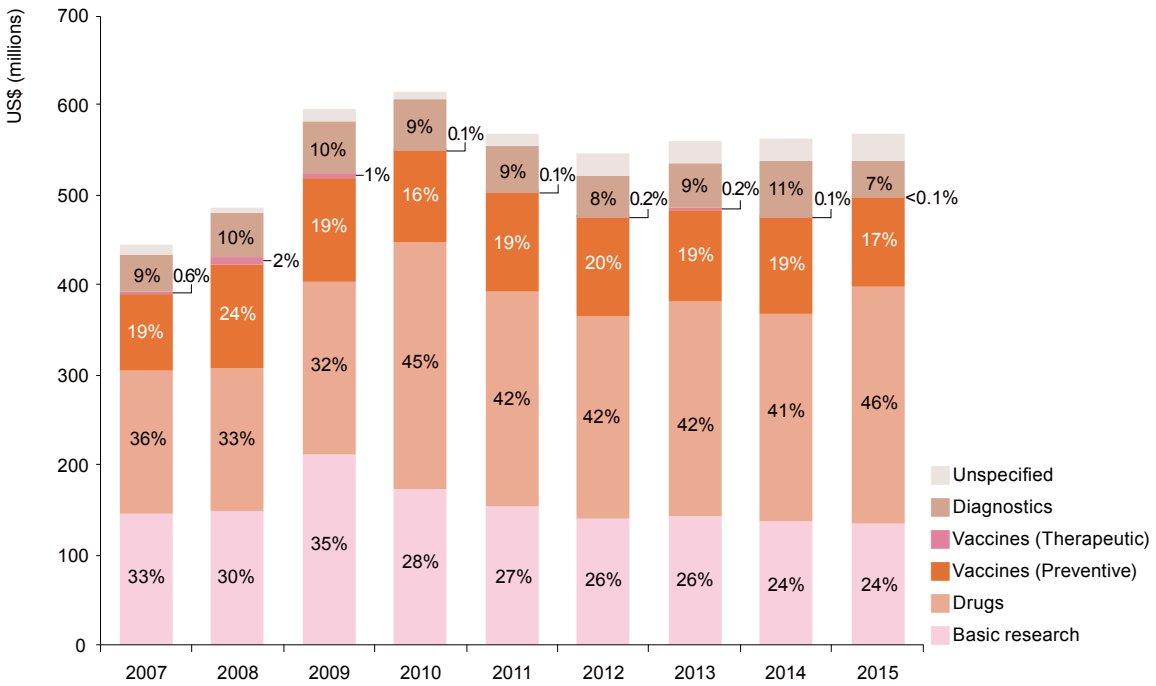
Global funding for TB R&D in 2015 was $567m, making it the second-highest funded neglected disease by a very small margin (malaria received $565m). Of this total, $538m was from YOY funders, with irregular survey participants providing the remaining $29m. YOY funding remained essentially unchanged in 2015 (up $2.4m, 0.5%), but it is worth noting that the steady, incremental growth of TB funding over the last four years (up $26m, 5.2% since 2012) stands in sharp contrast to the ongoing decline in HIV/AIDS funding over the same period.

Almost half of TB investment went to drug development ($263m, 46%), followed by basic research ($135m, 24%), preventive vaccines ($98m, 17%) and diagnostics ($42m, 7.4%). Funding for therapeutic vaccines was minimal, as it has been since the start of G-FINDER, at $0.2m (<0.1%).

Most of the fluctuations in funding for individual TB product areas in 2015 were the result of Gates Foundation funding patterns, despite little change in the Foundation's overall funding for TB R&D. The most significant change was the increase in YOY funding for TB drug development (up $27m, 12%). This was the result of increased drug R&D investment from the Gates Foundation (up $25m, 52%), much of which was for TB Alliance's Shortening Treatments by Advancing Novel Drugs (STAND) trial, a Phase III trial of the PaMZ regimen in MDR-TB, drug-sensitive TB, and TB/HIV co-infection. Funding for TB basic research also increased (up $4.5m, 3.6%), reflecting the increase in basic research investment from the Gates Foundation ($4.3m, up 63%).

Funding was lower for both diagnostics (down $21m, -39%) and preventive vaccines (down $11m, -10%). Again, this was the result of a sharp drop in disbursements from the Gates Foundation for both these areas (diagnostics down $24m, -91%; and preventive vaccines down $11m, -22%). Unlike the increase in drug funding – which was in response to funding needed for late-stage clinical trials – these reductions were largely cyclical, with reduced Foundation disbursements for diagnostic development to SMEs (down $13m, -93%) and the Foundation for Innovative New Diagnostics (FIND, down $7.0m, -91%), and to Aeras for vaccine development (down $20m, -41%), with this latter drop actually obscuring an increase in Gates Foundation grants for TB vaccine R&D given directly to researchers and developers.

Figure 7. TB R&D funding by product type 2007-2015



The top 12 funders in 2015 provided 92% of overall funding for TB R&D, and the top three funders three-quarters ($427m, 75%), with the US NIH contributing $196m (35%), the Gates Foundation $129m (23%) and industry $102m (18%).

The largest increase in TB funding in 2015 came from the US NIH (up $7.7m, 4.1%). Although the increases from the EU (up $7.5m, 51%) and UNITAID (up $5.6m, from a low base) were lower than the US NIH, they represented large increases for those individual funders. These increases were balanced by small drops in funding from the Gates Foundation (down $5.3m, -4.0%), the UK Medical Research Council (MRC, down $2.7m, -25%) and industry (down $2.3m, -2.5%).

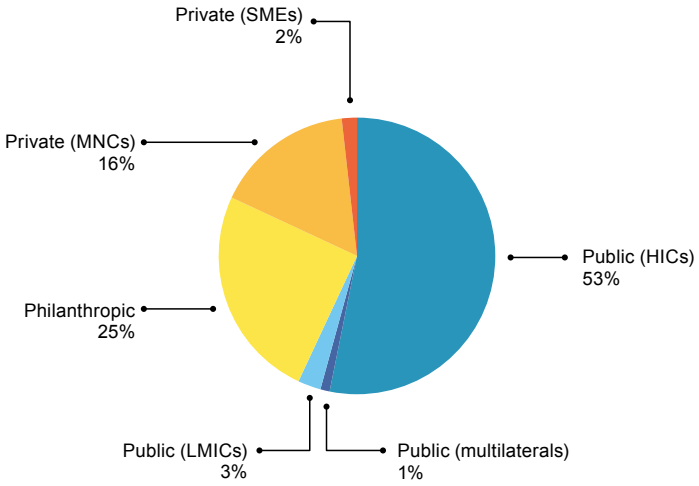
Table 4. Top TB R&D funders 2015

Funder / US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total	2007-2015 trend
US NIH	140	129	187	180	174	182	168	188	196	35	
Gates Foundation	133	151	111	117	99	104	128	134	129	23	
Aggregate industry	68	93	131	163	157	136	111	103	102	18	
EU	20	26	27	20	17	11	19	15	22	3.9	
UK DFID	1.7	3.3	17	21	12	1.6	14	15	13	2.3	
USAID	4.5	7.5	9.3	9.6	9.4	9.9	8.7	13	13	2.3	
Wellcome Trust	2.4	5.3	8.1	13	12	13	14	13	11	1.9	
US CDC	13	10	17	10	9.7	-	-	8.5	8.9	1.6	
Indian ICMR		1.0	2.2	3.4	3.5	6.8	8.2	8.2	7.9	1.4	
UK MRC	12	12	12	14	15	15	12	11	7.9	1.4	
German BMBF	4.1	0.4	4.6	3.9	3.7	4.7	4.7	5.7	6.5	1.1	
UNITAID			6.7			0.4	2.0	0.5	6.0	1.1	
Subtotal of top 12^	420	449	542	568	520	494	502	517	523	92	
Disease total	444	486	596	614	568	545	559	562	567	100	

^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015
- 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

Well over half of all TB funding came from public funders ($323m, 57%), with the remaining funding split between the philanthropic sector ($141m, 25%) and industry ($102m, 18%). HICs provided the vast majority of public funding ($301m, 93%), of which the US NIH provided two-thirds ($196m, 65%). MNCs were similarly responsible for most industry funding ($92m, 90%). The public sector was responsible for the largest YOY increase (up $12m, 4.1%), which was balanced by a decrease from the philanthropic sector (down $7.2m, -4.9%), primarily from the Gates Foundation.

Figure 8. **TB R&D funding by sector 2015**



MALARIA

Malaria is a parasitic disease transmitted through the bite of an infected mosquito. The two most common types of malaria are caused by *Plasmodium falciparum* and *Plasmodium vivax*. Left untreated, malaria can cause severe illness and death, with children and pregnant women being the most vulnerable (70% of malaria deaths are in children under five years of age[25]).

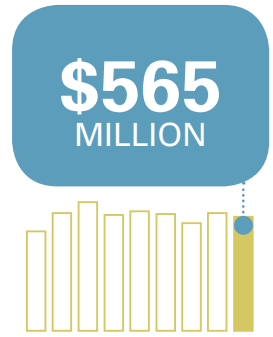
Malaria caused 56 million DALYs and at least 730,290 deaths in the developing world in 2015, making it the fourth highest cause of morbidity and fifth highest cause of mortality from neglected diseases. *P. falciparum* is by far the most deadly species, and in 2010 accounted for 98% of malaria cases in Africa.[26] Although *P. vivax* only accounts for about 8% of global cases, this proportion increases to 47% outside the African continent.[27]

New malaria drugs and insecticides are needed in response to the emergence of resistance to artemisinin-based combination therapies (ACTs) and pyrethroids. Cheap, sensitive and specific Rapid Diagnostic Tests (RDTs) are available, but their quality and heat stability can be problematic.[28] New diagnostics are particularly needed for non-*falciparum* species, to distinguish between malaria and other febrile illnesses, and to detect asymptomatic infections.[28]

Final Phase III trial results of the most advanced malaria vaccine candidate, RTS,S, showed a 36% and 26% decrease in clinical malaria cases in children and infants respectively over 3-4 years of follow-up.[29] The vaccine received a positive opinion from the European Medicines Agency (EMA), and the WHO-led Strategic Advisory Group of Experts (SAGE) and the Malaria Policy Advisory Committee (MPAC) have recommended large-scale implementation pilots to evaluate to what extent the results of the Phase III trial can be replicated in real world settings.[30] The next most advanced malaria vaccine candidates are in early stage clinical trials (Phase IIb).[31]

Seven new malaria treatments have received regulatory approval since G-FINDER began in 2007, including two ACT formulations designed specifically for children.[32,33] There are a number of promising drugs in late stage development for the treatment and prophylaxis of malaria, including OZ439/FQ, which is undergoing Phase IIb trials and has shown potential as a single exposure radical cure, and tafenoquine, which is in development for the treatment and relapse of *P. vivax* malaria, and is currently in Phase III clinical trials.[32]

The availability of a field molecular assay (LAMP test) has greatly reduced the time to diagnosis.[34] Diagnostic technologies in the pipeline include a urine dipstick malaria test (currently in clinical evaluation[35]).



TOTAL SPEND ON MALARIA R&D IN 2015

OF GLOBAL R&D FUNDING

Malaria R&D is needed in many areas including:

- Basic research
- Drugs
- Preventive vaccines
- Diagnostics
- Vector control products

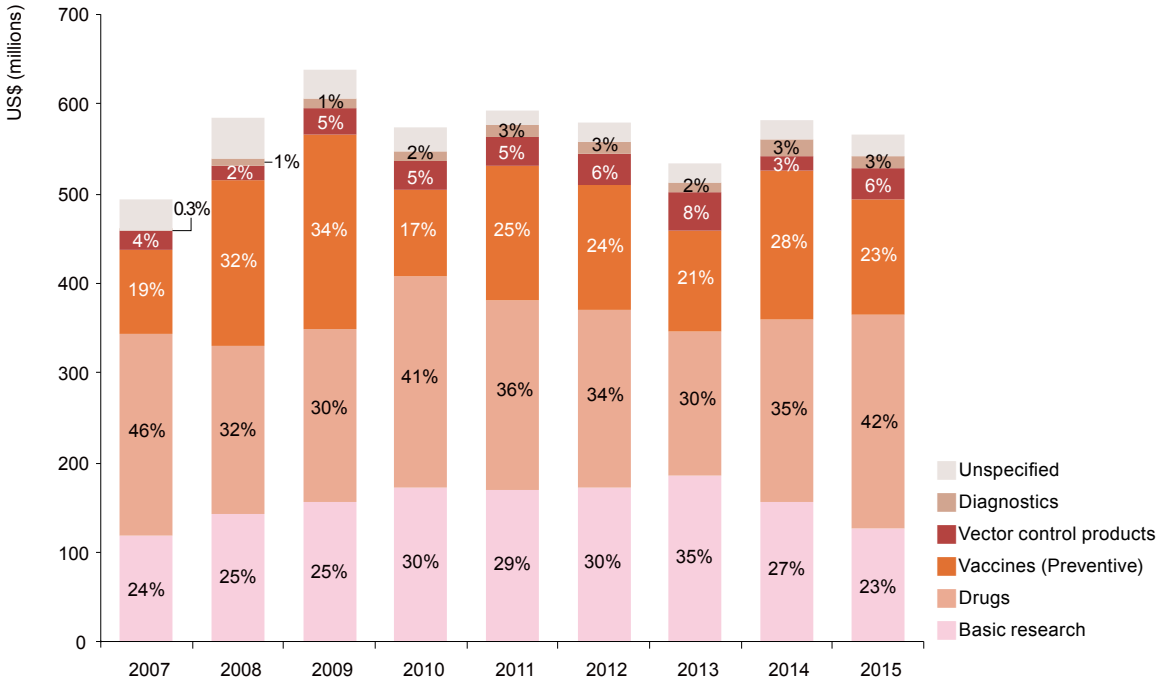
Malaria received $565m in R&D funding in 2015. YOY funding decreased slightly (down $17m, -3.0%) to $543m, with irregular participants providing the remaining $22m. With TB funding essentially steady, this drop meant that malaria fell one place to become the third highest-funded neglected disease in 2015, behind TB (which received $567m).

Nearly two-thirds of all malaria R&D funding went to developing new drugs ($238m, 42%) or vaccines ($128m, 23%), with a further quarter ($128m, 23%) going to basic research. Vector control products ($32m, 5.7%) and diagnostics ($15m, 2.6%) received significantly smaller investments.

The emphasis on malaria product development continued in 2015, with funding for basic research falling by $27m (-18%). Funding for drug development increased by $32m (up 16%), driven by increased industry investment in this area (up $21m, 25%), reflecting the progression of key candidates to late-stage clinical trials. Funding for vector control products also increased (up $16m, 119%), mainly due to increased disbursements from the Gates Foundation to the Innovative Vector Control Consortium (IVCC, which received $7.1m in 2015 after getting minimal funding the preceding year).

Funding for vaccine development fell sharply (down $36m, -22%), however this was largely due to reduced disbursements from the Gates Foundation to PATH (down $47m, -77%), after large grants in 2014 for RTS,S and general vaccine development. Funding for diagnostics was also down $3.9m (-22%).

Figure 9. Malaria R&D funding by product type 2007-2015



The top funders accounted for 94% of total malaria funding in 2015, with almost three-quarters of total funding coming from the US NIH, industry and the Gates Foundation (collectively $411m, 73%).

By far the most significant drop in funding came from the Gates Foundation (down $35m, -25%), as their funding to PATH returned to normal levels following large disbursements for vaccine R&D in 2014. A number of other top funders also reduced their funding for malaria R&D, including the Australian National Health and Medical Research Council (NHMRC, down $7.4m, -69%) – which dropped out of the top 12 funders as a result – the UK MRC (down $6.0m, -40%), the Wellcome Trust (down $5.6m, -23%) and the EU (down $4.8m, -25%).

The only groups to increase their investment in malaria R&D were industry (up $21m, 17%) – due to a novel combination drug entering Phase IIb – and US Government agencies, including the US DOD (up $10m, 54%), also mostly for drug development, the US NIH (up $6.9m, 4.6%), and the US Agency for International Development (USAID, up $3.7m, 68%).

Table 5. Top malaria R&D funders 2015

Funder / US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total	2007-2015 trend
US NIH	97	120	133	152	140	173	141	149	156	28	
Aggregate industry	86	87	98	120	97	110	78	124	147	26	
Gates Foundation	143	199	209	100	166	132	122	143	108	19	
US DOD	38	35	43	26	21	11	22	19	29	5.1	
UK DFID	3.7	3.6	3.5	22	20	6.4	28	20	19	3.3	
Wellcome Trust	26	26	27	32	30	30	27	24	19	3.3	
EU	20	23	23	23	20	13	20	19	14	2.5	
UK MRC	17	18	20	21	19	17	17	15	9.1	1.6	
USAID	11	9.4	9.4	10	8.9	11	6.5	5.4	9.1	1.6	
Indian ICMR		10	7.0	5.0	5.0	6.7	7.5	7.0	7.7	1.4	
UNITAID							5.7	8.2	7.2	1.3	
German BMBF	0.8	0.6	1.6	1.6	2.0	2.6	2.8	3.3	5.8	1.0	
Subtotal of top 12^	468	549	591	530	545	532	489	545	531	94	
Disease total	493	584	639	573	594	579	533	581	565	100	

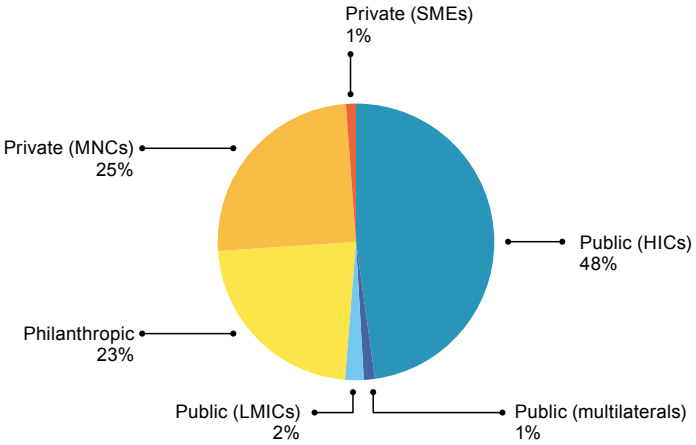
^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015

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, half of all malaria funding came from public funders ($290m, 51%). The vast majority of public sector funding came from HICs ($270m, 93%), with more than half of this coming from the US NIH ($156m, 58%).

There was a notable change in non-public sector funding for malaria R&D, with industry ($147m, 26%) investing more than the philanthropic sector ($128m, 23%) for the first time in the history of the G-FINDER survey. Although partly due to a drop in philanthropic funding (down $41m, -24%) – as funding from the Gates Foundation to PATH returned to normal levels – this change also reflected growing investment in drug development by MNCs (up $21m, 25%), who were responsible for the majority of industry investment overall ($141m, 96% of industry funding).

Figure 10. Malaria R&D funding by sector 2015



DIARRHOEAL DISEASES

Diarrhoeal diseases are a group of illnesses caused by viruses, bacteria or protozoa, that all present with fever and diarrhoea. They range from rotavirus and *E. coli*, which are relatively common in the West; to cholera and *Shigella*, which are mostly prevalent in DC settings. Diarrhoeal diseases mainly affect children under five years of age and are often transmitted by contaminated food or water. Although they rarely cause death in Western settings due primarily to better health care, their impact in the developing world is severe.

Diarrhoeal illnesses were collectively responsible for 66 million DALYs and 1.2 million deaths in the developing world in 2015, making them the third highest cause of neglected disease morbidity and second highest cause of mortality from neglected diseases.

Current vaccines against diarrhoeal diseases such as cholera are not always suitable for infants under the age of one, and some are relatively ineffective. New bi- and multivalent vaccines that are suitable for infants, and have longer durations of protection, are needed for most of the diarrhoeal diseases. New safe, effective and affordable drugs are needed for some diarrhoeal diseases to complement supportive interventions such as oral rehydration therapy (ORT) and zinc supplementation.[36] New rapid diagnostic tests capable of distinguishing between diarrhoeal diseases are also required.[37]

Several vaccine candidates are in Phase II and III trials, including ACE527 for enterotoxigenic *E. coli* (ETEC)[38] and WRSS1 for *Shigella*. A new $1 rotavirus vaccine (ROTAVAC®) was launched in India's private market in early 2015, with the government planning to add it to its Universal Immunization Program (UIP), making it free for all infants.[39] Other advanced candidates include BRV-TV, a rotavirus vaccine currently studied in a Phase III trial in infants in India.[40]

A low-cost and portable chip-scale microscope diagnostic test capable of distinguishing between causes of diarrhoeal diseases is also in development.[41]

TOTAL SPEND ON DIARRHOEAL DISEASE R&D IN 2015

OF GLOBAL R&D FUNDING

R&D needs for the diarrhoeal illnesses include:

- Basic research for cholera, *Shigella* and *Cryptosporidium*
- Drugs for cholera, *Shigella* and *Cryptosporidium*
- Vaccines for rotavirus, *E. coli*, cholera, *Shigella* and *Cryptosporidium*
- Diagnostics

Diarrhoeal diseases received $160m in R&D funding in 2015. YOY funding saw a similar cut to last year, down $18m (-11%) to $154m. Irregular participants provided the remaining $6.5m.

Almost a third of total diarrhoeal disease funding went towards rotavirus ($51m, 32%), which is also the disease that saw the largest drop in YOY funding (down $7.6m, -14%). YOY investment for the next two largest diseases also decreased: cholera (down $5.1m, -18%) and *Shigella* (down $2.9m, -14%). Funding for ETEC (up $7.3m, 84%) and *Cryptosporidium* (up $5.1m, 69%) increased considerably, making them account for almost one-fifth of total diarrhoeal funding (from one-tenth in 2014). There were minimal changes to the low funding of the other diarrhoeal diseases.

For diseases where all product areas are in scope (cholera, *Shigella* and *Cryptosporidium*), funding profiles varied only marginally across areas. Funding for cholera was predominantly for basic research ($15m, 65%) and vaccines ($6.7m, 29%). *Shigella* funding had a similar focus, with $9.4m (51%) going to vaccines and $6.5m (35%) towards basic research. *Cryptosporidium* funding was somewhat more balanced, with basic research receiving $6.4m (52%), drugs $3.7m (29%) and vaccines $2.0m (16%).

Funding for vaccines fell more than for any other product area (down $16m, -16%), reflecting both cyclical grant funding from the Gates Foundation to PATH (down $12m, -40%), and a drop in industry investment in rotavirus vaccine development (down $6.2m, -17%). Other decreases were smaller, with drugs down $2.3m (-37%) and diagnostics down $0.9m (-10%). Funding for basic research was fairly stable (up $1.0m, 2.7%).

Table 6. Diarrhoeal disease R&D funding 2015 (US$ millions)^

Disease	Basic Research	Drugs	Vaccines (Preventive)	Diagnostics	Unspecified	Total	%
Rotavirus			50		1.3	51	32
Cholera	15	0.4	6.7	1.2	-	23	15
Shigella	6.5	-	9.4	0.9	1.8	19	12
Enterotoxigenic *E. coli* (ETEC)			15	0.2	0.3	16	9.9
Cryptosporidium	6.4	3.7	2.0	0.3	-	12	7.8
Enteroaggregative *E.coli (EAggEC)*			0.4	0.1	0.2	0.7	0.4
Giardia				0.3	0.2	0.5	0.3
Multiple diarrhoeal diseases	11	-	8.8	4.9	13	37	23
Total	39	4.0	93	7.7	17	160	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

\- No reported funding

Category not included in G-FINDER

The top 12 funders in 2015 provided 97% of overall funding for diarrhoeal disease R&D, and the top three funders almost a quarter each, with the Gates Foundation contributing $40m (25%), the US NIH $38m (23%) and industry $33m (21%).

Investments from all but two of the top 12 funders were down or flat, including from all of the top three funders: industry investment was down $7.3m (-19%, mostly towards rotavirus vaccines), the US NIH decreased by $5.2m (-12%, all towards basic research) and the Gates Foundation dropped slightly (down $1.1m, -2.8%). Other decreases came from the UK DFID (down $3.6m, -40%) and the US DOD (down $2.3m, -24%). The only increases of note came from Gavi, the Vaccine Alliance (Gavi, up $3.3m, after not having reported any funding in 2014) and Médecins Sans Frontières (MSF, up $1.4m, which provided funding for diarrhoeal disease R&D for the first time).

Table 7. Top diarrhoeal disease R&D funders 2015

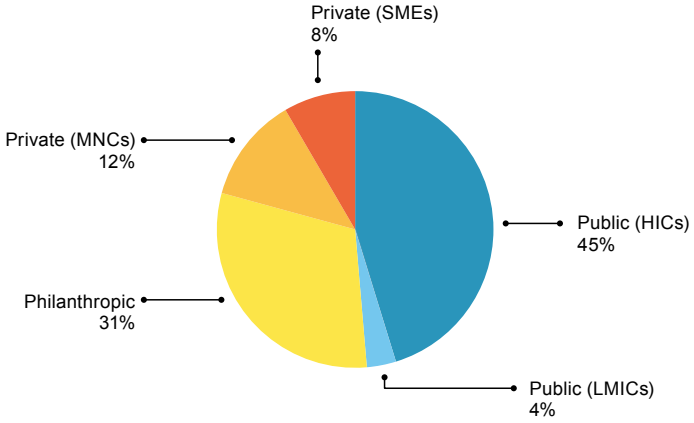
Funder (US$ millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total	2007-2015 trend
Gates Foundation	51	31	54	52	35	40	51	41	40	25	
US NIH	36	45	70	58	60	55	47	43	38	23	
Aggregate industry	13	26	41	33	27	30	44	39	33	21	
Inserm	0.3	0.3	1.3	1.5	7.9	8.3	12	10	11	6.7	
US DOD	6.2	6.8	13	6.8	5.5	8.4	9.4	9.3	7.0	4.4	
UK DFID	-	-	2.7	5.1	2.9	-	3.6	8.9	5.4	3.3	
Indian ICMR		4.4	3.8	4.7	2.8	2.7	4.7	4.6	5.1	3.2	
Wellcome Trust	1.0	0.4	0.3	0.5	0.5	4.2	3.2	5.2	4.3	2.7	
Institut Pasteur	3.1	3.5	4.8	3.9	4.0	3.8	3.7	3.7	3.6	2.2	
Gavi	12	17				4.0	7.3		3.3	2.1	
EU	0.6	0.5	0.5	0.7	2.6	2.7	3.0	3.1	2.9	1.8	
MSF							-	-	1.4	0.9	
Subtotal of top 12^	125	140	195	169	158	161	192	171	155	97	
Disease total	126	147	200	175	165	167	197	174	160	100	

^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2014
- 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

Around half of diarrhoeal disease R&D investment came from public funders ($78m, 49%); the majority of this was from HIC governments ($72m, 93%), and just over half of HIC funding came from the US NIH ($38m, 52%). The philanthropic sector accounted for about a third of funding ($49m, 31%) and industry a fifth ($33m, 21%). The share of industry funding by SMEs ($13m, 40%) increased considerably (up from 23% in 2014).

YOY funding from the public sector decreased by $10m (-12%) due to a drop in HIC funding (down $11m, -13%). The decrease from industry came entirely from MNCs (down $10m, -34%) which was only partially offset by an increase from YOY SME funders (up $3.0m, 35%). Philanthropic funding remained stable (down $0.7m, -1.4%).

Figure 11. Diarrhoeal disease R&D funding by sector 2015



KINETOPLASTIDS

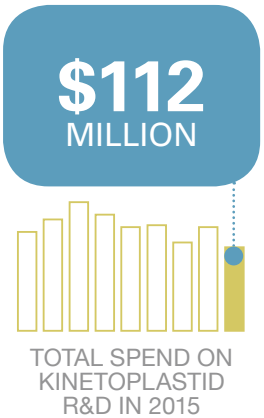
Kinetoplastid infections include three diseases: Chagas' disease, leishmaniasis and human African trypanosomiasis (HAT), also known as African sleeping sickness. Sleeping sickness initially presents with similar symptoms to a viral illness, but eventually infects the brain where it causes confusion, coma and death. Chagas' disease also has two stages, with late-stage Chagas' disease leading to heart failure and death. Leishmaniasis causes skin lesions and, in its more severe form, damages the spleen, liver and bone marrow. Kinetoplastid diseases are often fatal if left untreated. Kinetoplastid diseases are often fatal if left untreated.

In 2015, kinetoplastid diseases were responsible for 1.8 million DALYs and 35,160 deaths in the developing world. They ranked as the eleventh highest cause of morbidity and ninth highest cause of mortality from neglected diseases.

Chagas' disease needs preventive and therapeutic vaccines; safe, effective drugs that are suitable for children; treatments for the chronic form of the disease; and diagnostics that can reliably detect chronic disease and monitor treatment. The two drugs currently used (benznidazole and nifurtimox) are toxic, lack specificity and require multiple dosing for several months, increasing the likelihood of non-compliance and drug resistance.[42] A paediatric benznidazole formulation was registered in Brazil in 2011,[43] and the only drug in clinical development is an azole/benznidazole combination for chronic Chagas' disease.[5] A urine-based diagnostic is in Phase II development for the detection of congenital Chagas' disease,[44] while several vaccine candidates are in pre-clinical stages.

Sleeping sickness needs new, safe, oral drugs that are active against both stages of the disease to replace the injectable treatments now used,[45] as well as a vaccine. There are some promising sleeping sickness drug candidates, with fexinidazole, the first drug for the treatment of advanced stage sleeping sickness in 30 years, currently in Phase III clinical trials in Africa.[5] Another candidate – SCYX 7158, investigated for the treatment of late-stage sleeping sickness – is about to enter Phase II clinical trials.[46] There are currently no vaccine candidates for sleeping sickness.

Leishmaniasis is in need of 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 being evaluated for prophylactic and therapeutic indications[47] and there are several diagnostic tests in development for resource-limited settings. There are no novel leishmaniasis drugs on the immediate horizon and the only candidate currently in clinical trials is a topical formulation of amphotericin B for cutaneous leishmaniasis.



TOTAL SPEND ON KINETOPLASTID R&D IN 2015

OF GLOBAL R&D FUNDING

R&D needed for kinetoplastid in DCs includes:

- Basic research
- Drugs specific to DC needs
- Preventive vaccines
- Diagnostics
- Microbicides

Global funding for kinetoplastids was $112m in 2015. After a slight increase in 2014, YOY participants cut investment in 2015 by $21m (-18%), to $100m, continuing a sustained downward trend. Irregular participants contributed the remaining $12m.

The largest share of funding was for leishmaniasis ($38m, 34%), followed by sleeping sickness ($29m, 26%) and then Chagas' disease ($18m, 16%). It was the first time since 2012 that leishmaniasis received more funding than sleeping sickness; unfortunately this reflected the sharp drop in funding for sleeping sickness (down $17m, -38%) rather than an increase for leishmaniasis, which in fact fell slightly (down $1.0m, -2.9%). The drop in funding for sleeping sickness was partially a reflection of up-front funding (in 2014) of two multi-year grants from the Gates Foundation to the Drugs for Neglected Diseases initiative (DNDi) for drug development (worth a total of $12m). Funding for Chagas' disease also fell (down $3.9m, -23%).

Investment was down across all product areas, with the largest change reflecting the drop in funding from the Gates Foundation towards drug development for sleeping sickness; total YOY investment for drugs across kinetoplastids decreased by $12m (-21%). Other relatively large decreases were seen in basic research (down $7.0m, -15%) and diagnostics (down $3.1m, -40%). Funding towards therapeutic vaccines was down by $1.1m (-82%) and preventive vaccines by $1.0m (-19%).

Table 8. Kinetoplastid R&D funding 2015 (US$ millions)

Disease	Basic Research	Drugs	Vaccines (Preventive)	Vaccines (Therapeutic)	Vector control products	Diagnostics	Unspecified	Total	%
Leishmaniasis	16	13	3.6	0.2		1.4	4.0	38	34
Sleeping sickness	17	9.4	-		-	2.1	0.6	29	26
Chagas' disease	7.2	8.2	0.6	0.6	-	1.2	0.1	18	16
Multiple kinetoplastids	2.6	24	<0.1	-	-	-	0.4	27	24
Total	43	54	4.2	0.8	-	4.7	5.0	112	100

- No reported funding
Category not included in G-FINDER

In 2015, the top 12 funders accounted for 92% of total kinetoplastid R&D funding, with just four of these (the US NIH, industry, the EU and the Wellcome Trust) accounting for three-quarters of all funding ($84m, 75% of total).

The Gates Foundation was the third-highest funder in 2014, but decreased its investment by $16m (-86%, mainly owing to the multi-year grants to DNDi) and became the eighth-highest funder in 2015. Other funders that decreased their funding toward kinetoplastids included the US NIH (down $6.0m, -14%, across all diseases), the German Research Foundation (DFG, down $2.3m, -60%) and the German BMBF (down $2.2m, -42%). Funders that featured in last year's top 12 but dropped out in 2015 included the Dutch DGIS, which decreased its funding by $2.9m (-79%) and the Swiss National Science Foundation (SNSF, down $2.2m, -98%, which may be due to underreporting).

Only four of the top 12 kinetoplastid funders increased their investment, mainly industry (up $3.5m, 33%), the EU (up $3.4m, 33%, mainly for leishmaniasis) and the US DOD (up $3.3m, all for leishmaniasis, after not having funded any kinetoplastid R&D for two years).

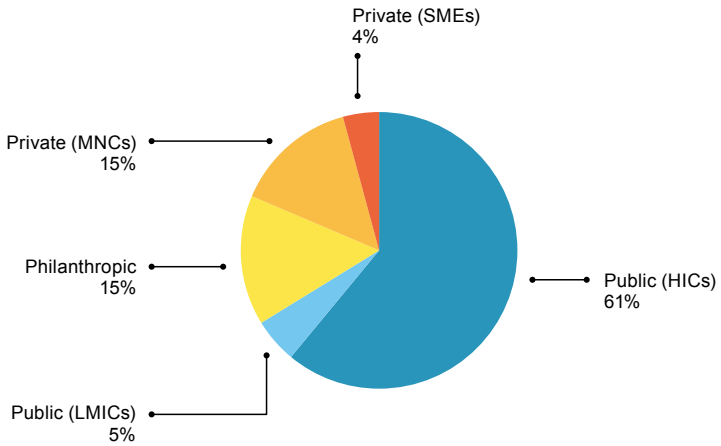
Table 9. **Top kinetoplastid R&D funders 2015**

Funder	US$ (millions)								2015 % of total	2007-2015 trend
	2007	2008	2009	2010	2011	2012	2013	2014	2015	
US NIH	32	56	61	64	54	52	46	41	35	31
Aggregate industry	5.0	2.9	5.2	12	14	18	17	19	21	19
EU	2.6	4.3	9.4	8.3	6.8	5.6	3.7	10	14	12
Wellcome Trust	14	12	11	9.0	9.9	13	11	14	14	12
US DOD	5.4	4.7	5.2	1.1	1.0	0.5	-	-	3.3	2.9
German BMBF			-	-	0.8	5.3	4.0	5.3	3.1	2.7
Indian ICMR		-	0.1	2.0	3.7	3.3	4.8	4.2	2.9	2.6
Gates Foundation	52	33	41	23	12	9.1	8.9	19	2.7	2.4
UK MRC	2.7	3.4	2.4	2.6	2.2	1.6	2.3	3.2	2.6	2.3
Institut Pasteur	-	2.7	2.9	5.4	4.6	2.8	2.4	2.5	2.1	1.9
German DFG	0.1		-	3.7	1.4	3.0	2.0	3.8	1.5	1.3
Indian CSIR		1.3	0.9	0.6	0.6	0.1	0.7	0.2	1.4	1.3
Subtotal of top 12^	132	136	158	144	125	129	108	128	103	92
Disease total	134	149	173	156	140	142	119	140	112	100

^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015
- 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 two-thirds ($74m, 66%) of total kinetoplastid R&D funding in 2015, dominated by high-income country (HIC) investment ($68m, 92% of public funding). Just over half of HIC funding came from the US NIH ($35m, 52%). Industry provided $21m (19%), most of which came from MNCs ($16m, 77% of industry funding). The philanthropic sector funded $17m (15%) and saw the largest decrease (down $17m, -50%), driven by the decrease in funding from the Gates Foundation. The decrease in public funding (down $8.3m, -11%) came from both HICs (down $5.9m, -8.4%) and low- and middle-income countries (LMICs, down $2.3m, -32%). The only sector to increase its funding was industry (up $3.5m, 33%, all from MNCs).

Figure 12. **Kinetoplastid R&D funding by sector 2015**



DENGUE

Dengue is transmitted by *Aedes* mosquitoes and causes a severe flu-like illness. In its most severe form, dengue haemorrhagic fever, it is a leading cause of serious illness and death among children in regions of Asia, with outbreaks also occurring frequently in Central and South America.

Dengue was responsible for 1.9 million DALYs and 18,298 deaths in 2015. It ranked as the tenth highest cause of morbidity and mortality from neglected diseases.

Dengue differs from many other tropical diseases in that it does have some degree of commercial market, driven by demand from travellers, the military and its high prevalence in several wealthier DCs in South-East Asia and Latin America. As there is a strong commercial programme for the development of dengue vaccines, investment into vaccine R&D is excluded from G-FINDER. The first dengue vaccine – Dengvaxia (CYD-TDV) was registered in December 2015 for use in individuals 9-45 years of age living in endemic areas.

Currently there is no curative treatment available for dengue; management is focused on control of transmission and supportive therapy to minimise patient dehydration or shock from haemorrhagic fever, therefore new drugs to treat dengue are needed. A diagnostic that is able to detect early-stage disease and distinguish dengue from other causes of fever is needed.[48] There is also a need for evaluation of the currently available diagnostic kits.[48]

There is very little activity in the dengue drug pipeline, and no products have reached the clinical stage. Although a new diagnostic test that can detect the presence of all four dengue virus types was approved by the US Food and Drug Administration (FDA) in 2012 (CDC DENV-1-4), independent evaluation showed that this product has lower clinical sensitivity than initially thought.[49] This real-time reverse transcription polymerase chain reaction (RT-PCR) assay also has limited practicality in DCs.[50] An RT-PCR that may be better suited to resource limited settings is the Liat™ Analyser (currently in clinical development), which is portable and can be used in non-laboratory settings.[51]

R&D needed for dengue includes:

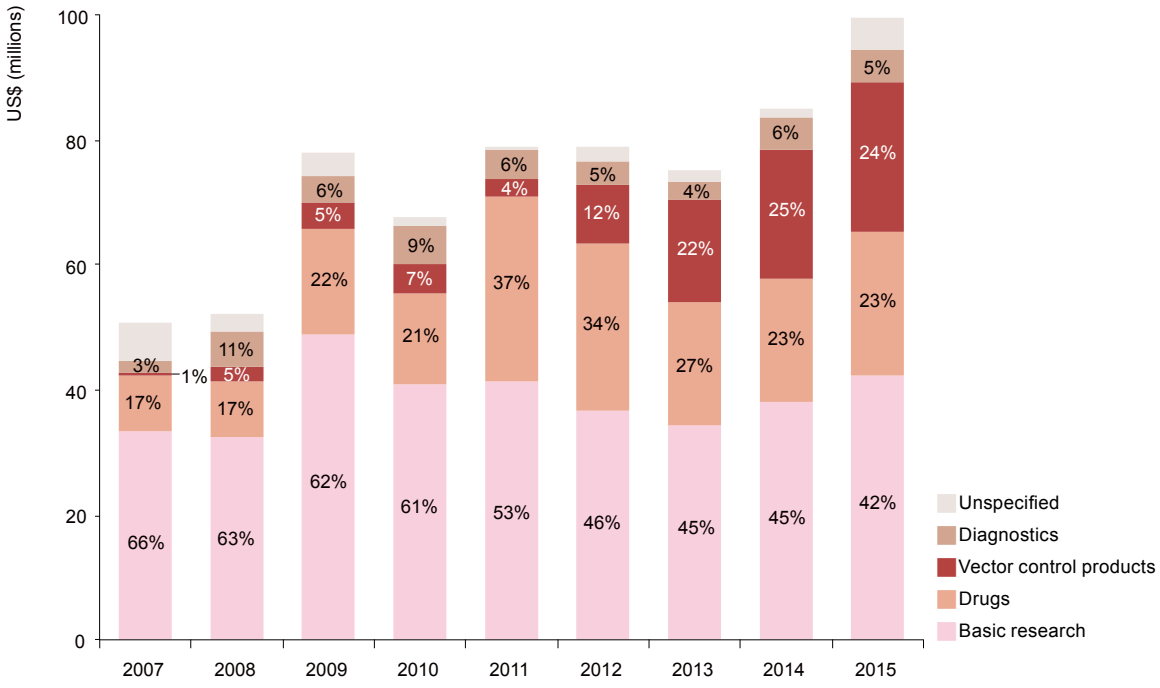
- Basic research
- Drugs
- Diagnostics
- Vector control products

In 2015, funding for dengue R&D within the scope of G-FINDER totalled $100m (this does not include investment in dengue vaccine development, which was removed from the G-FINDER scope in 2014, once it became clear that a significant commercial market had emerged). YOY funding for dengue R&D increased to $96m (up $12m, 14%), with irregular participants reporting $3.4m. This continues the long-term trend of increased funding for dengue R&D over the past nine years, which has accelerated in 2014 and 2015 on the back of increased funding from the US NIH, industry and the French National Institute of Health and Medical Research (Inserm).

Most dengue funding was in basic research ($42m, 42%), followed by vector control products ($24m, 24%) and drug development ($23m, 23%). Diagnostics only received 5.0% of total dengue funding ($5.0m).

The overall increase in funding was fairly evenly shared among most product areas, with drugs receiving a slightly higher increase (up $3.2m, 16%) than basic research (up $2.8m, 7.4%) and vector control products (up $2.7m, 13%). Investment in the development of new diagnostics decreased slightly (down $0.4m, -8.5%).

Figure 13. Dengue R&D funding by product type 2007-2015



In 2015, the top 12 funders accounted for the vast majority (96%) of total dengue R&D investment, with the US NIH accounting for nearly half ($45m, 45%). Most changes in funding from the top 12 contributors were relatively small, with the largest increases coming from industry (up $6.2m, 87%), the US NIH (up $5.3m, 13%) and Inserm (up $3.2m, from zero, and featuring in the top funders of dengue R&D for the first time). The US DOD also became a top 12 funder, albeit with an investment of just $1.0m. The only notable drops came from the Australian NHMRC (down $2.3m, -79%) and the Gates Foundation (down $1.1m, -6.1%).

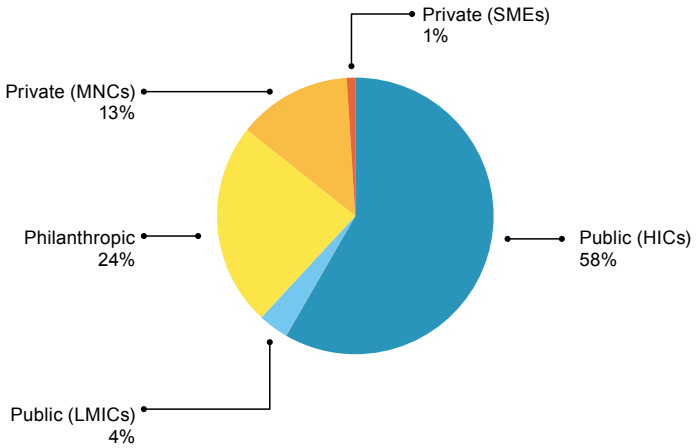
Table 10. Top dengue R&D funders 2015

Funder	US$ (millions)								2015 % of total	2007-2015 trend
	2007	2008	2009	2010	2011	2012	2013	2014	2015	
US NIH	29	24	44	41	48	43	35	40	45	45
Gates Foundation	1.2	2.1	1.7	1.1	0.1	5.3	17	19	18	18
Aggregate industry	7.2	3.6	5.1	7.2	11	8.4	7.3	7.6	14	14
Wellcome Trust	1.0	1.1	1.6	2.2	6.6	5.3	3.7	6.6	6.2	6.2
Inserm	-	-	-	-	-	-	-	-	3.2	3.2
EU	1.8	1.6	1.0	0.5	0.4	1.8	2.5	2.3	2.4	2.4
Institut Pasteur	3.6	2.2	2.0	3.0	2.3	1.8	1.8	1.8	1.9	1.9
Indian ICMR		0.6	1.0	1.4	1.3	1.2	1.8	1.6	1.8	1.8
UK MRC	0.2	0.3	0.2	0.1	0.8	0.5	0.5	0.8	1.7	1.7
US DOD	1.3	2.5	4.9	0.4	1.0	0.4	0.2	0.2	1.0	1.0
Australian NHMRC	0.7	1.1	1.1	1.3	1.9	2.8	1.6	2.9	0.6	0.6
US CDC	-	-	1.2	1.1	-	1.2	0.5	0.7	0.6	0.6
Subtotal of top 12^	50	49	71	64	76	76	73	84	96	96
Disease total	51	52	78	68	79	79	75	85	100	100

^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015
- 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, almost two-thirds of dengue funding came from the public sector ($62m, 62%). Most public sector funding was from HICs ($58m, 94%), and more than three-quarters of HIC funding came from the US NIH ($45m, 77%). The philanthropic sector accounted for $24m (24%) and industry for $14m (14%), mostly from MNCs ($13m, 93%). Public funding increased by $7.6m (up 15%), with HICs (up $7.7m, 16%) responsible for all of this increase. Investment from LMICs remained stable (down $0.1m, -4.9%). Funding from industry also increased (up $6.2m, 87%, all from MNCs), which was all for drug development (the only dengue product area within the G-FINDER scope that received industry investment). The only sector to see a small decrease was the philanthropic sector (down $1.6m, -6.4%)

Figure 14. Dengue R&D funding by sector 2015



BACTERIAL PNEUMONIA & MENINGITIS

Pneumonia is a lung infection transmitted by the cough or sneeze of infected patients. It presents with coughing, fever, chest pain and shortness of breath, and can be fatal, especially in young children and elderly patients. Although caused by a range of bacteria and viruses, *Streptococcus pneumoniae* is by far the most common cause of pneumonia in the developing world.

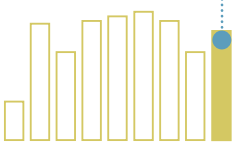
Bacterial meningitis is an infection of the fluid that surrounds the brain and spinal cord and is most commonly caused by *S. pneumoniae* and *Neisseria meningitidis*. Meningitis is transmitted from person to person through droplets of respiratory or throat secretions. Symptoms include severe headache, fever, chills, stiff neck, nausea and vomiting, sensitivity to light and altered mental state. Even with early diagnosis and treatment, 5-10% of patients die within 24-48 hours of the onset of symptoms.

Bacterial pneumonia & meningitis were responsible for 75 million DALYs and 1.6 million deaths in the developing world in 2015, and ranked as the highest cause of morbidity and mortality from neglected diseases.

The MenAfriVac™ vaccine protects against serogroup A meningococci, which historically accounted for the majority of epidemic and endemic disease in the meningitis belt of Africa. Its introduction via mass vaccination campaigns broke the cycle of epidemics in this region[52] and an infant version was WHO prequalified in early 2015.[53] However, vaccines are still needed for other meningitis serotypes, with only one polyvalent meningococcal conjugate vaccine currently in early development.

Traditional polysaccharide pneumococcal vaccines are unsuitable for DC use.[54] The conjugate pneumococcal vaccines PCV10 and PCV13 are effective against the strains included,[54] but expensive. New vaccines are therefore needed that are more affordable and that can provide either focused protection for children against strains prevalent in DCs or broad protection across all pneumococcal strains.[55] Pneumococcal protein vaccines (PPVs) are less expensive to manufacture and several of these new types of vaccines are in Phase II clinical trials.[56]

$92.1 MILLION



TOTAL SPEND ON BACTERIAL PNEUMONIA & MENINGITIS R&D IN 2015

OF GLOBAL R&D FUNDING

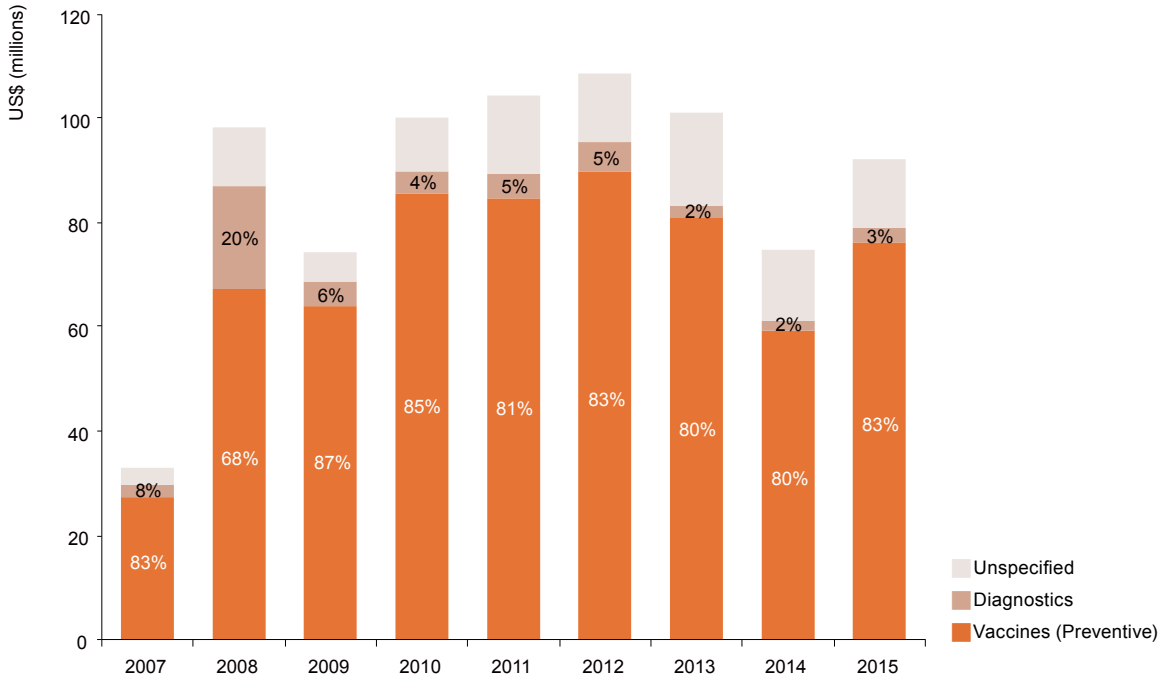
New products needed for pneumonia & meningitis are:

- Vaccines that include developing world strains (and possibly DC-specific vaccines that exclude Western strains)
- Diagnostics

A total of $92m was invested in bacterial pneumonia & meningitis R&D in 2015. $80m of this came from YOY funders, with irregular participants providing the remaining $12m. YOY funding increased by $8.7m (up 12%). Total funding still remains well below 2012 levels, however, as a result of the significant funding reductions seen in each of the two preceding years.

The only bacterial pneumonia & meningitis investments tracked by G-FINDER are for vaccines and diagnostics. As in previous years, funding was dominated by vaccine investment ($76m, 83%) with most of this going towards pneumococcal vaccines ($70m, 92% of total vaccine funding). Only $2.6m (2.8%) went to diagnostics. In a reverse of the last two years, YOY funding increased for both product areas, with vaccines increasing by $7.1m (up 12%) and diagnostics doubling (up $0.9m, 54%).

Figure 15. Bacterial pneumonia & meningitis R&D funding by product type 2007-2015



Funding for bacterial pneumonia & meningitis R&D was highly concentrated, with industry and the Gates Foundation collectively accounting for three-quarters of all funding ($69m, 75%). Of these two groups, only the Gates Foundation increased its funding in 2015 (to $33m, up from just $5.3m in 2014). This was a return to more customary funding levels from the Foundation, primarily reflecting the uneven disbursement of large, multi-year grants. In contrast, YOY industry funding fell sharply (down $17m, -34%), in large part due to the conclusion of regulatory trials for pneumococcal vaccines. The other notable change from the top funders came from Gavi, which provided $6.2m in 2015 after not having reported any funding the previous year.

Table 11. Top bacterial pneumonia & meningitis R&D funders 2015

Funder	US$ (millions) 2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total	2007-2015 trend
Aggregate industry	14	53	35	32	38	40	48	48	36	39	
Gates Foundation	6.4	30	24	45	38	43	14	5.3	33	36	
Inserm	-	0.1	-	-	4.1	4.2	13	9.9	10	11	
Gavi				2.5		5.4	11		6.2	6.8	
German DFG	-		0.5	0.6	-	0.4	2.4	2.6	1.6	1.8	
US NIH	4.8	4.6	4.2	10	16	8.6	6.4	2.2	1.2	1.3	
Wellcome Trust	0.2	0.2	0.1	0.3	0.8	3.5	2.0	2.1	1.2	1.3	
UK MRC	1.7	1.9	2.0	1.0	0.7	0.3	0.6	0.6	0.9	1.0	
EU	-	-	-	0.6	1.1	0.2	-	0.8	0.8	0.9	
French ANR		0.3	-	-	-	-	1.0	-	0.8	0.8	
Institut Pasteur	0.4	0.2	0.3	0.3	0.7	0.5	0.3	0.3	0.4	0.5	
Meningitis Research Foundation		<0.1	<0.1	<0.1			<0.1	0.1	0.2	0.3	
Subtotal of top 12^	33	97	73	98	104	108	100	74	92	100	
Disease total	33	98	74	100	104	108	101	75	92	100	

^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015
- 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

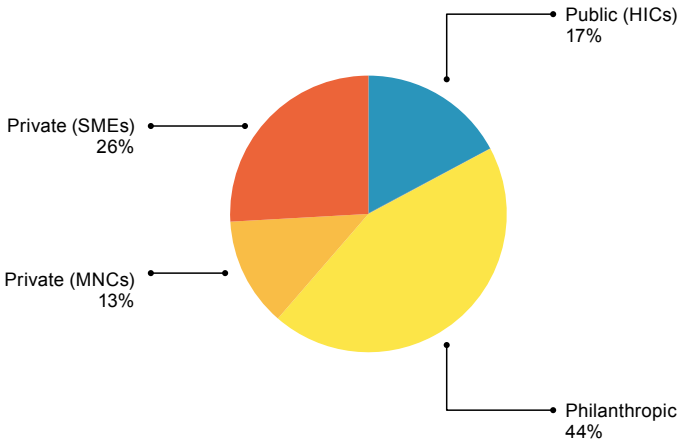
The philanthropic sector ($41m, 44%) was the source of just under half of all funding for bacterial pneumonia & meningitis in 2015, closely followed by industry ($36m, 39%) and the public sector ($16m, 17%). All public sector funding was from HICs, but just 7.8% of this came from the US NIH – its lowest share of HIC funding out of all the neglected diseases the organisation funds.

This is a very different picture compared to 2014, when industry was responsible for 65% of total funding – an all-time high – and the philanthropic sector just 10%. Part of the reason for the huge variability in funding share between the various sectors is the minor role played by the public sector, which often provides a stable base level of funding – indeed, there was little change in public sector investment in 2015 compared to the preceding year (down $1.6m, <-0.1%). But as noted above, public sector funding accounted for less than a fifth of total funding for bacterial pneumonia & meningitis R&D in 2015. As a result, the cyclical funding patterns of philanthropic organisations and the project-dependent investments of industry have a major impact on the overall funding picture.

Two years of reduced disbursements from the Gates Foundation in 2013 and 2014 meant that the share of philanthropic funding was relatively low during those years (27% and 10%, respectively). The increase in Gates Foundation funding in 2015 – along with $6.2m from Gavi, which did not report any funding in 2014 – helped return this share to more historically normal levels.

The drop in industry investment affected both pneumonia vaccines (down $13m, -30%) and meningitis vaccines (down $3.9m, -68%). All of this drop came from MNCs, who reduced their investments in bacterial pneumonia & meningitis R&D by $19m (-62%). As a result of this drop in MNC investment, SMEs accounted for a remarkable two-thirds (67%) of all industry funding for bacterial pneumonia & meningitis, with virtually all of this SME investment ($24m, 99%) coming from Indian firms.

Figure 16. **Bacterial pneumonia & meningitis R&D funding by sector 2015**



HELMINTH INFECTIONS

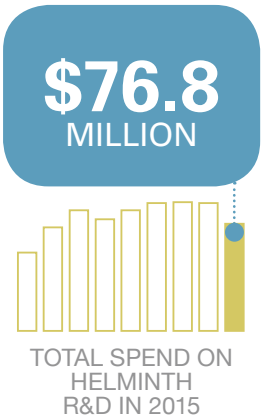
Helminths are parasitic worms and flukes that can infect humans. Helminth infections include ancylostomiasis and necatoriasis (hookworm), ascariasis (roundworm), trichuriasis (whipworm), strongyloidiasis and cysticercosis/taeniasis (tapeworm), collectively referred to as soil-transmitted helminths. Other helminth infections include elephantiasis (lymphatic filariasis), river blindness (onchocerciasis) and schistosomiasis. Adult worms live in the intestines and other organs, and infection is transmitted through food, water, soil or other objects.

Helminths can cause 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 elephantiasis causes painful, disfiguring swelling of the legs and genitals.

Helminth infections are the ninth highest cause of morbidity from neglected diseases globally and the eleventh highest cause of mortality; they were responsible for 9.5 million DALYs and 7,443 deaths in 2015.

There is no vaccine against any of these helminth infections and with the increase in mass drug administration programmes, drug resistance is a real concern.[57] Current diagnostic products for detection of some helminths are also outdated, meaning new effective diagnostics that are able to measure infection intensity and detect drug resistance are needed.[57]

Three drug candidates are in Phase III clinical trials for helminth infections: Moxidectin for onchocerciasis, Co-Arinate FDC for schistosomiasis and Oxantel pamoate for trichuriasis. Development of an orodispersible praziquantel tablet for children from three months to six years old is also underway, with Phase II trials having commenced in mid-2016.[58] There are several schistosomiasis vaccines in development, the most advanced being Bilhvax in Phase III.[59] There are two vaccine candidates against human hookworm infection in Phase I, and two against onchocerciasis in pre-clinical stages. There are several diagnostic tests in development for helminth diseases, including a UCP-LF CAA assay for schistosomiasis diagnosis in low-prevalence settings (clinical development)[60] and a dual detection POC test for onchocerciasis and lymphatic filariasis (pre-clinical development).[61]



TOTAL SPEND ON HELMINTH R&D IN 2015

OF GLOBAL R&D FUNDING

Helminth R&D is needed in many areas including:

- Basic research for all listed infections
- Drugs for all listed infections
- Vaccines for strongyloidiasis, onchocerciasis, schistosomiasis and hookworm
- Diagnostics for strongyloidiasis, onchocerciasis and schistosomiasis
- Vector control products for lymphatic filariasis, onchocerciasis, schistosomiasis and tapeworm

Helminth infections received $77m in R&D funding in 2015. Funding from YOY funders fell by $10m (-13%) to $70m, with irregular survey participants providing the remaining $6.5m.

Just three diseases accounted for well over half ($46m, 60%) of helminth R&D funding: schistosomiasis ($20m), lymphatic filariasis ($13m) and onchocerciasis ($12m). All other helminth infections received less than $6.0m each. The overall decrease in funding was driven by a marked drop in funding for lymphatic filariasis (down $9.1m, -44%). Funding was also lower for schistosomiasis (down $2.6m, -13%), strongyloidiasis (down $1.7m, -51%) and hookworm (down $0.6m, -8.8%), with small increases for onchocerciasis (up $2.5m, 27%) and roundworm (up $1.0m, from a low base).

Most helminth funding was for basic research ($30m, 39%), closely followed by drug development ($28m, 36%), although it should be noted that these are the only two product areas that are included for *all* helminth infections. These are also the areas that saw the largest YOY cuts, with funding for drugs down $5.4m (-17%) and basic research falling by $4.8m (-15%). The only product area that saw an increase in investment was diagnostics (up $2.7m, 79%), as funding returned to more normal levels.

Table 12. Helminth R&D funding 2015 (US$ millions)

Disease	Basic Research	Drugs	Vaccines (Preventive)	Vector control products	Diagnostics	Unspecified	Total	%
Schistosomiasis (bilharziasis)	9.6	2.9	3.5	-	2.4	1.4	20	26
Lymphatic filariasis (elephantiasis)	5.7	6.3		<0.1	0.2	1.3	13	18
Onchocerciasis (river blindness)	1.6	7.5	<0.1	<0.1	3.3	-	12	16
Hookworm (ancylostomiasis & nectoriasis)	1.2	0.9	3.6	-		<0.1	5.8	7.5
Tapeworm (cysticercosis/taeniasis)	1.2	1.4		0.1		-	2.7	3.5
Strongyloidiasis & other intestinal roundworms	0.7	0.5	<0.1		0.3	0.2	1.7	2.2
Whipworm (trichuriasis)	1.2	0.1				<0.1	1.4	1.8
Roundworm (ascariasis)	1.0	<0.1				<0.1	1.1	1.4
Multiple helminths	7.9	7.9	2.7	-	-	-	18	24
Total	30	28	9.9	0.1	6.3	3.0	77	100

- No reported funding
Category not included in G-FINDER

Funding for helminth R&D remained extremely concentrated in 2015, with the top 12 funders accounting for 98% of total funding, and the US NIH, the Gates Foundation and industry collectively responsible for three-quarters ($57m, 75%). Most of the top funders reduced their investments in 2015. The largest drop came from the Gates Foundation (down $5.5m, -24%), followed by the EU (down $1.8m, -28%), the UK MRC (down $1.3m, -48%) and the US NIH (down $1.1m, -3.8%). The only notable increases came from industry (up $3.1m, 48%), and the German DFG (with an investment of $2.0m, after not having funded helminth R&D last year).

Table 13. Top helminth R&D funders 2015

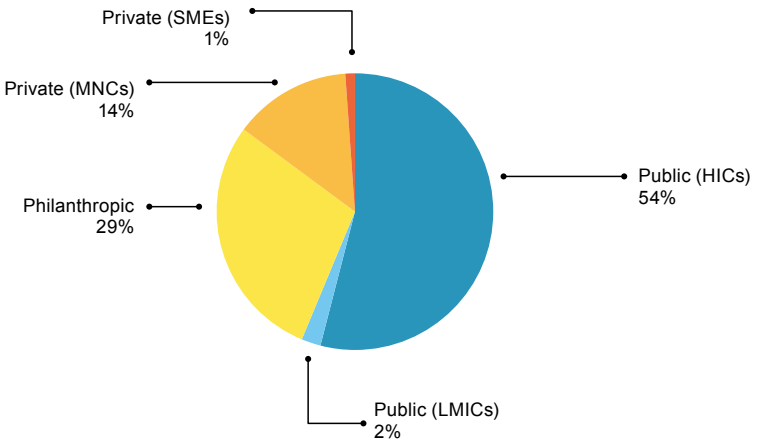
Funder	US$ (millions) 2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total	2007-2015 trend
US NIH	32	27	32	34	27	37	29	29	28	37	
Gates Foundation	8.3	24	18	17	21	20	22	23	18	23	
Aggregate industry	0.8	5.5	9.7	6.7	7.6	4.1	8.3	15	11	15	
EU	3.9	2.9	2.7	7.3	6.1	7.1	6.8	6.5	4.7	6.1	
Wellcome Trust	3.0	3.8	4.9	5.4	8.2	6.2	7.5	4.9	4.0	5.2	
German DFG	-		6.3	0.5	0.6	2.5	2.8	-	2.0	2.6	
Texas Children's Hospital					0.1	0.8	1.3	1.1	1.5	1.9	
UK MRC	1.0	1.4	1.1	1.1	3.3	2.3	2.0	2.8	1.4	1.9	
Indian ICMR		0.4	0.4	1.0	1.2	1.4	1.5	1.4	1.3	1.7	
Inserm	0.3	0.5	1.9	<0.1	1.7	1.9	2.2	1.5	1.2	1.6	
Dutch DGIS	-	-	-	0.5	1.5	0.2	1.8	1.5	0.9	1.1	
Science Foundation Ireland						0.4	0.4	-	0.6	0.8	
Subtotal of top 12^	55	70	82	77	81	86	88	89	75	98	
Disease total	56	74	86	80	87	92	92	92	77	100	

^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015
- 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 majority of helminth R&D funding came from the public sector ($43m, 56%), whilst the philanthropic sector provided $22m (29%), and industry the remaining $11m (15%). Most public sector funding was from HICs ($41m, 96% of public funding), and two-thirds of HIC funding came from the US NIH ($28m, 68%). Industry funding was dominated by MNC investment ($11m, 92% of total industry funding), with SMEs only providing $0.9m (7.5%).

YOY funding fell from both the public sector (down $6.9m, -15%) and philanthropic sector (down $6.3m, -22%), with industry increasing its investment slightly (up $3.1m, 48%, all from MNCs).

Figure 17. Helminth R&D funding by sector 2015



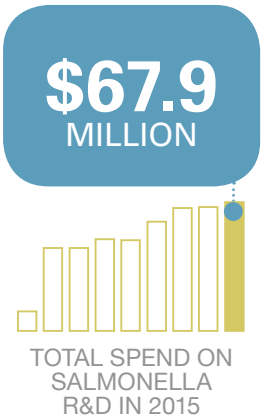
SALMONELLA INFECTIONS

Salmonella infections are a group of diseases caused by bacteria transmitted through contaminated food or drink. These infections can broadly be grouped into typhoid and paratyphoid fever (*Salmonella typhi, Salmonella paratyphi A*), which cause disease only in humans; and non-typhoidal *Salmonella enterica* (NTS), which has more than 2,000 serotypes that cause gastroenteritis in humans, as well as some serotypes that almost exclusively cause disease in animals.

Symptoms include high fever, malaise, headache, constipation or diarrhoea, rose-coloured spots on the chest, and enlarged spleen and liver. Young children, immunocompromised patients and the elderly are the most vulnerable to severe disease. In 2015, salmonella infections were responsible for 18 million DALYs and 265,947 deaths.

Although data from endemic regions show that antimicrobial resistance in salmonella infections is common, increasingly rendering these conditions untreatable,[62] there are no new drugs in the pipeline. Rapid disease progression and the existing drugs' unsuitability for young children mean that vaccine development is an important priority in achieving disease control. There are currently two safe and effective vaccines for preventing typhoid fever caused by *S. typhi*, however, there is no vaccine that targets both typhoid and paratyphoid fever, even though the latter is becoming the main causative agent of enteric fever in Asia.[63] Similarly, no typhoid or NTS vaccine is readily available for HIV-infected individuals or children under two years of age.[64]

There are some bivalent vaccines in development, but the most advanced product is a conjugated typhoid vaccine (Vi-CRM 197) that completed Phase II trials in 2012.[65] Results from this trial, reported in 2014, found the candidate to be safe and immunogenic in populations of all ages.[66] Most NTS vaccines are in pre-clinical stages.



R&D needed for salmonella infections includes:

- Basic research
- Drugs
- Diagnostics
- Vaccines

Salmonella infections received $68m in R&D funding in 2015, showing a slight increase in funding from YOY funders (up $2.0m, 3.2%) to $64m. Irregular survey participants provided the remaining $3.8m.

Typhoid and paratyphoid fever ($54m, 80%) received the bulk of R&D funding for salmonella infections in 2015, far more than went to NTS ($3.5m, 5.1%). This represented the highest recorded share of total funding for typhoid and paratyphoid fever since the salmonella category was expanded to include NTS in the second year of the survey. YOY funding for typhoid and paratyphoid fever increased by $6.9m (up 15%), while YOY funding for NTS halved (down $2.8m, -49%).

More than half of all funding for salmonella went to basic research ($35m, 52%), followed by vaccine investment ($27m, 39%). Vaccine development was particularly heavily focused on typhoid and paratyphoid fever ($24m, 91% of vaccine funding), with only minimal investment in NTS vaccines ($0.7m, 2.5% of vaccine funding). As in previous years, both diagnostics ($3.3m, 4.9%) and drugs ($2.6m, 3.8%) received very small proportions of total funding.

The small increase for YOY salmonella funding went mainly to basic research (up $2.7m, 9.1%). Vaccines (down $0.9m, -3.4%), drugs (up $0.5m, 24%) and diagnostics (down $0.2m, -7.1%) all saw only minor changes.

Table 14. Salmonella R&D funding 2015 (US$ millions)

Disease	Basic Research	Drugs	Vaccines (Preventive)	Diagnostics	Total	%
Typhoid and paratyphoid fever (*S. typhi, S. paratyphi A*)	26	2.0	24	2.3	54	80
Non-typhoidal *S. enterica* (NTS)	1.5	0.5	0.7	0.9	3.5	5.1
Multiple *Salmonella* infections	8.3	0.2	1.7	0.2	10	15
Total	35	2.6	27	3.3	68	100

The top 12 funders in 2015 provided essentially all funding (99%) for salmonella R&D, with the US NIH and industry collectively providing almost two-thirds of total funding ($42m, 63%). The only notable funding increases in 2015 came from the Gates Foundation (up $5.7m, 84%), primarily in basic research and vaccine development for typhoid and paratyphoid fever, and Science Foundation Ireland (up $2.1m, from no investment in 2014), which entered the top 12 funders for the first time. Decreases from top funders were relatively small, and mainly came from the US NIH (down $1.8m, -5.9%), industry (down $1.5m, -10%, all for vaccines) and the German DFG (down $1.4m, -78%).

Table 15. Top salmonella R&D funders 2015

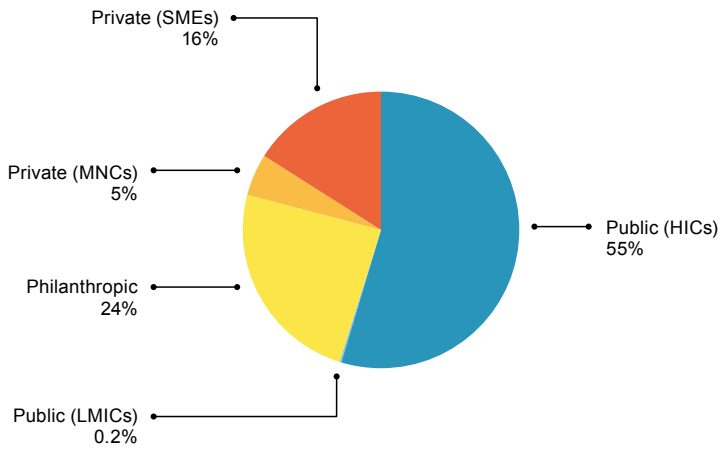
Funder	US$ (millions)									2015 % of total	2007-2015 trend
	2007	2008	2009	2010	2011	2012	2013	2014	2015		
US NIH	9.3	23	29	31	25	34	31	30	28	42	
Aggregate industry	-	14	3.9	3.2	4.9	4.4	10	15	14	21	
Gates Foundation	-	-	1.9	3.7	4.4	5.3	9.5	6.8	12	18	
Wellcome Trust	-	1.0	2.0	2.8	4.8	5.6	5.2	4.1	3.7	5.4	
UK MRC	0.9	1.2	0.9	0.7	1.6	1.3	1.5	2.0	2.5	3.6	
Science Foundation Ireland						0.4	0.4	-	2.1	3.1	
Institut Pasteur	-	1.3	1.5	1.4	2.2	1.4	1.6	1.9	1.7	2.5	
French ANR		0.5	-	-	-	-	1.6	-	0.6	0.9	
Chilean FONDECYT				0.1	0.7	0.6	0.7	0.6	0.5	0.8	
German DFG	-		0.5	1.2	1.1	0.9	1.2	1.8	0.4	0.6	
Swedish Research Council		0.4	0.3	0.4	0.5	0.5	0.5	0.4	0.4	0.5	
Australian NHMRC	-	0.5	0.5	0.5	0.1	0.3	0.5	0.7	0.3	0.5	
Subtotal of top 12^	10	44	44	47	47	56	64	65	67	99	
Disease total	10	44	44	48	48	58	65	66	68	100	

^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015
- 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

Public funders accounted for just over half of total salmonella funding ($37m, 55%), essentially all from HICs, with more than three-quarters of this coming from the US NIH ($28m, 76%). The philanthropic sector ($16m, 24%) and industry ($14m, 21%) each contributed similar amounts. As in previous years, the majority of industry funding came from SMEs ($11m, 76% of industry funding) rather than MNCs ($3.3m, 24% of industry funding).

Philanthropic funding for salmonella R&D increased in 2015 (up $5.2m, 48%), driven entirely by the increase from the Gates Foundation, whilst funding from both the public sector (down $1.7m, -4.8%) and industry (down $1.5m, -10%) was slightly lower. The latter drop could be considered more of a 'levelling off', with industry investment in salmonella R&D having tripled between 2012 and 2014, driven by growing investment in vaccine development by Indian SMEs.

Figure 18. Salmonella R&D funding by sector 2015



HEPATITIS C

In 2013, the G-FINDER scope expanded to include DC-specific R&D for hepatitis C genotype 4. Last year genotypes 5 and 6 were added to this category to capture further DC-relevant investments. The data reported here includes costs for R&D into either one of the specific genotypes as well as DC-specific R&D costs of products targeted at all genotypes including genotypes 4, 5 and 6.

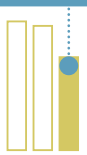
Hepatitis C is a blood-borne virus that causes inflammation of the liver. There are an estimated 26 million people infected with hepatitis C genotypes 4, 5 or 6 worldwide.[67] However, these genotypes are most prevalent in DCs, with genotype 4 accounting for more than 65% of infections in North Africa and the Middle East, genotype 5 accounting for 36% of infections in Southern Sub-Saharan Africa and genotype 6 accounting for 31% of infections in Southeast Asia.[68] Due to their low prevalence in the US and Europe they are significantly under-researched compared with other hepatitis C genotypes, and diagnostic, treatment and prevention tools are far less developed.

Hepatitis C can be successfully and safely treated with a pan-genotypic regimen of sofosbuvir/daclatasvir, including in hepatitis C/HIV co-infection.[12] However, the high cost of these drugs severely limits DC access. There are a number of new treatments in development that are either pan-genotypic or focused on genotypes prevalent in the West. Some of these have also shown efficacy in DC-relevant genotypes. Interim results of a Phase III trial of simeprevir + peginterferon/ribavirin showed comparable efficacy in patients with hepatitis C genotype 4 as those with hepatitis C genotype 1.[69] A Phase III study showed efficacy of a grazoprevir/albasvir FDC in genotypes 1, 4 and 6.[70] A Phase II trial of ombitasvir/paritaprevir/ritonavir showed a high virological response in patients infected with hepatitis C genotype 4.[71]

Most diagnostic tools were developed for the detection of hepatitis C genotype 1, making accurate epidemiological studies in countries with heavy hepatitis C genotype 4, 5 or 6 burdens challenging. In a recent advancement however, the WHO prequalified its first ever hepatitis C RDT for genotypes 3, 4 and 5.

There is no vaccine for hepatitis C and most vaccine R&D is focused on genotypes prevalent in the West. However, there are some pan-genotypic early-stage candidates, such as the Burnet Institute's Delta3 candidate.[72]

$33.5 MILLION



TOTAL SPEND ON HEPATITIS C R&D IN 2015

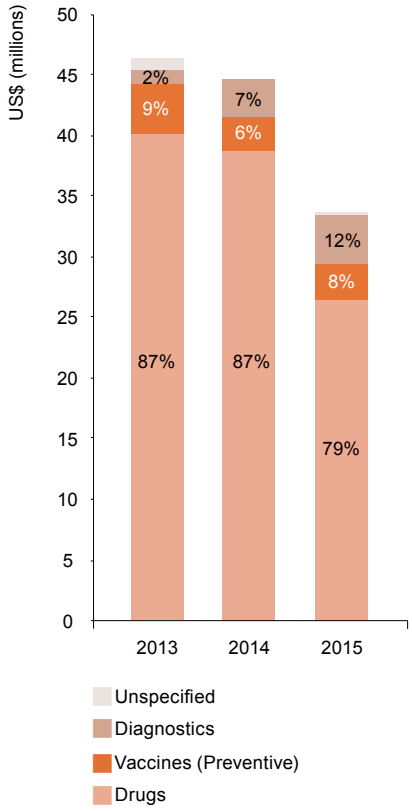
OF GLOBAL R&D FUNDING

R&D needed for hepatitis C genotypes 4,5 & 6 includes:

- Drugs
- Diagnostics
- Preventive vaccines

A total of $34m was invested in DC-specific R&D for hepatitis C genotypes 4, 5 and 6 in 2015 (this includes only research that is specifically for genotypes 4, 5, 6, or DC-specific investment in multi- or pan-genotypic technologies), with all but $0.4m of this reported by YOY participants. YOY funding dropped significantly in 2015 (down $11m, -25%), following a much smaller drop the previous year.

Figure 19. Hepatitis C (genotypes 4, 5 & 6) R&D funding by product type 2013-2015



Drug development ($26m, 79%) once again accounted for the vast majority of hepatitis C funding in 2015, with only modest investment in diagnostics ($4.1m, 12%) and vaccines ($2.8m, 8.5%). It was also the only area for which funding fell (down $13m, -33%), mainly due to reduced investment from the French National Agency for Research on AIDS and Viral Hepatitis (ANRS, down $5.0m, -58%), the US NIH (down $3.0m, -64%) and several industry funders. Funding for other product categories saw very small increases, with funding for diagnostics up by $1.1m (up 38%) and vaccines by $0.4m (up 19%).

Industry (collectively) remained top funder of hepatitis C R&D by some margin, contributing nearly two-thirds ($21m, 62%) of total investment. This share was relatively unchanged from 2014 despite industry funding falling by $4.6m (-18%), due to decreases from the second- and third-largest funders: French ANRS (down $4.6m, -53%, after a large contribution in 2014) and the US NIH (down $1.9m, -30%). Investment from other organisations is too low to provide meaningful analysis of funding trends for individual funders from year to year.

All of industry's investment in DC-relevant hepatitis C R&D came from two MNCs. In both cases, these investments represented a small part of overall funding for one or more multi-genotypic drugs. Both of these MNCs reported reduced investment in 2015, with a collective drop of $4.6m (-18%).

Table 16. Top hepatitis C (genotypes 4, 5 & 6) R&D funders 2015

Funder	US$ (millions)			2015 % of total	2013-2015 trend
	2013	2014	2015		
Aggregate industry	27	26	21	62	
US NIH	10	6.5	4.6	14	
French ANRS	1.8	8.6	4.0	12	
EU	0.6	2.8	2.8	8.4	
UK MRC	0.4	0.4	0.4	1.3	
Indian DBT	1.1	<0.1	0.3	1.0	
Thailand GPO	0.1	<0.1	0.2	0.7	
Brazilian FINEP	-	-	0.2	0.5	
German BMBF	-	-	0.1	0.3	
Wellcome Trust	0.1	0.1	<0.1	0.1	
Australian ACH[2]	<0.1	0.2			
Anonymous funder		0.2			
Disease total	46	45	34	100	

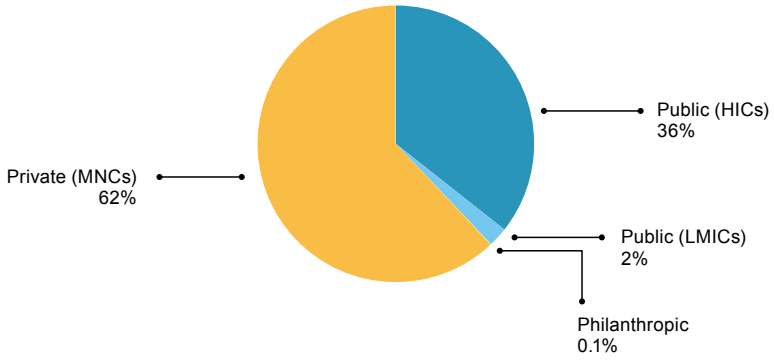
Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete

- No reported funding

The public sector contributed most of the remaining funding ($13m, 38%), of which almost all came from HICs (94%). Unlike in other neglected diseases, most of this came from European public funders ($7.4m, 62% of public HIC investment). The US NIH, on the other hand, contributed only a third of HIC funding ($4.6m, 38%). Decreases from several organisations meant that the public sector was responsible for most of the decline in YOY funding for hepatitis C (down $6.3m, -34%), despite the sector only accounting for a relatively small propotion of total funding.

There was minimal contribution from the philanthropic sector (less than $0.1m, 0.1%), which was stable between 2014 and 2015.

Figure 20. Hepatitis C (genotypes 4, 5 & 6) R&D funding by sector 2015



MOST NEGLECTED DISEASES

The most poorly funded neglected diseases, or 'third tier' diseases, are defined as those that receive less than 0.5% each of global funding for neglected disease R&D. These include leprosy, cryptococcal meningitis, trachoma, rheumatic fever, Buruli ulcer and leptospirosis.

These most neglected diseases cannot be analysed in the same way as better-funded diseases, simply because they receive so few grants from so few funders in any given year. Completion or initiation of even one grant by one funder can lead to large annual swings in reported funding, making analysis of funding trends meaningless. As a result, no trend analysis is included for these micro-funded diseases.

The table below summarises the R&D needs for the most neglected diseases.

EACH DISEASE RECEIVES

<0.5%

OF TOTAL GLOBAL FUNDING

Table 17. R&D needs for the most neglected diseases

Disease	Basic Research	Drugs	Vaccines (Preventive)	Diagnostics
Leprosy	Y	Y		Y
Cryptococcal meningitis		Y		
Trachoma			Y	Y
Rheumatic fever			Y	
Buruli ulcer	Y	Y	Y	Y
Leptospirosis				R

'R' denotes a category where only some investments are eligible, as defined in the neglected disease R&D scope document
'Y' denotes a category where a disease or product is included in the survey

LEPROSY

Leprosy is caused by *Mycobacterium* bacteria transmitted via droplets from the nose and mouth of untreated patients. Leprosy mainly affects the skin and nerves, and if left untreated causes nerve damage that leads to muscle weakness and wasting, as well as permanent disabilities and deformities.

Leprosy was responsible for 30,797 DALYs in 2015. A successful leprosy eradication programme, which has resulted in improved diagnosis and treatment with multidrug therapy (MDT), means that incidence is decreasing. Nevertheless, around a quarter of a million new cases are still recorded each year.[73]

The current MDT regimen for leprosy has been standard treatment for 30 years and, although highly effective, it requires 6-24 months of treatment.[74] Further research is needed to improve and simplify drug regimens, to provide products for the management of nerve function, and to develop and improve leprosy diagnostics.[75,76]

Bedaquiline, an antibiotic approved for the treatment of MDR-TB, has been found effective in the treatment of leprosy in mice[77] and may hold some promise. The Infectious Disease Research Institute (IDRI) is currently developing rapid diagnostic tests and a defined subunit vaccine.[78]

$10.8 MILLION

TOTAL SPEND ON LEPROSY R&D IN 2015

Funding for leprosy R&D in 2015 was $11m, exactly half of which was for basic research ($5.4m, 50%). Only $1.0m (10%) was allocated to product development, with diagnostics receiving $0.8m and drugs $0.3m. The large unspecified amount ($4.4m, 40%) was primarily core funding for leprosy R&D given to the Indian National JALMA Institute for Leprosy and Other Mycobacterial Diseases.

Table 18. Leprosy R&D funding by product type 2007-2015

Product \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total
Basic research	4.5	5.9	6.9	4.9	7.2	9.8	12	6.8	5.4	50
Diagnostics	0.7	0.6	1.5	1.4	1.2	1.4	0.8	0.2	0.8	7.3
Drugs	<0.1	0.8	0.9	1.1	0.3	0.8	0.2	0.1	0.3	2.5
Unspecified	0.6	3.4	2.5	2.8	-	2.8	0.1	3.4	4.4	40
Total	5.9	11	12	10	8.8	15	13	10	11	100

- No reported funding

Once again, the majority of leprosy R&D funding came from the public sector ($9.0m, 83%), and just two public funders (the US NIH and the Indian Council of Medical Research [ICMR], with a collective investment of $8.7m) were responsible for 81% of total leprosy R&D funding. The philanthropic sector provided $1.1m (10%) and industry $0.7m (6.3%, all from MNCs).

Table 19. Top leprosy R&D funders 2015

Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total
Indian ICMR		3.3	2.0	3.0	2.4	0.8	3.4	3.4	4.5	42
US NIH	2.3	3.6	5.8	3.7	4.4	10	5.9	5.6	4.2	39
Aggregate industry	-	-	-	0.1	0.1	-	0.1	0.1	0.7	6.3
LRI									0.5	5.0
TLMI				0.3	0.4	0.4	0.6	0.6	0.5	4.8
Institut Pasteur	0.1	0.2	0.2	0.2	0.1	0.2	0.1	0.1	0.1	0.8
Philippines DOH									0.1	0.7
UK MRC	-	-	-	-	-	-	-	<0.1	0.1	0.6
Wellcome Trust	-	<0.1	<0.1	-	-	<0.1	<0.1	<0.1	<0.1	0.2
EU	-	-	-	<0.1	<0.1	-	<0.1	0.1	<0.1	0.2
Fontilles				0.1	<0.1	<0.1	<0.1	<0.1	<0.1	0.1
Damien Foundation							0.1	<0.1	<0.1	0.1
Subtotal of top 12^	5.9	11	11	9.9	8.7	15	12	10	11	100
Disease total	5.9	11	12	10	8.8	15	13	10	11	100

^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015
- 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 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 2015).

CRYPTOCOCCAL MENINGITIS

Cryptococcal meningitis is an infection that causes inflammation of the tissue covering the brain and spinal cord. It is caused by *Cryptococcus*, a fungus found in soil. The disease predominantly affects people with weakened immune systems, such as those with HIV/AIDS. Approximately 1 million new cases occur each year, resulting in 625,000 deaths, mostly in countries with a high burden of HIV/AIDS.[79]

Cryptococcal meningitis can be effectively treated with amphotericin B (AmB) and flucytosine, but these are poorly suited to DC use. AmB is expensive and requires hospital administration, and flucytosine requires careful blood monitoring. As a result, cryptococcal meningitis in DCs is usually treated with fluconazole, which is only partially effective.[80]

A new long-acting azole-like compound (VT-1129) is currently being developed and received orphan drug status from the US FDA in 2014.[81] Furthermore, several oral formulations of AmB are in early stages of development.[82]

$5.8 MILLION

TOTAL SPEND ON CRYPTOCOCCAL MENINGITIS R&D IN 2015

Table 20. Cryptococcal meningitis R&D funders 2015

Funder	US$ (millions)			2015 % of total
	2013	2014	2015	
US NIH	1.4	4.1	3.5	60
UK MRC	1.5	1.3	2.2	38
Wellcome Trust	0.3	<0.1	0.1	1.4
Fondation Mérieux	<0.1	<0.1	<0.1	0.2
Australian NHMRC	0.1	0.1	-	-
Disease total	3.2	5.7	5.8	100

- No reported funding

A total of $5.8m was invested in cryptococcal meningitis R&D in 2015. We note that the only cryptococcal meningitis investments tracked by G-FINDER are for drug R&D.

Only four organisations reported providing funding for cryptococcal meningitis R&D in 2015. The two public HIC organisations (the US NIH and the UK MRC) accounted for essentially all of this funding ($5.7m, 98%). The rest came from two philanthropic funders: the Wellcome Trust and Fondation Mérieux ($0.1m, 1.6%).

TRACHOMA

Trachoma is an eye infection spread by contact with eye and nose discharge from an infected person, and by eye-seeking flies. It is the leading infectious cause of blindness in the world.[83]

Trachoma is endemic in 51 countries with an estimated 1.8 million people visually impaired or blind from the disease (of whom 0.5 million are irreversibly blind).[83] Trachoma was responsible for 278,190 DALYs in 2015, making it the thirteenth highest cause of morbidity from neglected diseases. Although debilitating, trachoma is not a fatal disease.

Current treatment involves either surgery (which has low acceptance and high recurrence rates) or treatment with azithromycin (where over-reliance on a single drug increases the risk of drug resistance). There are several *Chlamydia trachomatis* vaccines in development; however all of these are in pre-clinical/discovery stages.

Clinical diagnosis of trachoma is not always reliable, but current diagnostic tests are not a viable alternative due to their cost and complexity.[84] Recent studies showed that an antibody-based multiplex assay could be used to diagnose trachoma in low prevalence settings.[84]

$4.8 MILLION

TOTAL SPEND ON TRACHOMA R&D IN 2015

Funding for trachoma R&D was $4.8m in 2015. We note that the only trachoma investments tracked by G-FINDER are for vaccine and diagnostic R&D. Vaccines received just under two-thirds ($3.1m, 63%) of total funding, and diagnostics received the remainder ($1.8m, 37%).

Table 21. Trachoma R&D funding by product type 2007-2015

Product \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total
Vaccines (Preventive)	-	1.1	1.5	2.1	4.2	4.7	2.9	4.7	3.1	63
Diagnostics	0.9	0.1	0.4	3.1	6.8	4.7	2.5	2.0	1.8	37
Unspecified	0.7	0.9	0.1	-	-	0.5	0.5	0.2	-	-
Total	1.6	2.2	2.0	5.2	11	9.9	6.0	6.8	4.8	100

- No reported funding

The funder base for trachoma R&D contracted to only two organisations in 2015. The US NIH accounted for almost all funding ($4.6m, 96%), with the rest coming from the Wellcome Trust ($0.2m, 4.1%).

Table 22. Trachoma R&D funders 2015

Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total
US NIH	-	1.2	1.9	3.0	6.3	9.3	5.2	6.3	4.6	96
Wellcome Trust	1.4	-	-	-	-	0.6	0.5	0.3	0.2	4.1
Institut Pasteur	-	<0.1	-	<0.1	<0.1	-	0.1	0.1	-	-
US CDC	-	-	-	-	-	-	-	0.1	-	-
German DFG	-		-	-	-	-	0.2	-	-	-
Aggregate industry	0.1	0.1	-	2.2	4.5	-	-	-	-	-
TI Pharma					0.1					
Swedish Research Council		<0.1	0.1	-	-	-	-	-	-	-
SSI	-	0.6	-	-	-	-	-	-	-	-
Brazilian DECIT	-	0.2	-	-	-	-	-	-	-	-
All other funders	0.1	-	-	-	-	-	-	-	-	-
Disease total	1.6	2.2	2.0	5.2	11	9.9	6.0	6.8	4.8	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

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 an untreated bacterial throat infection and can lead to rheumatic heart disease, in which the heart valves are permanently damaged. It may progress to heart failure and stroke.

Rheumatic fever was responsible for 10 million DALYs and 278,996 deaths in 2015. It was the seventh highest cause of morbidity and mortality from neglected diseases.

Acute rheumatic fever can be treated using currently available drugs (although post-infection prophylaxis requires multiple dosing with 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 being developed, the most advanced being a Group A *streptococcus* vaccine in Phase I.[85]

$2.2 MILLION

TOTAL SPEND ON RHEUMATIC FEVER R&D IN 2015

A total of $2.2m was invested in rheumatic fever R&D in 2015. We note that the only rheumatic fever product area tracked by G-FINDER is preventive vaccine development.

Table 23. Rheumatic fever R&D funding by product type 2007-2015

Product	US$ (millions)									2015 % of total
	2007	2008	2009	2010	2011	2012	2013	2014	2015	
Vaccines (Preventive)	1.6	2.2	3.2	2.0	0.8	0.8	0.9	1.2	2.2	98
Unspecified	0.3	0.3	0.2	-	0.1	0.1	-	0.1	<0.1	1.7
Total	1.9	2.5	3.4	2.0	0.9	0.9	0.9	1.3	2.2	100

- No reported funding

There were three funders of rheumatic fever R&D in 2015. The US NIH invested $1.0m (46%), with the remaining funding provided by two new rheumatic fever funders: the Brazilian Development Bank ($0.6m, 27%) and the Health Research Council of New Zealand (New Zealand HRC, $0.6m, 26%).

Table 24. Rheumatic fever R&D funders 2015

Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total
US NIH	1.5	0.7	0.9	0.9	0.4	0.5	0.6	0.5	1.0	46
Brazilian Development Bank								-	0.6	27
New Zealand HRC	-	-	-	-	-	-	-	-	0.6	26
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	0.9	0.9	1.3	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

BURULI ULCER

Buruli ulcer begins as a painless lump that becomes an ulcer that can lead to disfiguration and functional impairment. It typically affects the rural poor, with the greatest number of cases in children under 15. Although HIV infection is not a risk factor of Buruli ulcer, co-infection complicates the management of the patient[86] and may impact its severity.[87]

Buruli ulcer occurs in more than 33 countries, predominantly in Western Africa. No DALY figures are available, although the WHO estimates that 2,200 new cases were reported in 2014 by 12 of the 33 countries.[88]

Treatment options including antibiotics and surgery are effective if the disease is diagnosed early, however, current diagnostics are both costly and insufficiently sensitive.[89] 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, emphasising the need for new drugs that are less complicated to administer or can be given for a shorter period. The BCG vaccine (designed for TB) provides short-term protection, but this is insufficient.

There are no new drugs in development for Buruli ulcer and the only vaccine in the pipeline is in pre-clinical stages (TMX 201[90]). FIND is developing several Buruli ulcer tests in collaboration with the WHO and other partners. These include an instrument-free POC test and tests to be used at a district hospital or microscopy level laboratory.[91]

$1.8 MILLION

TOTAL SPEND ON BURULI ULCER R&D IN 2015

Funding for Buruli ulcer R&D in 2015 was $1.8m. The majority went to basic research ($0.8m, 47%), with the rest going to product development: $0.4m (23%) to diagnostics and $0.2m (8.7%) to drugs. Like last year, there was no reported funding for vaccine R&D.

Table 25. Buruli ulcer R&D funding by product type 2007-2015

Product	US$ (millions)									2015 % of total
	2007	2008	2009	2010	2011	2012	2013	2014	2015	
Basic research	1.0	1.4	1.0	1.3	0.9	1.7	3.4	1.4	0.8	47
Diagnostics	<0.1	0.1	0.3	0.7	0.3	1.0	0.7	1.2	0.4	23
Unspecified	1.4	0.2	0.1	0.7	2.0	0.8	0.7	0.8	0.4	21
Drugs	-	0.2	0.3	0.7	0.7	0.7	0.8	0.2	0.2	8.7
Vaccines (Preventive)	-	<0.1	0.2	2.0	1.9	1.8	0.8	-	-	-
Total	2.4	1.9	1.8	5.5	5.7	6.0	6.4	3.6	1.8	100

- No reported funding

There were eight funders that invested in Buruli ulcer in 2015, none of which provided more than $0.5m. Funding provided by the R. Geigy Foundation ($0.1m, 4.1%) was captured for the first time. Contributions from the philanthropic ($1.0m, 54%) and public ($0.8m, 46%) sectors were fairly equal. There was no industry investment in Buruli ulcer R&D in 2015.

Table 26. Buruli ulcer R&D funders 2015

Funder / US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total
Institut Pasteur	0.6	0.3	0.3	0.4	0.2	0.4	0.3	0.4	0.4	24
Medicor Foundation				0.4	0.1	0.2	0.2	0.2	0.4	23
UBS Optimus Foundation		0.1	0.1	1.0	1.8	2.0	1.5	2.2	0.4	20
French ANR		-	-	-	-	0.1	-	-	0.2	14
UK MRC	-	-	-	-	-	-	0.2	0.2	0.1	7.6
Volkswagen-Stiftung					0.1	<0.1	<0.1	<0.1	0.1	6.0
R. Geigy Foundation									0.1	4.1
Wellcome Trust	-	<0.1	<0.1	<0.1	0.3	0.3	0.3	0.2	<0.1	1.0
FRF				-	-	0.2	0.2	0.2		
ALM	-	-	-	-	-	<0.1	0.2	0.2	-	-
German DFG	-		-	-	-	-	1.8	-	-	-
US NIH	0.8	0.5	0.9	1.2	1.3	1.0	1.0	-	-	-
Disease total	2.4	1.9	1.8	5.5	5.7	6.0	6.4	3.6	1.8	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

LEPTOSPIROSIS

Leptospirosis is an infection caused by *Leptospira* bacteria, transmitted by the urine of domestic or wild animals. It typically affects those living in tropical climates, involved in animal husbandry or living in slums.[92] Experts estimate that approximately 1 million people contract leptospirosis annually, resulting in nearly 60,000 deaths per year.[93]

The flu-like symptoms of leptospirosis make diagnosis difficult, with diagnostic tests limited to specialised laboratories. There is an urgent need to develop new, easy to use techniques for quick diagnosis at the acute stage of the disease.

A promising rapid POC test using chromatographic immunoassay technology is currently in development, with early studies demonstrating an overall sensitivity of 85% and specificity of 90%.[94]

$1.2 MILLION

TOTAL SPEND ON LEPTOSPIROSIS R&D IN 2015

Table 27. Leptospirosis R&D funders 2015

Funder	US$ (millions)			2015 % of total
	2013	2014	2015	
Institut Pasteur	0.4	0.9	0.9	76
US NIH	-	0.3	0.3	24
Colombian Colciencias		0.1	-	-
ALRA	<0.1	-	-	-
Disease total	0.4	1.2	1.2	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

There was $1.2m in reported funding for DC-specific leptospirosis R&D in 2015. We note that the only leptospirosis investments tracked by G-FINDER are for diagnostics.

Only two organisations funded leptospirosis R&D in 2015, both from the public sector. The Institut Pasteur provided more than three-quarters of total funding ($0.9m, 76%), with the rest coming from the US NIH ($0.3m, 24%).

Table 28. Disease and product R&D funding 2015 (US$ millions)

Disease or R&D area	Basic research	Drugs	Vaccines (Preventive)	Vaccines (Therapeutic)	Microbicides	Vector control products	Diagnostics	Unspecified	Total
HIV/AIDS	175.12	26.20	618.54		147.29		19.41	25.82	1,012.38
Tuberculosis	135.31	262.78	97.67	0.16			41.86	29.04	566.81
Malaria	127.87	238.38	128.45			32.47	14.64	23.17	564.98
P. falciparum	69.63	113.12	99.88			7.98	7.58	6.31	304.51
P. vivax	11.76	58.89	4.98			0.26	0.44	0.53	76.85
Other and/or unspecified malaria strains	46.48	66.37	23.60			24.23	6.62	16.33	183.62
Diarrhoeal diseases	38.96	4.04	92.70				7.75	16.57	160.01
Rotavirus			49.92					1.26	51.17
Cholera	15.21	0.38	6.73				1.16	-	23.48
Shigella	6.53	-	9.42				0.85	1.78	18.58
Enterotoxigenic *E.coli* (ETEC)			15.40				0.16	0.32	15.87
Cryptosporidium	6.42	3.66	2.05				0.29	-	12.42
Enteroaggregative *E.coli* (EAggEC)			0.43				0.08	0.20	0.70
Giardia							0.29	0.23	0.52
Multiple diarrhoeal diseases	10.80	-	8.76				4.91	12.79	37.26
Kinetoplastids	43.27	54.24	4.21	0.81		-	4.72	5.01	112.26
Leishmaniasis	16.18	13.00	3.58	0.24			1.45	3.97	38.42
Sleeping sickness	17.29	9.38	-			-	2.11	0.55	29.33
Chagas' disease	7.20	8.22	0.61	0.56		-	1.16	0.10	17.85
Multiple kinetoplastids	2.60	23.64	0.02	-		-	-	0.39	26.66
Dengue	42.11	23.34				24.05	5.00	5.23	99.73
Bacterial pneumonia & meningitis			76.27				2.61	13.18	92.06
S. pneumoniae			70.22				0.73	1.55	72.50
N. meningitidis			6.05				0.34	1.03	7.42
Both bacteria							1.54	10.60	12.14
Helminths (worms & flukes)	29.96	27.54	9.88			0.11	6.28	3.03	76.80
Schistosomiasis (bilharziasis)	9.58	2.94	3.50			-	2.44	1.39	19.86
Lymphatic filariasis (elephantiasis)	5.66	6.32				0.02	0.20	1.27	13.46
Onchocerciasis (river blindness)	1.58	7.47	0.02			0.02	3.35	-	12.43
Hookworm (ancylostomiasis & necatoriasis)	1.15	0.94	3.63					0.05	5.77
Tapeworm (cysticercosis/taeniasis)	1.22	1.36				0.08		-	2.67
Strongyloidiasis & other intestinal roundworms	0.68	0.48	<0.01				0.29	0.24	1.69
Whipworm (trichuriasis)	1.19	0.15						0.05	1.38
Roundworm (ascariasis)	1.04	0.03						0.03	1.09
Multiple helminths	7.87	7.86	2.73			-	-	-	18.45
Salmonella infections	35.46	2.59	26.56				3.30	-	67.91
Typhoid and paratyphoid fever (*S. typhi, S. paratyphi A*)	25.64	1.97	24.22				2.26	-	54.09
Non-typhoidal *S. enterica* (NTS)	1.48	0.47	0.67				0.88	-	3.49
Multiple *Salmonella* infections	8.34	0.15	1.67				0.16	-	10.32
Hepatitis C (genotypes 4, 5 & 6)		26.48	2.83				4.09	0.10	33.50

Disease or R&D area	Basic research	Drugs	Vaccines (Preventive)	Vaccines (Therapeutic)	Microbicides	Vector control products	Diagnostics	Unspecified	Total
Leprosy	5.38	0.27					0.79	4.36	10.79
Cryptococcal meningitis		5.76							5.76
Trachoma			3.06				1.77	-	4.83
Rheumatic fever			2.17					0.04	2.21
Buruli ulcer	0.85	0.16	-				0.42	0.37	1.79
Leptospirosis							1.25		1.25
Core funding of a multi-disease R&D organisation									118.35
Unspecified disease									76.87
Platform technologies	General diagnostic platforms			Adjuvants and immunomodulators			Delivery technologies and devices		
	13.66			11.95			7.45		33.06
Total R&D funding									**3,041.36**

- No reported funding

Category not included in G-FINDER

NEGLECTED DISEASE FUNDERS

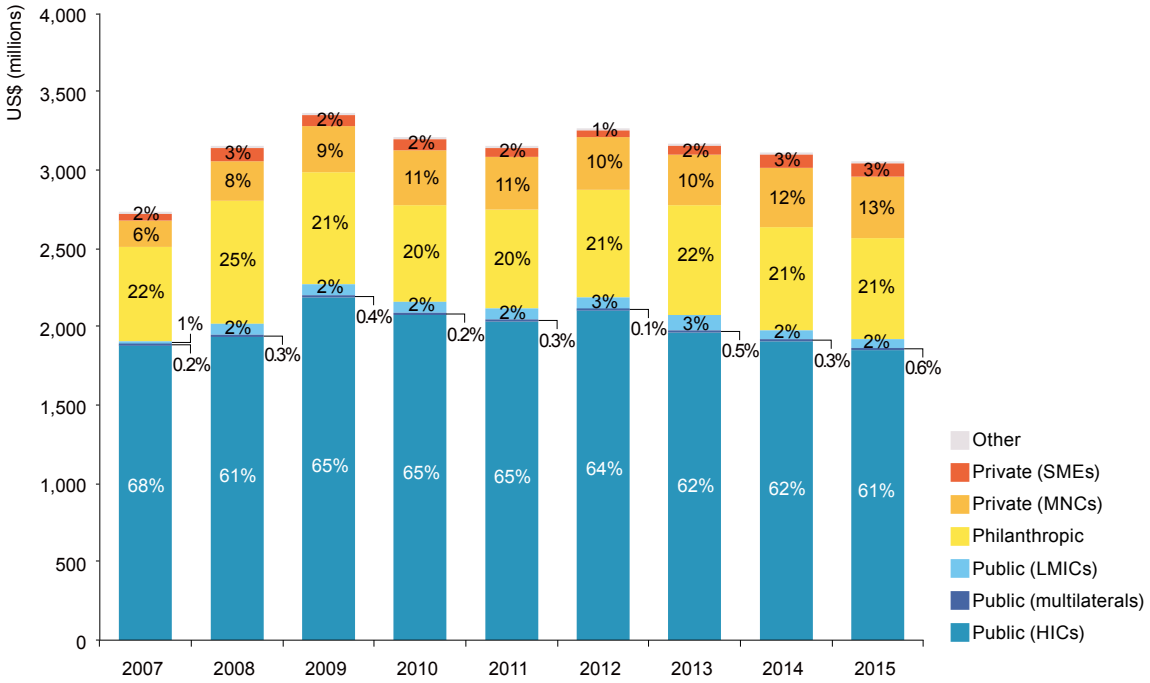
FUNDER OVERVIEW

Public sector funding for neglected disease R&D fell once again in 2015 – extending the decline seen since 2012 – while industry investment edged slightly higher, following a significant increase in 2014. Coupled with a small drop in philanthropic funding, these changes resulted in both the lowest public sector funding share and the highest industry funding share ever recorded in the history of the G-FINDER survey.

The public sector remained by far the most significant source of neglected disease R&D funding in 2015, providing almost two-thirds ($1,925m, 63%) of the global total, with almost all public funding coming from HIC governments and multilaterals ($1,866m, 97%). The philanthropic sector provided 21% ($645m), and industry contributed 15% ($471m).

YOY public funding fell by $53m (-2.8%) – entirely driven by HIC governments and multilaterals (down $56m, -3.0%) – and philanthropic funding was $22m lower (down 3.5%). Industry funding increased marginally (up $7.1m, 1.7%). SMEs were responsible for more than half of the industry increase – YOY SME investment increased by $4.7m (up 9.9%) – despite representing only 18% of all industry investment.

Figure 21. Total R&D funding by sector 2007-2015



Ebola and other African VHFs

In response to the 2014 West African Ebola epidemic, last year's G-FINDER survey tracked funding for Ebola R&D for the first time (capturing FY2014 investments). This year, the survey scope was expanded to also include funding for R&D into African viral haemorrhagic fevers (VHFs) other than Ebola, as well as funding targeted at multiple African VHFs.

However, because of the unprecedented nature of the global response to the Ebola threat – and its distorting effect on investments in 'traditional' neglected disease R&D – funding for Ebola and other African VHFs (for both 2014 and 2015) has been analysed separately in this year's G-FINDER report.

As noted at the beginning of this report, the true scale of the global response to the Ebola outbreak became apparent in the 2015 survey. Globally, a total of $631m was invested in R&D for Ebola and other African VHFs in 2015. This was an increase of nearly half-a-billion dollars compared to 2014 (up $464m, 288%), and meant that Ebola and other African VHFs received more R&D funding than any neglected disease except for HIV/AIDS.

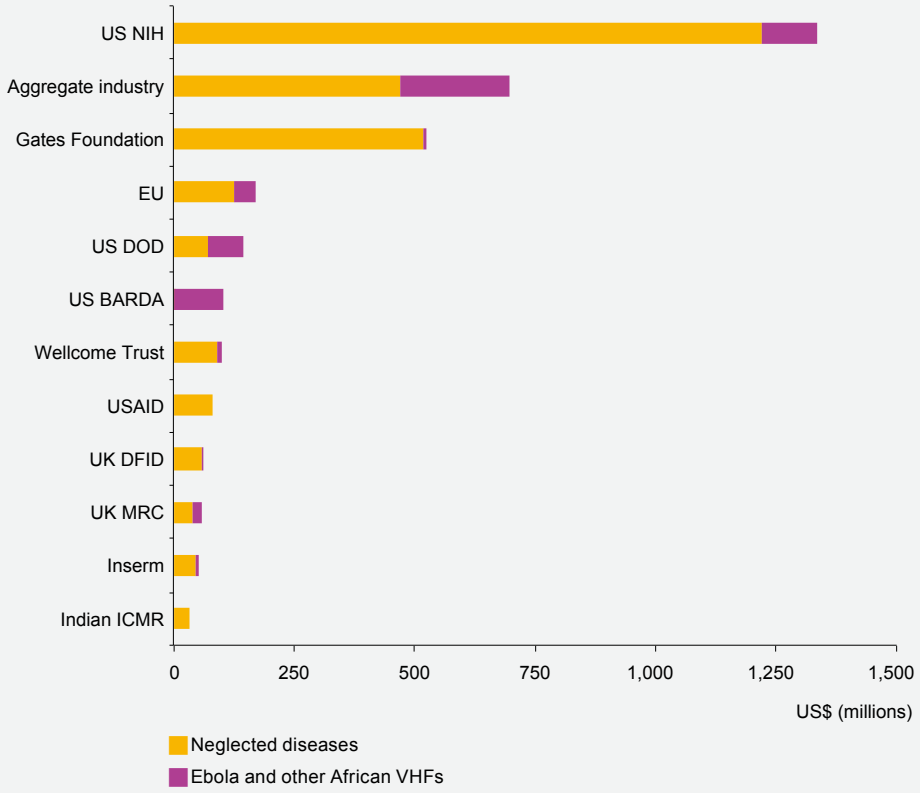
The funder landscape looks markedly different when funding for Ebola and other African VHFs is included along with investment in 'traditional' neglected diseases. The relative contribution of the public sector remains unchanged, with its $2,307m investment representing 63% of all funding. But in a major change, industry ($697m, 19%) leapfrogs the philanthropic sector ($667m, 18%) to become the second most significant funding sector.

With funding for Ebola included, total YOY public sector funding actually increased (up $157m, 7.8%), and industry investment nearly doubled (up $201m, 44%) compared to 2014 levels. Total philanthropic funding would still have dropped slightly (down $15m, -2.3%), despite a small increase in philanthropic funding for Ebola in 2015.

Including funding for Ebola and other African VHFs has no impact on the ranking of top public sector funders by country: the US ($1,685m) remains the top contributor, providing 73% of all public funding, and the EU ($171m, 7.4%) is still the second-largest public funder globally. Notably, however, total US public funding – including Ebola and other African VHFs – increased by $156m (up 10%) compared to 2014, despite the US investing less in neglected diseases. The EU was responsible for the second largest public sector funding increase globally (up $62m, 57%) when its 2015 Ebola R&D investment of $45m is included.

The list of top funding organisations does change slightly when investment in Ebola and other African VHFs is included. The most notable change is that the aggregate pharmaceutical industry ($697m) collectively invested more than the Gates Foundation ($526m), making it the second-largest 'individual' funder behind the US NIH ($1,334m). The US DOD moves from 7th to 5th when its funding for Ebola and other African VHFs is included, and the US Biomedical Advanced Research and Development Authority (BARDA) moves into the top funders list (in 6th place), causing the German BMBF to drop out of the top 12.

Figure 22. Top R&D funders 2015 with Ebola and other African VHFs included



PUBLIC FUNDERS

As has been the case in each of the past eight years, the top three public funders in 2015 were the US, the UK and the EU[ii]. The US was responsible for nearly three-quarters of all global public funding ($1,387m, 72%), with a contribution more than 11 times larger than that of the next biggest public funder. In 2015 this position was held by the EU, which contributed $125m (6.5% of global public funding) – the first time since 2008 that the EU has provided more neglected disease R&D funding than the UK.

YOY public funding for neglected disease R&D fell by $53m in 2015 (-2.8%), further extending the decline that started in 2012. Of the top three funders, only the EU (up $21m, 20%) significantly increased funding in 2015, reflecting its expanded contributions under the second phase of EDCTP. US public sector funding fell by $44m (-3.0%), led by the US DOD (down $24m, -25%), although we note that some of this decrease may be due to more accurate reporting of HIV/AIDS investments in 2015 by the US DOD. UK public funding fell by $22m (-18%), with decreases from the UK DFID (down $15m, -21%), reflecting the cyclical nature of DFID's funding to product development partnerships (PDPs), and the UK MRC (down $6.5m, -14%).

Outside of the top three, the most significant drops in public funding came from Australia and the Netherlands. Australian funding nearly halved (down $16m, -47%), entirely due to a marked drop in funding reported by the Australian NHMRC (down $16m, -62%, to $9.8m), which in the past has consistently invested between $20m and $25m annually in neglected disease R&D. The Netherlands fell out of the Top 12 public funders for the first time since the G-FINDER survey began, due to a sharp drop in funding from the Dutch DGIS (down $13m, 76%) as it transitioned between PDP funding rounds. These drops were partially offset by smaller increases from Germany (up $6.6m, 39%), Switzerland (up $3.9m, 40%)[iii] and Ireland (up $3.3m, 150%).

Table 29. Top public R&D funders 2015

Country	US$ (millions)									2015 % of total
	2007	2008	2009	2010	2011	2012	2013	2014	2015	
United States of America	1,409	1,431	1,650	1,572	1,538	1,638	1,462	1,430	1,387	72
EU	111	120	110	84	99	87	105	104	125	6.5
United Kingdom	98	100	141	153	125	87	119	124	102	5.3
France	14	27	44	37	56	50	73	60	60	3.1
Germany	11	3.5	32	35	30	51	41	45	51	2.6
India		39	26	40	44	44	52	40	44	2.3
Australia	20	28	25	28	35	44	23	34	20	1.0
Switzerland	7.6	4.8	8.7	15	15	17	17	19	16	0.8
Japan	4.1	6.6	5.6	8.5	3.3	2.5	10	10	12	0.6
Canada	21	25	17	9.0	9.1	17	19	13	9.6	0.5
Ireland	22	8.1	4.8	6.0	5.8	6.9	11	2.7	8.8	0.5
Sweden	19	22	28	17	17	16	5.9	6.0	8.3	0.4
Subtotal of top 12^	1,801	1,883	2,147	2,022	2,002	2,084	1,960	1,904	1,844	96
Total public funding	1,905	2,014	2,269	2,153	2,120	2,185	2,077	1,978	1,925	100

^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015
No funding organisations from this country participated in the survey for this year

[ii] The term 'European Union' is used here and throughout the report to refer to funding from the EU budget that is managed by the European Commission or related EU partnerships and initiatives (such as the EDCTP and IMI)

[iii] The apparent drop in total Swiss public funding shown in Table 29 is due to partial underreporting of funding from the Swiss National Science Foundation (SNSF), with around $4m in funding data provided too late to be included in the G-FINDER analysis. This does not affect YOY analysis, as SNSF has not participated in every year of the G-FINDER survey

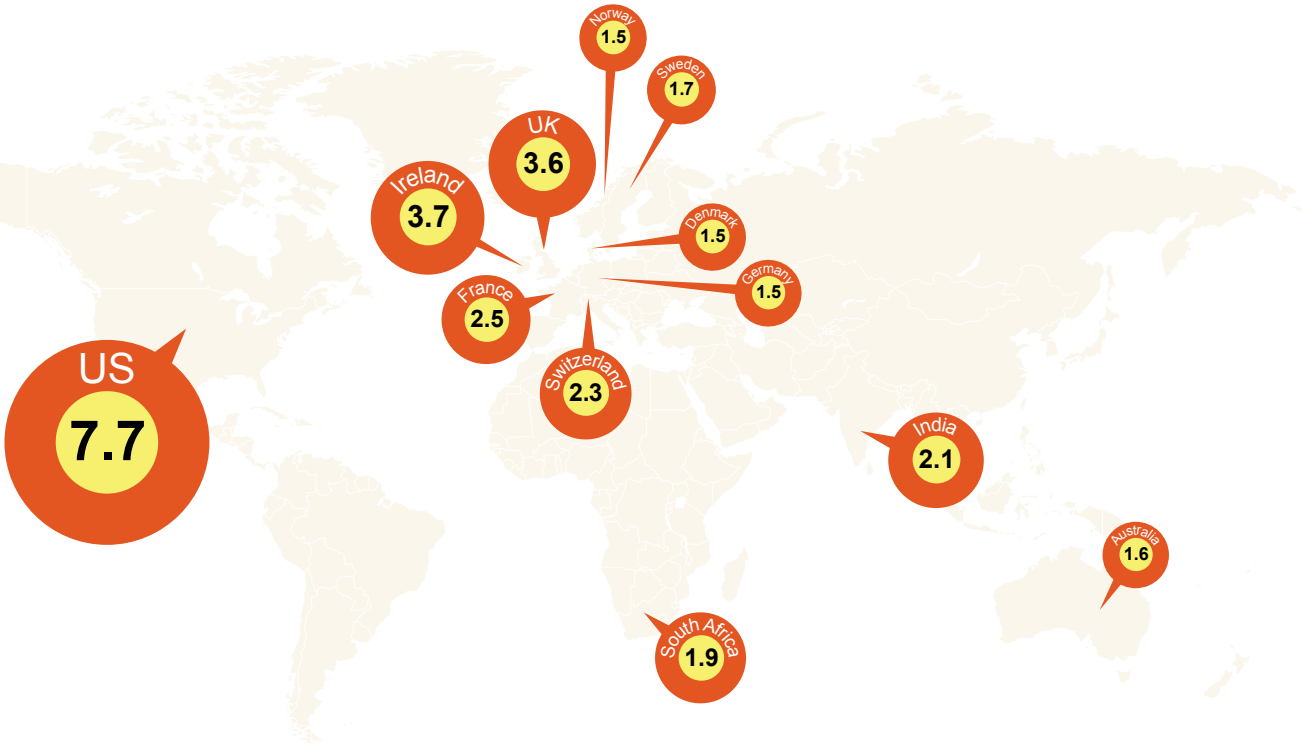
Overall IDC[iv] public funding increased by $3.5m (7.1%), due to increases from India (up $4.7m, 12%) and South Africa (up $2.2m, 58%). Funding from the Indian Department of Biotechnology (Indian DBT) rose to $6.3m, after an unusually low year in 2014 (up $3.4m, 116%). The South Africa Medical Research Council (MRC) increased funding by $2.3m from a low base.

PUBLIC FUNDING BY GDP

Absolute funding can be a misleading measure of public R&D investment, as it can underplay the 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 when ranked by contribution relative to GDP: South Africa, Norway and Denmark. Conversely, Japan and Canada drop out of the list when GDP is factored in, as does the EU (which cannot be fairly analysed by this measure). The US, UK, France, Germany, India, Australia, Switzerland, Ireland and Sweden are all ranked in the top 12 using both metrics. Ireland provided the second highest contribution as a percentage of GDP of all countries in 2015 (second only to the US), even though it ranks eleventh by absolute funding amount ($8.8m).

Figure 23. Public R&D funding by GDP 2015^*
(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

[iv] IDC increases or decreases refer to organisations that participated in both 2014 and 2015 (rather than in every year of the survey, as is the case in the remainder of the report), as IDC survey participation is inconsistent from year to year

HIGH-INCOME COUNTRIES AND MULTILATERALS

HIC governments and multilaterals provided $1,866m in neglected disease R&D funding in 2015 (97% of public funding). YOY funding fell by $56m (down 3.0%), with substantial reductions from the US (down $44m, -3.0%), the UK (down $22m, -18%) and Australia (down $16m, -47%) far outweighing the increases that came from the EU (up $21m, 20%), Germany (up $6.6m, 39%) and Switzerland (up $3.9m, 40%).

As in previous years, the top three diseases (HIV/AIDS, TB and malaria) received three-quarters ($1,408m, 75%) of all HIC and multilateral funding. YOY funding for HIV/AIDS fell by $56m (-6.5%), with the US DOD responsible for $34m of this drop. TB received more HIC and multilateral funding than it has in any year since 2009, with the slight increase in YOY investment (up $11m, 3.9%) coming largely from the EU (up $7.5m, 51%). Funding for malaria was essentially unchanged (up $0.3m, 0.1%).

Funding for most other diseases was either lower or flat. Outside of HIV/AIDS, the largest drop was for diarrhoeal diseases (down $11m, -13%), driven by reduced funding from the US NIH (down $5.2m, -12%) and the UK DFID (down $3.6m, -40%). Funding for hepatitis C also fell (down $6.6m, -36%), as funding from the French ANRS (down $4.6m, -53%) returned to more moderate levels after a large contribution in 2014. The only disease other than TB to receive notably more HIC and multilateral funding in 2015 was dengue (up $7.7m, 16%), primarily due to increased investment by the US NIH (up $5.3m, 13%).

Table 30. Public (HIC and multilaterals) R&D funding by disease 2007-2015

Disease or R&D area	US$ (millions)									2015 % of total
	2007	2008	2009	2010	2011	2012	2013	2014	2015	
HIV/AIDS	1,057	1,039	1,067	994	957	986	909	876	824	44
Tuberculosis	235	224	332	305	278	272	279	298	307	16
Malaria	231	251	284	306	284	282	284	279	277	15
Diarrhoeal diseases	49	66	101	83	92	84	86	83	72	3.9
Kinetoplastids	50	86	102	103	95	91	74	79	68	3.7
Dengue	39	42	57	50	57	53	44	49	58	3.1
Helminths (worms & flukes)	41	36	51	49	47	58	49	45	41	2.2
Salmonella infections	10	29	36	37	33	40	40	39	37	2.0
Bacterial pneumonia & meningitis	11	10	13	18	27	16	25	19	16	0.8
Hepatitis C (genotypes 4, 5 & 6)							14	19	12	0.6
Cryptococcal meningitis							2.9	5.6	5.7	0.3
Trachoma	-	1.9	2.0	3.0	6.3	9.3	5.5	6.5	4.6	0.2
Leprosy	3.8	4.0	6.9	3.9	4.5	11	6.0	5.7	4.4	0.2
Rheumatic fever	1.9	1.3	1.5	1.8	0.9	0.9	0.9	1.2	1.6	0.1
Leptospirosis							0.4	1.2	1.2	0.1
Buruli ulcer	2.2	1.5	1.6	3.7	3.4	3.4	4.0	0.6	0.8	<0.1
Platform technologies	3.2	5.9	7.6	11	11	26	29	11	13	0.7
General diagnostic platforms	1.2	2.2	2.1	5.6	8.5	7.3	8.4	5.8	9.5	0.5
Adjuvants and immunomodulators	<0.1	0.8	3.0	4.0	1.9	18	16	3.3	3.2	0.2
Delivery technologies and devices	2.0	2.9	2.5	1.2	0.4	0.4	4.0	1.6	0.6	<0.1
Core funding of a multi-disease R&D organisation	91	82	64	68	83	66	65	61	77	4.1
Unspecified disease	54	63	74	46	66	101	67	44	43	2.3
Total public funding (HICs/multilaterals)	1,879	1,942	2,200	2,083	2,044	2,100	1,983	1,922	1,866	100

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

LOW- AND MIDDLE-INCOME COUNTRIES

Public funders in LMICs provided $59m for neglected disease R&D in 2015, accounting for 3.0% of global public funding.[v] Inconsistent survey participation by many LMIC organisations makes long-term or multi-year comparisons of funding difficult, but funding from LMIC public funders who participated in both 2014 and 2015 grew by $3.2m (up 5.8%).[vi]

[v] Overall LMIC funding is under-reported as FAPESP, a major Brazilian funder, was unable to provide data in time to be included in the G-FINDER analysis. FAPESP invested $5.3m in neglected disease R&D in 2015, with approximately half of that being for kinetoplastid R&D.

[vi] 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 2014 and 2015 (rather than in every year of the survey, as is the case in the remainder of the report). This group of funders provided $57m of the $59m in total LMIC public funding for 2015.

In 2015, 92% of LMIC public funding was provided by the three IDCs: India ($44m, 76%), South Africa ($6.0m, 10%) and Brazil ($3.3m, 5.6%). If the State of Sao Paulo Research Foundation's (FAPESP) funding had been included, Brazil's total investment would have been $8.6m.

YOY LMIC funding for TB, malaria and HIV/AIDS R&D increased by $5.6m (up 21%), driven by malaria, which increased by more than a third (up $3.1m, 35%), due in large part to a $2.1m increase from the Indian DBT, from a low base. The Indian Council of Scientific and Industrial Research (Indian CSIR) tripled its funding for TB (up $2.0m, 202%), returning to levels seen before 2014, supporting an overall increase of $1.7m (up 13%). A large jump in HIV/AIDS R&D investment from the South African MRC (up $2.4m from a low base) offset a reduction of $1.5m from Indian ICMR (-83%). Overall, HIV/AIDS R&D funding from LMICs rose $0.7m (up 17%).

Table 31. Public (LMIC) R&D funding by disease 2010-2015

Disease or R&D area	US$ (millions)						2015 % of total
	2010	2011	2012	2013	2014	2015	
Tuberculosis	11	17	17	25	13	15	26
Malaria	9.9	13	20	19	9.1	12	21
Kinetoplastids	9.6	7.7	11	7.4	7.6	5.9	10
HIV/AIDS	17	18	12	18	5.8	5.5	9.4
Diarrhoeal diseases	7.1	9.1	4.7	5.3	5.5	5.5	9.3
Leprosy	3.5	2.5	2.0	4.6	3.5	4.6	7.8
Dengue	5.7	4.3	6.4	3.3	3.2	3.5	6.0
Helminths (worms & flukes)	1.2	1.9	2.9	1.7	2.6	1.7	3.0
Hepatitis C (genotypes 4, 5 & 6)				5.3	0.2	0.8	1.3
Rheumatic fever	-	-	-	-	-	0.6	1.0
Salmonella infections	0.6	0.5	0.3	0.5	0.6	0.1	0.2
Bacterial pneumonia & meningitis	0.3	0.1	0.2	<0.1	0.3	-	-
Leptospirosis				-	0.1	-	-
Platform technologies	3.3	0.4	4.4	0.5	0.3	1.3	2.1
Delivery technologies and devices	1.9	<0.1	3.9	0.4	0.3	1.2	2.0
General diagnostic platforms	0.9	0.4	0.5	<0.1	0.1	0.1	0.2
Adjuvants and immunomodulators	0.6	-	-	-	-	-	-
Core funding of a multi-disease R&D organisation	0.4	0.3	-	0.4	0.3	1.5	2.5
Unspecified disease	-	0.4	3.7	2.2	3.9	0.1	0.2
Total public funding (LMICs)	70	76	85	94	56	59	100

- No reported funding

New disease added to G-FINDER in 2013

PHILANTHROPIC FUNDERS

Philanthropic funders invested $645m in neglected disease R&D in 2015 (21% of the total). The two largest contributors – the Gates Foundation and the Wellcome Trust – together contributed $610m (95% of philanthropic funding).

YOY philanthropic funding decreased slightly (down $22m, -3.5%). While funding from the Gates Foundation was steady (down $2.3m, -0.4%), the Wellcome Trust decreased investment by $27m (down 22%), but the organisation remained by far the second largest philanthropic funder of neglected disease R&D.

Table 32. Top philanthropic R&D funders 2015

Funder / US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total	2007-2015 trend
Gates Foundation	518	691	627	517	513	509	526	520	518	80	
Wellcome Trust	56	59	64	75	89	138	127	119	92	14	
Gavi	12	17		2.5		9.6	18		9.9	1.5	
MSF	6.6	6.7	4.2	4.3	4.8	5.4	5.5	4.4	5.8	0.9	
Fundació La Caixa		0.3		0.3	3.2	2.6	2.9		3.4	0.5	
UBS Optimus Foundation	0.5	1.1	1.1	6.7	5.0	3.1	2.5	3.3	1.4	0.2	
Funds raised from the general public	2.3	1.4	0.5	0.4	0.5	0.4	0.7	0.9	1.2	0.2	
Medicor Foundation			0.5	0.8	0.6	0.5	0.7	0.5	0.7	0.1	
All other philanthropic organisations	8.5	16	17	18	15	20	12	6.8	12	1.9	
Total philanthropic funding	604	792	715	625	631	688	696	655	645	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

The most notable change in disease funding from philanthropic organisations was a $41m reduction in malaria R&D investment (-24%). This is the lowest level of philanthropic funding for malaria since the G-FINDER survey began, and was the result of decreases from both the Gates Foundation (down $35m, -25%) and the Wellcome Trust (down $5.6m, -23%). Philanthropic funding for kinetoplastid R&D fell by $17m (-50%), driven by a $16m decrease from the Gates Foundation (down 86%), although this followed a large upfront grant disbursement to DNDi in 2014.

Philanthropic funding for bacterial pneumonia & meningitis more than tripled (up $27m), reflecting a return to more traditional funding levels from the Gates Foundation (up $28m, 519%).

Table 33. Philanthropic R&D funding by disease 2007-2015

Disease or R&D area	US$ (millions)									2015 % of total
	2007	2008	2009	2010	2011	2012	2013	2014	2015	
Tuberculosis	135	158	123	135	116	121	143	148	141	22
Malaria	172	228	239	137	199	167	152	169	128	20
HIV/AIDS	116	199	151	152	151	160	148	136	128	20
Diarrhoeal diseases	63	48	54	52	36	48	62	46	49	7.6
Bacterial pneumonia & meningitis	7.0	31	26	50	39	52	27	7.5	41	6.3
Dengue	2.2	3.2	3.2	4.5	6.9	11	21	25	24	3.7
Helminths (worms & flukes)	12	30	25	23	30	27	33	29	22	3.4
Kinetoplastids	73	53	58	32	24	22	21	34	17	2.6
Salmonella infections	0.1	1.0	3.8	7.3	9.7	13	15	11	16	2.6
Leprosy	0.8	1.1	1.1	2.6	1.7	2.2	2.0	1.2	1.1	0.2
Buruli ulcer	-	0.2	0.3	1.8	2.3	2.7	2.4	3.0	1.0	0.1
Trachoma	1.4	-	-	-	0.1	0.6	0.5	0.3	0.2	<0.1
Cryptococcal meningitis							0.3	<0.1	0.1	<0.1
Hepatitis C (genotypes 4, 5 & 6)							0.1	0.1	<0.1	<0.1
Leptospirosis							<0.1	-	-	-
Rheumatic fever	-	0.1	0.2	0.2	-	-	-	-	-	-
Platform technologies	2.3	9.3	16	15	6.8	19	15	11	18	2.8
Adjuvants and immunomodulators	-	1.5	2.5	5.6	3.8	9.3	4.9	5.0	8.5	1.3
Delivery technologies and devices	0.1	4.7	6.3	5.0	1.4	0.7	1.6	2.4	5.7	0.9
General diagnostic platforms	2.3	3.1	7.7	3.9	1.6	9.2	8.2	3.8	4.0	0.6
Core funding of a multi-disease R&D organisation	15	11	6.3	5.8	4.8	42	43	22	30	4.7
Unspecified disease	3.7	20	8.5	7.4	3.2	2.3	11	12	27	4.2
Total philanthropic funding	604	792	715	625	631	688	696	655	645	100

New disease added to G-FINDER in 2013

- No reported funding

PRIVATE SECTOR FUNDERS

The private sector invested $471m in neglected disease R&D in 2015 (15% of the total). This is both the largest amount and the highest share of funding from industry in the history of the G-FINDER survey. The proportion of industry investment that came from MNCs ($388m, 82%) compared to SMEs ($83m, 18%) was similar to 2014 (when it was 83% and 17%, respectively).

YOY industry funding increased by $7.1m (up 1.7%). This increase came primarily from SMEs, which invested $4.7m more than in 2014 (up 9.9%). MNC investment was steady (up $2.4m, 0.6%).

MULTINATIONAL PHARMACEUTICAL COMPANIES

In 2015, almost three quarters ($280m, 72%) of MNC investment in neglected disease R&D was directed to three diseases (malaria, TB and HIV/AIDS), compared to 66% in 2014.

More than a third ($141m, 36%) of all MNC investment in 2015 was in malaria. YOY industry investment in malaria R&D rose substantially (up $20m, 18%) for the second year in a row, as key drug candidates from a number of MNCs moved into later stage clinical trials. TB received a quarter ($92m, 24%) of all MNC investment. YOY MNC investment in TB was essentially steady (down $2.4m, -2.5%), suggesting that the trend of declining industry support for TB R&D – which has been apparent since 2010 – may be slowing. MNCs invested $47m in HIV/AIDS in 2015 (up $7.5m, 19%), more than in any previous year in the history of the survey. As was the case in 2014, the vast majority (85%) of this investment was in vaccine R&D.

YOY MNC investment in bacterial pneumonia & meningitis R&D fell by $19m (down 62%) in 2015, in large part due to the conclusion of regulatory trials to support LMIC uptake of the latest generation of pneumococcal vaccines. MNC investment in diarrhoeal diseases (down $10m, -34%) and hepatitis C (down $4.6m, -18%) also fell.

Of the third tier diseases, only leprosy received any contributions from MNCs ($0.7m).

Table 34. MNC R&D funding by disease 2007-2015

Disease or R&D area	US$ (millions)									2015 % of total
	2007	2008	2009	2010	2011	2012	2013	2014	2015	
Malaria	75	78	79	109	90	103	72	118	141	36
Tuberculosis	52	78	114	146	143	127	106	95	92	24
HIV/AIDS	7.5	21	19	17	14	15	9.6	39	47	12
Hepatitis C (genotypes 4, 5 & 6)							27	26	21	5.4
Diarrhoeal diseases	9.8	24	35	32	22	27	38	30	20	5.1
Kinetoplastids	5.0	1.3	3.8	10	9.8	17	16	12	16	4.2
Dengue	4.8	3.4	4.2	6.7	11	8.0	7.0	7.1	13	3.4
Bacterial pneumonia & meningitis	14	32	26	24	32	35	30	31	12	3.0
Helminths (worms & flukes)	0.1	4.5	9.3	3.6	2.5	3.3	8.2	6.6	11	2.7
Salmonella infections	-	1.2	2.0	3.0	4.9	4.1	4.1	3.7	3.3	0.9
Leprosy	-	-	-	-	-	-	0.1	0.1	0.7	0.2
Buruli ulcer	-	0.1	-	-	-	-	-	-	-	-
Rheumatic fever	-	1.1	1.7	-	-	-	-	0.1	-	-
Trachoma	0.1	0.1	-	-	-	-	-	-	-	-
Core funding of a multi-disease R&D organisation	-	-	-	-	-	-	2.5	8.9	9.2	2.4
Unspecified disease	-	-	-	-	3.4	1.6	8.0	4.0	2.3	0.6
Total MNC funding	168	244	293	352	332	341	329	381	388	100

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

SMALL PHARMACEUTICAL AND BIOTECHNOLOGY FIRMS

SMEs invested $83m in neglected disease R&D in 2015 (representing 18% of total industry funding). Innovative developing country (IDC) firms contributed the majority of this ($55m, 66%), with developed country firms contributing the remainder ($28m, 34%).

Irregular survey participation among SMEs makes analysis of funding trends difficult, but regular funders[vii] increased their investment in several diseases, including bacterial pneumonia & meningitis (up $6.6m, 39%), diarrhoeal diseases (up $4.8m, 55%) and TB (up $1.9m, 24%). Funding from this group of participants decreased for helminth R&D (down $3.2m, -79%), after unusually high funding levels in 2014 related to late-stage vaccine development costs.

As was the case in 2014, there was no funding for third tier diseases from SMEs.

[vii] SME increases or decreases refer to organisations that had funding data included in both 2014 and 2015, rather than in every year of the survey, as SME survey participation is inconsistent from year to year

Table 35. SME R&D funding by disease 2007-2015

Disease or R&D area	US$ (millions)									2015 % of total
	2007	2008	2009	2010	2011	2012	2013	2014	2015	
Bacterial pneumonia & meningitis	0.5	21	9.0	7.6	5.9	5.4	18	17	24	29
Diarrhoeal diseases	2.8	1.9	5.3	0.7	5.1	2.6	6.3	8.8	13	16
Salmonella infections	-	13	1.9	0.2	0.1	0.3	6.0	12	11	13
Tuberculosis	17	15	18	18	15	9.1	5.0	8.1	10	12
HIV/AIDS	12	28	19	14	9.5	7.4	6.2	6.3	8.3	10
Malaria	10	9.7	19	11	7.1	7.0	5.8	6.3	6.6	7.9
Kinetoplastids	<0.1	1.7	1.3	1.4	3.8	0.8	0.6	6.9	4.7	5.7
Dengue	2.4	0.2	0.9	0.5	0.5	0.5	0.3	0.5	1.0	1.2
Helminths (worms & flukes)	0.7	1.1	0.4	3.1	5.1	0.7	0.1	8.1	0.9	1.0
Trachoma	-	-	-	2.2	4.5	-	-	-	-	-
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	1.7	5.0	3.3	4.0
Total SME funding	46	92	75	59	57	34	50	79	83	100

- No reported funding

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 have not been included in G-FINDER due to the difficulty of accurately quantifying or allocating them to neglected disease 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 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 36. Typical industry in-kind contributions 2015

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 & Johnson MSD Novartis Otsuka Sanofi
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 & Johnson MSD Novartis Otsuka Pfizer Sanofi
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 & Johnson MSD Novartis Otsuka Sanofi
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 Eisai GSK Johnson & 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	Eisai GSK Johnson & Johnson 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 continued to rely heavily on a handful of funders, with 12 funders (including aggregate industry) contributing 91% of all global funding ($2,781m). The US NIH, the Gates Foundation and industry once again accounted for almost three quarters of global funding ($2,210m, 73%, compared to 72% in 2014).

Although there was little change from the two largest funders – funding from both the US NIH (down $14m, -1.2%) and the Gates Foundation (down $2.3m, -0.4%) was essentially steady compared to 2014 – there were some significant changes among the remainder of the top 12.

Only four of the 11 individual organisations in the top 12 (i.e. excluding aggregate industry) increased their neglected disease R&D funding in 2015. With the exception of the EDCTP-related increase from the EU (up $21m, 20%), these increases were generally modest: the German BMBF increased its funding by $6.6m (up 39%), entering the list of top 12 funders for the first time, Inserm by $6.3m (up 16%) and USAID by $3.6m (up 4.6%).

Reductions in funding were much larger than the increases. The most significant came from the Wellcome Trust (down $27m, -22%) and the US DOD (down $24m, -25%) – although the latter may be partly due to more accurate reporting of HIV/AIDS investment by the US DOD in 2015. These were followed by a $16m reduction in funding from the Australian NHMRC (down 62%) – which dropped out of the top 12 for the first time since 2009 – and a grant cycle-related drop from the UK DFID (down $15m, -21%).

Table 37. Top neglected disease R&D funders 2015

Funder	US$ (millions)									2015 % of total	2007-2015 trend
	2007	2008	2009	2010	2011	2012	2013	2014	2015		
US NIH	1,210	1,231	1,423	1,377	1,345	1,453	1,273	1,236	1,221	40	
Gates Foundation	518	691	627	517	513	509	526	520	518	17	
Aggregate industry	214	336	369	412	389	375	379	460	471	15	
EU	111	120	110	84	99	87	105	104	125	4.1	
Wellcome Trust	56	59	64	75	89	138	127	119	92	3.0	
USAID	92	96	97	99	93	94	81	77	80	2.6	
US DOD	84	77	106	74	83	81	95	96	72	2.4	
UK DFID	45	42	83	91	71	42	69	74	59	1.9	
Inserm	1.6	2.9	25	18	35	37	52	40	46	1.5	
UK MRC	48	51	51	57	50	45	47	46	40	1.3	
Indian ICMR		24	19	23	22	23	35	33	33	1.1	
German BMBF	4.8	0.9	6.5	8.8	8.1	15	14	17	23	0.8	
Subtotal of top 12^	2,462	2,775	3,004	2,871	2,825	2,918	2,812	2,830	2,781	91	
Total R&D funding	2,738	3,144	3,354	3,190	3,140	3,254	3,153	3,094	3,041	100	

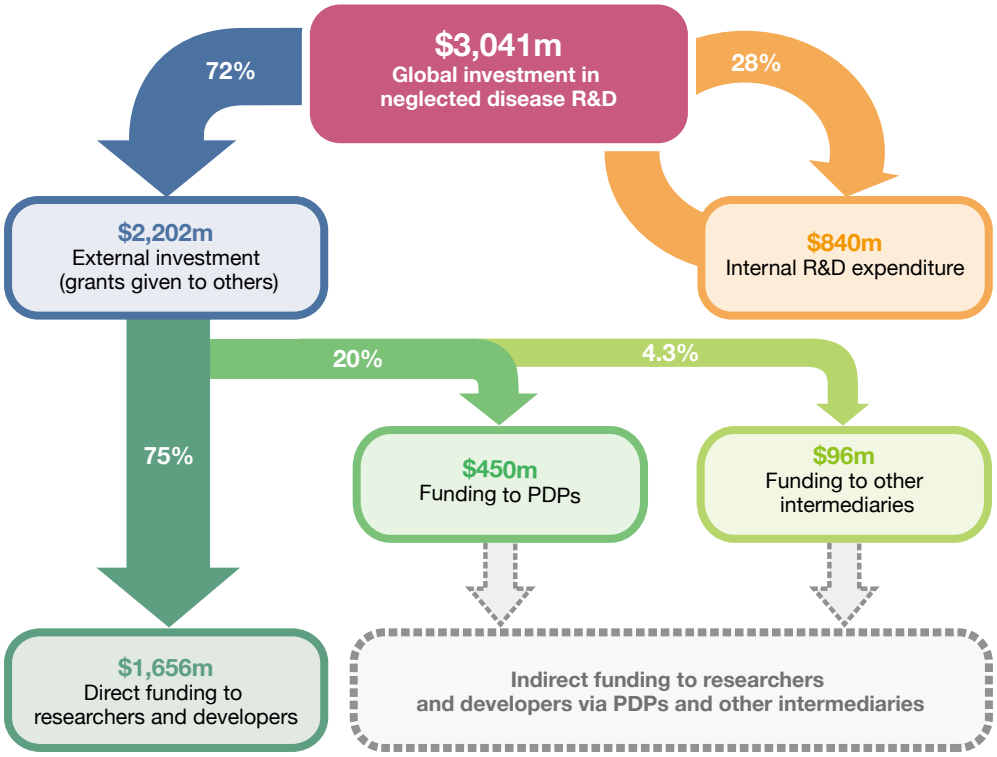
^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015

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

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[viii] 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 24. R&D funding flows 2015



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); while philanthropic and aid agency funders are the source of the vast majority of PDP funding (usually over 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 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.

[viii] PDPs are public health driven, not-for-profit organisations that typically use private sector management practices to drive product development in conjunction with external partners. Some PDPs focus on a single neglected 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 DC use. While their primary aim is the advancement of public health rather than commercial gain, they 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 target neglected diseases

FUNDING FLOW TRENDS

Nearly three-quarters ($2,202m, 72%) of all funding for neglected disease R&D in 2015 was given externally in the form of grants (or contracts) to other organisations, with internal investment ($840m, 28%) making up the remainder. YOY external investment fell for the third year in a row (down $72m, -3.3%), but self-funding continued its slow and steady growth (up $3.8m, 0.5%), largely reflecting the ongoing growth in industry investment in neglected disease R&D.

Exactly three-quarters ($1,656m, 75%) of all external funding disbursed in 2015 was given directly to researchers and developers. Of this, three-quarters came from S&T agencies ($1,252m, 76%), with philanthropic funders providing the bulk of the remainder ($360m, 22%). YOY direct funding to researchers and developers fell slightly compared to 2014 (down $38m, -2.3%). This was primarily due to a $36m drop in external investment from the US DOD[ix], although funding from S&T agencies also fell (down $16m, -1.3%), driven by markedly lower funding from the Australian NHMRC (down $16m, -62%). Philanthropic funding for researchers and developers increased (up $11m, 3.2%). This was entirely due to increased funding from the Gates Foundation (up $38m, 18%), which masked a drop in funding from the Wellcome Trust (down $26m, -23%).

As noted above, not all external grant funding for neglected disease R&D is given directly to researchers and developers. A quarter ($546m, 25%) of all external funding disbursed in 2015 was given to fund managers (PDPs and other intermediary organisations), who then pass this funding on to researchers and developers or invest it in their own internal R&D activities. A total of $450m (20% of all external funding) was channelled through PDPs in 2015, most of which came from philanthropic organisations ($268m, 59%) and aid agencies ($145m, 32%). This was a drop in YOY PDP funding of $65m (-13%) compared to 2014, reflecting the highly cyclical nature of grant funding to PDPs, especially from the Gates Foundation.

Other intermediary organisations received $96m (4.3% of all external funding) in 2015. YOY funding for intermediaries increased substantially (up $31m, 50%), primarily driven by increased funding from S&T agencies (up $22m, 83%) related to the second phase of EDCTP, along with a smaller increase in philanthropic funding (up $6.5m, 88%) to the Global Health Innovative Technology Fund (GHIT Fund).

A more in-depth analysis of funding for PDPs and other intermediaries is presented on the following pages.

[ix] The apparent drop in external funding by US DOD may be partly artefactual, as a breakdown of internal vs external expenditure was not available for all programmes

Figure 25. R&D funding flow trends 2007-2015

FUNDING FOR PRODUCT DEVELOPMENT PARTNERSHIPS

PDPs received a total of $450m in 2015, accounting for 15% of all funding for neglected disease R&D, and a fifth (20%) of all external investment.

However, the central role of PDPs is somewhat obscured by the 'NIH factor'. The US NIH is by far the largest funder of neglected disease R&D, but allocates only a small portion of its funding to PDPs ($4.6m in 2015, or 0.4% 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 well over a third (39%) of all non-NIH grant funding in 2015.

As was the case in 2014, half of all PDP funding in 2015 ($223m, 50%) went to three PDPs – this time comprising the Medicines for Malaria Venture (MMV), PATH and TB Alliance.

Funding to PDPs fell by $65m (down 13%) compared to 2014, although this was almost entirely due to the cyclical pattern of large grant disbursements to PDPs from the Gates Foundation. PATH (down $47m, -39%), Aeras (down $23m, -42%) and DNDi (down $22m, -43%) all saw large reductions in YOY funding, marking a return to more normal levels after each received significant disbursements from the Gates Foundation in 2014. The biggest increases went to the International AIDS Vaccine Initiative (IAVI, up $25m, 62%) and IVCC (up $19m, 188%), reflecting large disbursements from the Gates Foundation to both of these organisations in 2015.

Table 38. Funds received by PDPs 2007-2015

PDPs \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of total
MMV	84	50	45	74	77	52	68	75	78	17
PATH	44	128	142	76	100	85	83	120	75	17
TB Alliance	44	38	39	53	38	45	52	56	70	16
IAVI	85	93	76	70	64	63	60	40	65	14
DNDi	28	22	33	34	37	32	34	54	33	7.2
Aeras	44	72	59	43	43	39	40	55	32	7.1
IVCC	-	11	15	17	<0.1	10	22	10	29	6.4
IPM	46	64	35	32	14	23	30	27	25	5.7
FIND	26	34	23	27	23	22	24	24	16	3.5
IVI	15	2.3	13	9.6	5.6	8.2	9.6	6.4	7.0	1.5
IDRI	9.3	16	19	13	23	11	5.9	14	6.1	1.4
CONRAD	18	16	24	19	25	31	26	17	3.8	0.8
EVI	7.0	4.0	3.5	4.8	7.1	2.0	6.0	2.8	3.4	0.8
Sabin Vaccine Institute	8.7	17	10	4.2	8.8	6.4	6.5	5.4	3.1	0.7
WHO/TDR[A]	34	38	35	29	31	-	-	2.3	2.5	0.6
TBVI	-	-	0.1	3.8	3.5	4.9	5.3	1.3	1.5	0.3
OWH[B]	31	33	17	23	11	7.2	-	-	-	-
FHI 360	14	19	19	19	12	5.9	4.5	0.2	-	-
Total funding to PDPs	538	657	606	550	524	449	477	511	450	100

[A] TDR's mission extends beyond product development, but it operated as a de facto PDP from the mid-1970s until 2012, when it decided to focus on implementation research and research capacity strengthening. Funds received in 2014 and 2015 are related to the pooled fund demonstration projects

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

- No reported funding

FUNDERS OF PDPs

Philanthropic organisations provided well over half ($268m, 59%) of all funding to PDPs in 2015. Almost all of the remaining funding came from HIC governments ($164m, 36%), mostly via their aid agencies ($145m, 89% of HIC funding to PDPs). The Gates Foundation's contribution of $254m made it once again the single largest funder of PDPs by a considerable margin, providing 56% of all PDP funding.

Funding from almost all of the top PDP funders was either lower or flat compared to 2014, but the $65m overall drop in PDP funding in 2015 was largely driven by reduced funding from three organisations, all due to grant funding cycles. The largest reduction came from the Gates Foundation (down $41m, -14%). However, this followed a big increase in the Foundation's PDP funding in 2014, when it made several major up-front grant disbursements. Similarly, the drop in the UK DFID's PDP funding (down $19m, -25%) came after two years of increased disbursements at the start of its current five-year PDP funding stream; and the sharp drop from the Dutch DGIS (down $13m, -76%) was the result of 2015 being a transition year between PDP funding rounds. Irish Aid was one of the few top PDP funders to contribute more than in 2014 (up $3.3m, 150%), but this represented a rebound after a marked drop in funding in 2014.

Public sector multilateral organisations gave $17m to PDPs in 2015 (3.9% of total PDP funding). Almost all multilateral funding to PDPs came from UNITAID, which has been playing an increasingly important role in supporting paediatric drug development for TB, malaria, and HIV/AIDS. UNITAID's $16m investment in PDPs in 2015 was larger than in any previous year of the survey, primarily due to increased funding to the TB Alliance to support the successful development of two new TB drug formulations designed specifically for children.

Table 39. Top funders of PDPs 2015

Funder \ US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of org's funds given to PDPs	2015 % of total PDP funding
Gates Foundation	267	390	326	290	260	246	239	294	254	49	56
USAID	77	77	79	78	76	75	62	57	58	72	13
UK DFID	31	27	76	91	71	42	69	74	56	95	12
UNITAID			6.7				8.4	10	16	100	3.5
German BMBF			-	-	1.2	5.7	4.8	6.6	8.2	35	1.8
Swiss SDC	2.3	2.3	2.5	4.7	3.7	3.4	4.5	6.8	7.9	84	1.8
Australian DFAT						8.1	-	7.7	7.5	100	1.7
Irish Aid	22	6.3	4.8	5.9	5.8	5.6	7.8	2.2	5.5	100	1.2
US NIH	4.7	3.8	8.6	2.9	21	8.0	11	9.3	4.6	0.4	1.0
MSF	6.6	6.7	4.2	4.3	4.6	5.4	5.5	4.4	4.4	76	1.0
Dutch DGIS	29	18	18	15	19	11	21	17	4.1	100	0.9
Wellcome Trust	3.7	3.6	3.5	2.5	3.0	4.2	3.7	4.3	3.9	4.2	0.9
Subtotal top 12 funders of PDPs^	492	602	559	518	485	420	444	493	429		
Total PDP funding	538	657	606	550	524	449	477	511	450		
% of total PDP funding (top 12)	92	92	92	94	93	94	93	97	95		

^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015
- 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

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 received $96m in 2015, representing 3.1% of total neglected disease R&D funding and 4.3% of external investment. The intermediaries that received the most funding in 2015 were the EDCTP ($49m), the GHIT Fund ($28m), the International Union Against Tuberculosis and Lung Disease (The Union, $8.5m) and the Barcelona Institute for Global Health (ISGlobal, $6.2m).

Funding to intermediaries increased substantially in 2015 (up $31m, 50%). The most significant driver of this was new funding for EDCTP2, the second iteration of the EU's partnership for facilitating product development for infectious diseases that affect Sub-Saharan Africa. Funding for the EDCTP more than doubled in 2015 (up $28m, 128%), reaching a level not seen since the mid-point of EDCTP1 in 2007-08.

Most funding to intermediaries in 2015 ($81m, 84%) was not earmarked for a specific disease by the funder. Of the intermediary funding that was disease-specific, $8.6m was for TB, $3.2m was for HIV/AIDS and $2.7m was for malaria.

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. In 2015, 50% of funding to other intermediaries came from S&T agencies, 18% from development agencies, and 16% from philanthropic funders.

Almost all of the increases in funding to intermediaries from the top funders were associated with EDCTP2. The biggest increase came from the EU (up $19m, 85%), making it the source of 41% of all intermediary funding in 2015 (compared to 35% in 2014). However, $9.2m in new funding from the UK DFID, the UK MRC and the Swedish International Development Agency (Swedish SIDA) for EDCTP2 – none of whom contributed any intermediary funding in 2014 – meant that the share of total funding coming from the top three funders was actually slightly lower in 2015 (62%, compared to 65% in 2014).

Table 40. Top funders of intermediaries 2015

Funder / US$ (millions)	2007	2008	2009	2010	2011	2012	2013	2014	2015	2015 % of org's funds given to intermediaries	% of 2015 total intermediary funding
EU	38	36	18	2.0	23	24	24	22	41	32	43
Japanese Government							9.3	9.2	10	100	11
USAID	<0.1	4.2	5.3	5.8	5.7	5.5	5.0	9.2	8.5	11	8.9
Gates Foundation	11	8.3	13	5.9	5.2	4.2	6.8	7.4	7.4	1.4	7.8
Aggregate industry	-	1.3	3.2	-	-	-	3.4	7.5	5.0	1.1	5.2
US NIH	-	1.0	3.4	3.1	1.3	2.1	1.8	3.5	3.2	0.3	3.4
UK DFID	13	15	6.8	-	-	-	-	-	3.1	5.3	3.3
UK MRC	-	-	-	4.4	-	<0.1	-	-	3.1	7.7	3.2
Swedish SIDA	4.0	1.9	2.1	1.9	<0.1	-	0.6	-	3.0	100	3.1
Spanish MAEC	-	-	-	-	-	0.3	-	2.7	2.2	80	2.3
Subtotal top 10 funders of intermediaries^	71	76	54	29	41	52	54	62	84		
Total funding to intermediaries	71	77	55	32	41	53	56	62	96		
% of total intermediary funding (top 10)	100	99	98	92	99	97	97	100	88		

^ Subtotals for 2007–2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015
- 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

There are only a small number of intermediary organisations, and government funding (in particular) to intermediaries is usually very geographically-driven. For example, essentially all funding to intermediaries from the EU, the Swedish SIDA, the UK DFID and the UK MRC went to the EDCTP; USAID channelled its intermediary funding through The Union; the Japanese Government contributed to the GHIT Fund; and Spanish public sector organisations funded ISGlobal.

EBOLA AND OTHER AFRICAN VIRAL HAEMORRHAGIC FEVERS

In response to the 2014 West African Ebola epidemic, last year's G-FINDER survey tracked funding for Ebola R&D for the first time, capturing FY2014 investments. This year, the survey scope was expanded to include four more African VHFs: Marburg, Lassa fever, Rift Valley fever and Crimean-Congo haemorrhagic fever. Of these additional diseases, only Marburg received any significant R&D investment in its own right. Funding for R&D into the remaining three VHFs – as well as that for R&D targeting multiple VHFs – has been combined into a single category for analysis.

In this year's G-FINDER report, funding for Ebola and other African VHFs (for both 2014 and 2015) has been analysed separately from the neglected diseases traditionally included in G-FINDER. This is a change from last year's report, when Ebola funding was included in the neglected disease analysis. This revised approach reflects the different nature of the threat posed by Ebola and other emerging infectious diseases – and the unique characteristics of the resulting market failure – compared to 'traditional' neglected diseases, and means that the unprecedented global response to the Ebola epidemic does not distort our understanding of the R&D funding landscape for neglected diseases.

For an analysis of how the neglected disease funding landscape changes when funding for Ebola and other African VHFs is included, please see the textboxes at the beginning of the Diseases and Funders sections of this report.

$631 MILLION

TOTAL SPEND ON EBOLA AND OTHER AFRICAN VHF R&D IN 2015

THIS WAS EQUIVALENT TO

21%

OF GLOBAL R&D FUNDING FOR NEGLECTED DISEASE R&D

MORE MONEY WAS INVESTED IN R&D FOR EBOLA AND OTHER AFRICAN VHFS IN 2015 THAN IN ANY NEGLECTED DISEASE EXCEPT HIV/AIDS

Viral haemorrhagic fevers can be caused by a diverse range of viruses, although the majority of these fall within four distinct taxonomic families: Arenaviridae, Bunyaviridae, Flaviviridae and Filoviridae. Although they share many common features, the diseases that fall under this definition vary significantly in terms of geographic distribution and the threat they pose to humans.

Based on the G-FINDER criteria, we have included five diseases within the scope of our tracking efforts, all of which predominantly occur on the African continent: Ebola virus disease, Marburg virus disease, Crimean-Congo haemorrhagic fever (which has also been documented in southern and central Europe, the Middle East and central Asia), Rift Valley fever and Lassa fever. Collectively referred to in our analysis as 'African VHFs', these diseases represent the five most important zoonotic viral haemorrhagic fevers for humans.[95]

The initial signs and symptoms of most VHFs may include fever, fatigue, dizziness, muscle aches, loss of strength, and exhaustion; the similarity of these symptoms to those of many other acute febrile illnesses can make early clinical diagnosis challenging. Signs of progression to severe disease include bruising, internal and external bleeding, organ failure and shock.

Ebola virus disease and Marburg virus disease are caused by filoviruses. The natural reservoir of both viruses is believed to be infected fruit bats; once introduced into the human population, person-to-person transmission is the primary mechanism for the spread of infection.[96] Both are severe, acute illnesses that can be fatal if untreated; the case fatality rate for Ebola can be as high 90% in some outbreaks, and for Marburg is over 80%.[97,98]

The Global Burden of Disease Study estimates that Ebola was responsible for 295,350 DALYs and 5,498 deaths in the developing world in 2015 (although this mortality figure is higher than the 3,311 confirmed, probable and suspected deaths reported by the WHO for 2015).[99,100] This is fewer deaths than were caused by any of the neglected diseases within the scope of G-FINDER which are potentially fatal, and around the same morbidity as trachoma.

Crimean-Congo haemorrhagic fever and Rift Valley fever are both caused by viruses of the bunyavirus family, and are transmitted to humans via ticks and mosquitoes, respectively. In documented outbreaks of CCHF, fatality rates in hospitalised patients have ranged from 9% to as high as 50%.[101] Only 1 in 10 RVF cases go on to severe disease and haemorrhagic fever occurs in less than 1% of all cases, but the fatality rate among this group is around 50%.[102]

Lassa fever is caused by an arenavirus, and is primarily spread to humans through contact with infected rodents. Its onset is more gradual, and the case fatality rate is 1-15%.[103] There are an estimated 100,000 to 300,000 Lassa virus infections per year in west Africa, with approximately 5,000 deaths.[104]

No licensed drugs or vaccines exist for Ebola, so treatment is restricted to supportive and symptomatic therapy, and outbreak containment relies on prevention and control strategies. Early diagnosis is critical for both successful treatment and epidemic control, but is hampered by the lack of appropriate tests. The first ever rapid POC screening tests for Ebola were given emergency approval at the height of the 2014 epidemic, but laboratory confirmation is still required.[105] There is a need for inexpensive but accurate rapid POC tests for screening, as well as smaller, faster, more mobile molecular tests suitable for the African setting.[106] Novel and re-purposed drugs are currently being evaluated for treatment of Ebola, including the monoclonal antibody cocktail ZMapp™ (Phase III), and favipiravir (Phase II).[107] There are also several vaccine candidates in clinical development, the most advanced of these being rVSV-ZEBOV (Phase III) and ChAd3-EBOZ (Phase II).[107] However, despite the fact that clinical trials were fast-tracked during the recent outbreak, the lack of new cases presents a challenge for further development.

There are no approved drugs, vaccines, or cheap and reliable POC tests available for Marburg. All drug candidates (including BCX4430 and AVI-7288) and vaccine candidates are in very early stages of development (pre-clinical or Phase I). Current diagnostics include ELISA testing, PCR, and IgM-capture ELISA, which can confirm cases of Marburg within a few days of symptom onset. Virus isolation can also be performed but is limited to the few biosafety level 4 laboratories available in affected regions.[108]

No approved vaccine exists for Crimean-Congo haemorrhagic fever, and treatment is limited to ribavirin, which has limited efficacy and can have severe side-effects.[109] Diagnosis of CCHF through laboratory testing or an RT-PCR kit is available, with POC diagnostic assays still in early stage development. There are no treatments in the development pipeline, although protein antigen specific platform vaccines are in early stages of development.[110]

An inactivated vaccine for Rift Valley fever has been developed for experimental use but remains unregistered. There are a number of alternative candidates currently in the pipeline, one of which (RVF MP-12) has completed Phase II clinical trials.[111] Treatment for severe cases of RVF is generally limited to supportive care, and definitive diagnosis is limited to laboratory-based tests including RT-PCR, ELISA and virus isolation; we have not been able to identify any drug or diagnostic candidates specifically for RVF currently in development.

As for CCHF, there is no approved vaccine for Lassa fever, and treatment is reliant on ribavirin, which has limited efficacy.[112] A number of experimental antiviral drugs have been tested in vitro or in small animal models (favipiravir, T-705; ST-193; and small interfering RNAs), but none has progressed into clinical trials.[113] A number of vaccine candidates are also in development, all in pre-clinical stages.[113] The ReLASV® Antigen Rapid Test for Lassa received CE certification from European regulators in 2014 for diagnostic use in the EU and other international markets, however it is still not approved by the FDA.[114]

A total of $631m was invested in R&D for Ebola and other African VHFs in 2015. The vast majority of this was Ebola-specific ($574m, 91%). $17m (2.7%) was invested in Marburg-specific R&D, and $40m (6.4%) in other and/or multiple African VHFs (with the majority of this latter category being multi-filovirus R&D that included Ebola as a target).

Table 41. African VHF R&D funding 2014 (US$ millions)

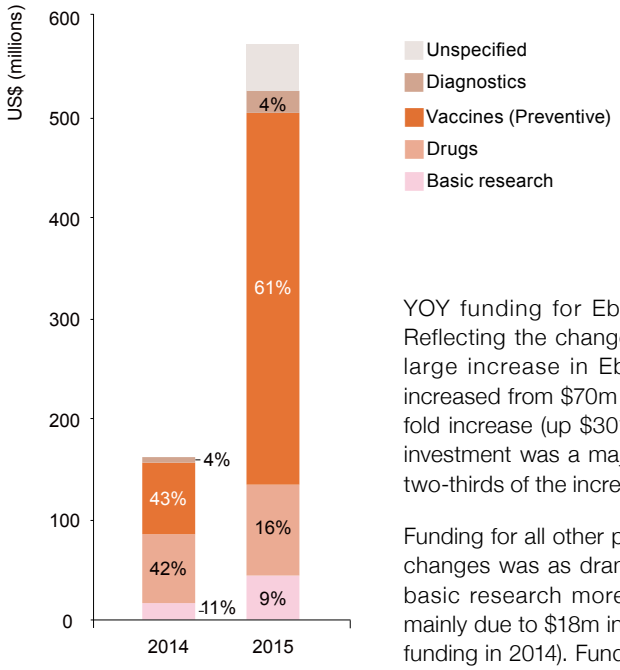
Disease	Basic Research		Vaccines (Preventive)	Diagnostics	Unspecified	Total	%
	Drugs						
Ebola	44	90	370	23	47	**574**	91
Marburg	4.0	3.0	5.7	2.8	1.7	**17**	2.7
Other and/or multiple VHFs	12	10	12	2.4	4.0	**40**	6.4
Total	59	103	388	28	53	631	100

In addition to the sheer volume of funding, one of the most remarkable – if not entirely unexpected – findings in this year's report is the massive increase in funding for Ebola R&D compared to 2014. We have restricted our analysis of YOY funding changes to Ebola alone, as it was the only VHF included in both the FY2014 and FY2015 surveys, although funding for African VHFs other than Ebola undoubtedly also increased.

Funding for Ebola R&D more than tripled (up $411m, 258%) from 2014 levels. The magnitude of this increase, which came primarily from public and industry funders, is unprecedented in any of the neglected diseases traditionally tracked by G-FINDER. For context, the 2015 *increase* in funding for Ebola alone (from already significant levels in 2014) was larger than the *collective* 2015 global investment in developing country-relevant R&D for dengue, bacterial pneumonia & meningitis, helminths, salmonella infections, hepatitis C, leprosy, cryptococcal meningitis, trachoma, rheumatic fever, Buruli ulcer and leptospirosis combined.

In 2015, the vast majority of R&D funding for Ebola and other African VHFs was focused on vaccines ($388m, 61%), with smaller amounts going to drugs ($103m, 16%), basic research ($59m, 9.4%) and diagnostics ($28m, 4.4%). This was a marked change from 2014, when vaccines and drugs each received a similar share of Ebola R&D funding (accounting for 43% and 42%, respectively), possibly reflecting the fact that vaccine clinical trials for Ebola started later and are more expensive to conduct.

Figure 26. African VHF R&D funding by product type 2014-2015



YOY funding for Ebola R&D increased for all product areas. Reflecting the change noted above, the vast majority of the very large increase in Ebola funding went to vaccine R&D, which increased from $70m in 2014 to $370m in 2015 – a more than five-fold increase (up $301m, 436%). The significant growth in industry investment was a major factor, with industry responsible for nearly two-thirds of the increase in Ebola vaccine investment.

Funding for all other product areas also grew, although none of the changes was as dramatic as that for vaccines. Funding for Ebola basic research more than doubled (up $26m, 149%) to $44m, mainly due to $18m in new investment from the UK MRC (after zero funding in 2014). Funding for Ebola drug development increased by $22m (up 33%) to $90m, as a result of increased US public sector investment, while Ebola diagnostic funding nearly tripled (up $15m, 263%) to $23m.

FUNDERS

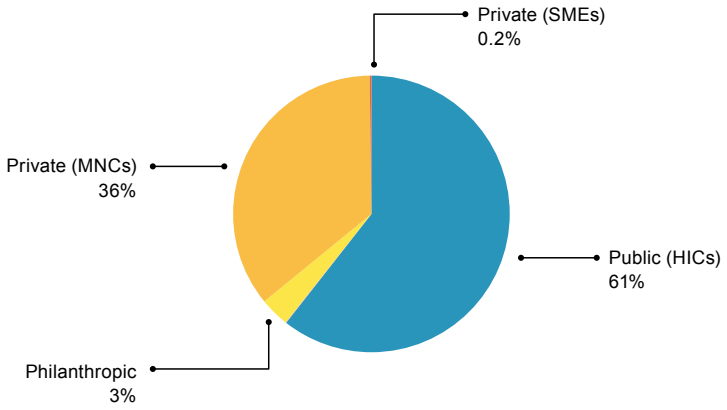
The public sector was the source of nearly two-thirds ($383m, 61%) of all reported funding for R&D into Ebola and other African VHFs in 2015. Industry provided just over a third ($226m, 36%), and the philanthropic sector just 3.4% ($22m).

This was a major change from the sectoral funding breakdown for 2014 Ebola investments (when the public sector funding share was 72%, industry 21% and philanthropic funders 7.3%), and is almost unparalleled amongst the diseases covered by the G-FINDER survey. Only hepatitis C and bacterial pneumonia & meningitis, for example, have greater of share of industry involvement – two diseases where there is significant overlap with commercially-driven R&D activities, neither of which receives anywhere close to the same level of funding. It is also one of the lowest shares of philanthropic funding seen in any of the diseases covered by the G FINDER survey.

More than three-quarters ($298m, 78%) of all public sector funding for Ebola and other African VHF R&D in 2015 came from US Government agencies. This share actually fell compared to 2014, despite the massive increase in US Government investment, as other countries also began to ramp up their investment in Ebola and other African VHF R&D. European governments in particular increased their share of public funding from 12% in 2014 to 22% in 2015.

Reported funding from LMIC governments represented less than 1% of total public funding for Ebola and other African VHF R&D in 2015. This figure is likely an underestimate – due to participation rates by African organisations in the G-FINDER survey – but may also reflect a focus on outbreak response and containment, rather than R&D. Virtually all industry investment came from MNCs, and was directed towards Ebola vaccine development (many SMEs are actively undertaking R&D in this area – particularly in drug development – but the majority of funding for these efforts comes from the public sector).

Figure 27. African VHF R&D funding by sector 2015



Public sector funding for Ebola R&D nearly tripled compared to 2014 (up $210m, 182%). This was driven by US Government funders (up $149m, 151%), but there was also a more than five-fold increase in European public funding for Ebola R&D (up $63m, 452%), much of which came from the EU's IMI Ebola+ initiative.

The increase in industry investment in Ebola R&D (up $194m, 614%) was nearly as large as that from the public sector, with almost all of this increase going to vaccine development (up $193m, 614%). Philanthropic funding for Ebola increased modestly (up $7.0m, 59%), with much of this increase also for vaccine R&D (up $5.6m, 271%).

TOP FUNDERS

In 2015, the top 12 funders accounted for 98% of funding for Ebola and other African VHF R&D. Although we generally avoid commenting on the aggregate industry contribution when discussing top funders (as it consists of the collective investment of many organisations), the funding picture here is remarkable: aggregate industry was by far the largest funder of Ebola and other African VHF R&D, providing over a third of all funding, twice the investment of the next largest funder (the US NIH).

In addition to the US NIH, two other US Government agencies (US BARDA and US DOD) round out the top three non-industry funders; they are also joined in the top 12 by the US CDC. Collectively, these four US Government agencies and the aggregate pharmaceutical industry were responsible for 83% ($524m) of all global investment in R&D for Ebola and other African VHFs in 2015.

Looking only at Ebola R&D funding for the sake of accurate comparison to 2014, the largest increase among the non-industry top funders in 2015 came from US BARDA (up $78m, 297%). This was followed by the US DOD (up $46m, 423%), and a ten-fold funding increase from the EU (up $40m, 900%, largely due to new investment under the IMI Ebola+ initiative). The two other organisations with increases in the double-digit millions were the US NIH (up $20m, 32%) and the UK MRC, whose $18m investment in Ebola basic research (from zero investment in 2014) put it in the top 12 for the first time.

Just two funders in the top 12 for 2015 reported reducing their investment in Ebola R&D, with small decreases coming from the Gates Foundation (down $4.0m, -34%) and Inserm (down $2.1m, -40%).

Table 42. Top African VHF R&D funders 2015

Funder	US$ (millions)		2015 % of total
	2014	2015	
Aggregate industry	34	226	36
US NIH	64	113	18
US BARDA	26	104	16
US DOD	11	73	12
EU	4.5	45	7.2
UK MRC	-	18	2.9
US CDC	-	8.3	1.3
Wellcome Trust	0.1	8.0	1.3
Gates Foundation	12	7.8	1.2
Inserm	5.3	6.4	1.0
UK DFID	1.5	4.6	0.7
MSF	-	3.5	0.6
Subtotal of top 12^	163	618	98
Disease Total	164	631	100

^ Subtotals for 2014 top 12 reflect the top funders for those respective years, not the top 12 for 2015
- 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

FUNDING FLOWS

R&D funding flows for Ebola and other African VHFs differ markedly from those for traditional neglected diseases in two main ways: the proportion of funding that is invested internally, and the way external funding is distributed.

More than half (54%) of all funding for Ebola and other African VHFs is invested in internal R&D programmes. This is almost double the self-funding share for neglected diseases (28%), and largely reflects the high level of industry investment.

Almost all external (grant or contract) funding was provided directly to researchers and developers, with fund managers essentially absent from the picture: PDPs received a single grant ($3.7m to FIND for diagnostic R&D), and no funding given to other intermediary organisations was specifically earmarked for African VHFs.[x] Accordingly, a much larger share (42%) of external funding for Ebola and other African VHFs was given directly to SMEs and MNCs than is normally the case in neglected disease R&D, where fund managers play a larger role and direct funding to industry accounts for less than 10% of all external funding.

[x] We note that some core funding given to intermediaries may subsequently be used to fund R&D for Ebola and other African VHFs. For example, EDCTP issued a diagnostic-focused call in 2015 for neglected and emerging infectious diseases, including Ebola (although ultimately no Ebola projects were selected)

DISCUSSION

The aim of the G-FINDER report is to describe the global funding landscape for neglected disease R&D. Following the 2014 outbreak of Ebola in West Africa, there was no question that the significant new global investment in R&D for this hitherto neglected disease should be tracked, and so Ebola was included in the scope of last year's report. But emerging infectious diseases like Ebola are different to 'classic' neglected diseases (those traditionally tracked by G-FINDER); the nature of the threat they pose to global health is different, and so too is the nature of the R&D investment this drives.

In this year's G-FINDER report we have treated neglected diseases and Ebola and other African VHFs as separate, distinct categories, in order both to acknowledge the differences between them, and to avoid these differences distorting our understanding of neglected disease R&D funding. But whether considered separately or together, the international response to the Ebola epidemic informs our understanding of – and is inseparable from – the global funding landscape for neglected disease R&D. It is also one of the biggest stories of this year's G-FINDER report.

The scale and nature of the global R&D funding response to the West African Ebola outbreak is now truly apparent

The rapid escalation of the 2014 Ebola epidemic captured global public and media attention. Ebola's status as a bioterror threat ensured military and government interest, and meant that there were existing (if semi-dormant) research programmes. The need to develop tools to combat the growing epidemic – followed by the need to conduct clinical trials before the epidemic subsided – provided a sense of urgency. Together, this helped catalyse the massive global investment in R&D seen in this report.

The global R&D funding response to the Ebola epidemic was impressive in both its scale and its speed, especially given the negligible level of investment prior to 2014. In 2015, a total of $631m was invested in R&D for Ebola and other African VHFs – more than in any neglected disease except for HIV/AIDS. And the *increase* in funding in 2015 for Ebola alone (from already significant levels in 2014) was larger than the *collective* global investment in 2015 in developing country-relevant R&D for dengue, bacterial pneumonia & meningitis, helminths, salmonella infections, hepatitis C, leprosy, cryptococcal meningitis, trachoma, rheumatic fever, Buruli ulcer and leptospirosis combined.

As is the case for neglected diseases, R&D funding for Ebola and other African VHFs is heavily reliant on the public sector; in 2015 this was again dominated by the US (which provided 78% of all public funding), despite a more than five-fold increase in Ebola R&D investment from European public funders. But after this, the picture diverges: Ebola and other African VHFs received comparatively little philanthropic funding, and intermediaries such as PDPs played little to no role – replaced instead by direct funding of researchers, including to industry. There was also massive investment by industry, which invested far more in Ebola and other African VHFs than in any neglected disease: industry's $226m investment in Ebola and other African VHFs in 2015 was $80m more than they invested in malaria (the neglected disease that received the most industry investment), and was larger than their combined investment in all neglected diseases other than malaria and TB.

Global funding for neglected disease R&D reached historic lows in 2015, driven by declining public sector investment

Unlike the dramatic increase in R&D funding for Ebola and other African VHFs, funding for neglected disease R&D in 2015 fell to its lowest level since 2007, with YOY global funding $180m lower than at its 2012 peak. This drop has been driven by the ongoing decline in public sector funding for neglected disease R&D, which in 2015 also fell to its lowest level since 2007.

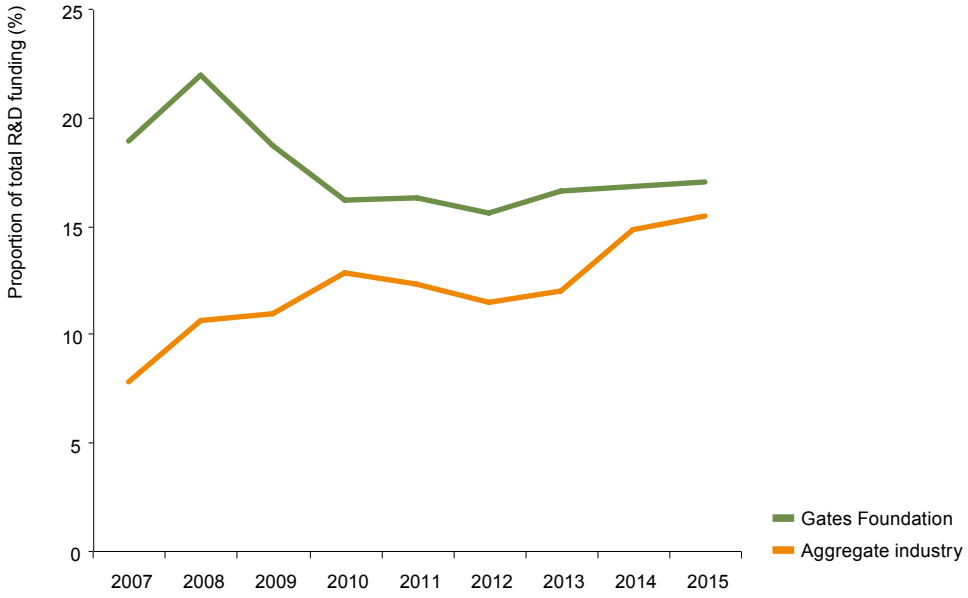
The decline in public funding has primarily been driven by the US. US Government funding for neglected disease R&D fell again in 2015 (down $44m, -3.0%), to the lowest level ever recorded in the history of the G-FINDER survey. It is however worth emphasising the outsized role played by the US Government, which is still by far the largest contributor to neglected disease R&D globally; it provided 46% of total global funding in 2015, and contributed twice as much as a proportion of GDP as the next largest government funder (the UK).

There are positive signs from the next two largest public funders behind the US. Increased funding from the EU (up $21m, 20%) made it the second-largest public funder of neglected disease R&D globally in 2015 – an increase that is likely to be sustained, given the expanded budget of Horizon 2020 (and EDCTP2 in particular). UK Government funding fell in 2015 (down $22m, -18%), but recently announced funding commitments for global health R&D should see the UK's contribution grow over the coming years.

In sharp contrast to the public sector, industry investment in neglected disease R&D reached historical highs

In a positive development, industry consolidated its status as a significant funder of neglected disease R&D in 2015. The small increase marked the fourth year in a row that industry has increased its investment in neglected disease R&D – the only sector to have recorded year-on-year growth for such a stretch – and confirmed that the sharp increase in industry investment in 2014 was not an anomaly. Taken collectively, the share of global funding contributed by industry is now comparable to that of the Gates Foundation. And all of this is without taking into account the major industry investment in Ebola and other African VHFs.

Figure 28. Comparative share of total R&D funding 2007-2015



It remains to be seen whether this level of industry contribution will be sustained. Industry funding is less concentrated than public and philanthropic funding – there are a large number of companies active in the field, with a relatively even spread of investment between them – and so has the potential to be a more stable funding source. But in the non-profit field of neglected diseases, industry involvement depends on adequate levels of public and philanthropic funding. A continued decline in public funding would likely put this level of involvement at risk.

It is important also to note that industry funding is limited to only a subset of neglected diseases, with malaria and TB alone accounting for more than half of all industry investment in neglected disease R&D in 2015.

The highly concentrated nature of neglected disease R&D funding remains an area of concern

Researchers and developers continue to rely upon a small number of large funders, particularly the US Government (the US NIH especially) and the Gates Foundation. While having a limited number of dependable funders can reduce the administrative burden for recipient organisations, it also makes them more susceptible to the vagaries of external political, economic, and other forces.

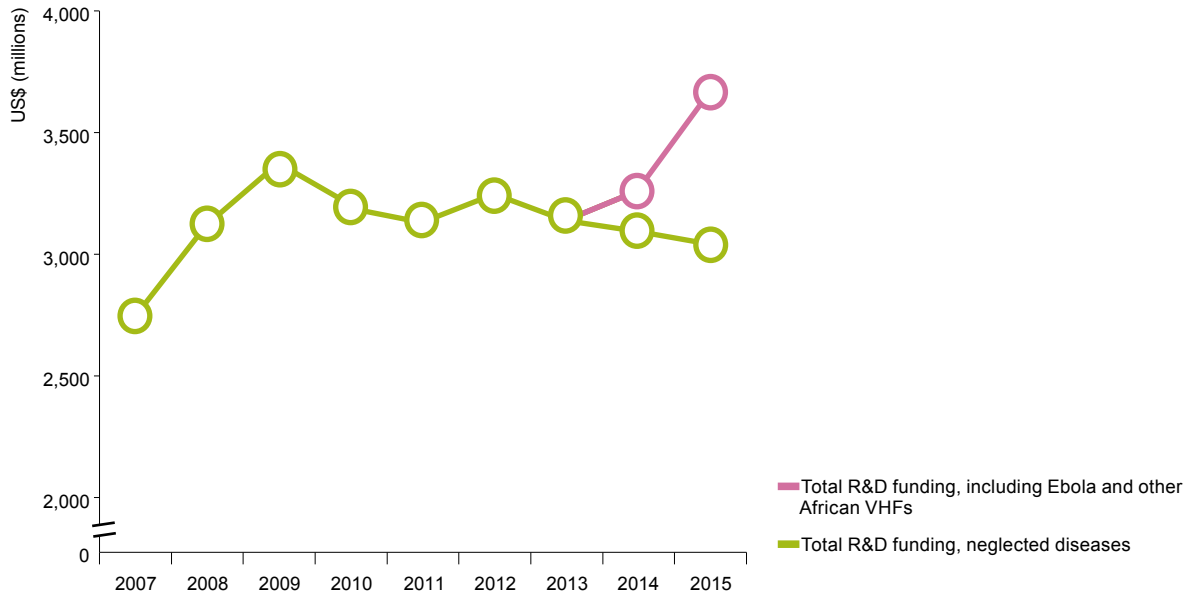
For example, 40% of all neglected disease R&D funding goes to organisations that receive more than 80% of their funding from the US Government, which has reduced its funding for neglected disease R&D by a quarter of a billion dollars since 2012. Similarly, PDPs are highly reliant on the Gates Foundation; in 2015, nearly half of all PDPs received more than half their funding from the Gates Foundation.

The reality is that this reliance on a small number of major funders is largely a product of the limited pool of organisations who invest large sums in neglected disease R&D – something that is especially true for PDPs, as some of the largest funders (for example the US NIH and the EU) prefer to fund researchers directly. Recipients will only be able to diversify their funding sources if other funders scale up their investments.

Conclusion

The findings presented in this report show that significant additional financial resources are available – including from the pharmaceutical industry – for R&D into infectious diseases that largely exist only in the developing world. When funding for Ebola and other African VHFs is added to that for neglected diseases, global investment in R&D increased by $396m (up 13%) in 2015 – the largest single year increase ever recorded by G-FINDER – with public funding growing by $210m (up 10%) and investment by industry nearly doubling (up $201m, 44%).

Figure 29. Total R&D funding with Ebola and other African VHFs 2007-2015



The impressive funding response to the Ebola epidemic has been accompanied by policy and coordination frameworks, including the release of the WHO *R&D Blueprint for action to prevent epidemics*, and the launch of the Coalition for Epidemic Preparedness Innovations (CEPI) – which in January 2017 had already secured $460m in funding commitments. With mechanisms like this in place, and growing global concern about the threat of bioterrorism, there is reason to hope that R&D funding for Ebola and other African VHFs will be sustained long enough (and at a sufficient level) to deliver the tools we currently lack.

It is critical, however, that the (vital) attention and funding given to emerging infectious diseases like Ebola does not come at the expense of neglected diseases – which are responsible for more mortality and morbidity, but rarely generate the same sense of urgency, or capture the same political and media attention.

There is an opportunity to capitalise on the lessons learned from the global response to the Ebola epidemic – not only to ensure that we are better prepared for the next emerging infectious disease outbreak, but also to secure adequate and sustainable R&D funding to address the existing and much larger challenge posed by neglected diseases.

ANNEXE CONTENTS

REPORT ANNEXES

ONLINE ANNEXES

To access the online annexes, please go to:
http://www.policycuresresearch.org/g-finder/

ANNEXE 1

ACRONYMS

Aggregate industry	Aggregate pharmaceutical and biotechnology companies
AIDS	Acquired Immune Deficiency Syndrome
ALM	American Leprosy Missions
ALRA	Austrian Leprosy Relief Association
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
Brazilian DECIT	Brazilian Ministry of Health: Department of Science and Technology
Brazilian FAPESP	State of Sao 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
Colombian Colciencias	Colombian Department for Science, Technology and Innovation
DALY	Disability adjusted life year
DC	Developing country
DNDi	Drugs for Neglected Diseases initiative
Dutch DGIS	Dutch Ministry of Foreign Affairs - Directorate General of Development Cooperation
EAggEC	Enteroaggregative *E. coli*
EDCTP	European & Developing Countries Clinical Trials Partnership
EMA	European Medicines Agency
ETEC	Enterotoxigenic *E. coli*
EU	European Union, including the budget managed by the European Commission, European partnerships and other European initiatives
EVI	European Vaccine Initiative
FDC	Fixed-dose combination
FIND	Foundation for Innovative New Diagnostics
French ANR	French National Research Agency
French ANRS	French National Agency for Research on AIDS and Viral Hepatitis
FRF	Fondation Raoul Follereau
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

ACRONYMS

German DFG	German Research Foundation
G-FINDER	Global Funding of Innovation for Neglected Diseases
GHIT Fund	Global Health Innovative Technology Fund
GSK	GlaxoSmithKline
HIC	High-income country
HIV	Human Immunodeficiency Virus
IAVI	International AIDS Vaccine Initiative
IDC	Innovative developing country
IDRI	Infectious Disease Research Institute
IMF	International Monetary Fund
Indian CSIR	Indian Council of Scientific and Industrial Research
Indian DBT	Indian Department of Biotechnology
Indian ICMR	Indian Council of Medical Research
Inserm	French National Institute of Health and Medical Research
IPM	International Partnership for Microbicides
ISGlobal	Barcelona Institute for Global Health
IVCC	Innovative Vector Control Consortium
IVI	International Vaccine Institute
LMIC	Low- and middle-income country
LRI	Leprosy Research Initiative
MDR-TB	Multidrug-resistant tuberculosis
MDT	Multidrug therapy
MIC	Middle-income country
MMV	Medicines for Malaria Venture
MNC	Multinational pharmaceutical company
MSD	Merck Sharp & Dohme (Merck)
MSF	Médecins Sans Frontières
New Zealand HRC	Health Research Council of New Zealand
NIAID	National Institute of Allergy and Infectious Diseases
NTS	Non-typhoidal *Salmonella enterica*
OECD	Organisation for Economic Cooperation and Development
OWH	OneWorld Health
PDP	Product development partnership
Philippines DOH	Philippines Department of Health
POC	Point-of-care
R&D	Research and development
RCDC	US NIH's Research, Condition, and Disease Categorization Process
RePORTER	US NIH's Research Portfolio Online Reporting Tools
RT-PCR	Reverse transcription polymerase chain reaction
S&T	Science & Technology
SME	Small pharmaceutical and biotechnology firms
South African MRC	South Africa Medical Research Council
Spanish MAEC	Spanish Ministry of Foreign Affairs and Cooperation for Development (MAEC) and/or Agency of International Cooperation for Development (AECID)
SSI	Statens Serum Institute
Swedish SIDA	Swedish International Development Agency
Swiss SDC	Swiss Agency for Development and Cooperation
TB	Tuberculosis
TBVI	TuBerculosis Vaccine Initiative
Thailand GPO	Thailand Government Pharmaceutical Organisation
The Union	International Union Against Tuberculosis and Lung Disease

ACRONYMS

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
US DOD	US Department of Defense, including Defense Advanced Research Projects Agency (DARPA)
US FDA	US Food and Drug Administration
US NIH	US National Institutes of Health
USAID	US Agency for International Development
VHF	Viral haemorrhagic fevers
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

ANNEXE 2

Advisory Committee members & additional experts

ADVISORY COMMITTEE MEMBER	ORGANISATION	TITLE
Ripley Ballou	GlaxoSmithKline Biologicals	Vice President and Head, Clinical Research and Translational Science
Graeme Bilbe	Drugs for Neglected Diseases initiative (DNDi)	Research & Development Director
François Bompart	Sanofi	Vice President, Deputy Head and Medical Director, Access to Medicines
Wanderley de Souza	Financiadora de Estudos e Projetos (FINEP)	President
Alan Fenwick	Imperial College London	Professor of Tropical Parasitology
Carole Heilman	US National Institute of Allergy and Infectious Diseases (NIAID)	Director, Division of Microbiology and Infectious Diseases
Vishwa Mohan Katoch	Indian Council of Medical Research (ICMR)	Former Director General
Sue Kinn	UK Department for International Development (DFID)	Team Leader and Research Manager
Line Matthiessen	European Commission	Head of Infectious Diseases and Public Health Unit, Directorate-General for Research and Innovation
Carl Mendel	Global Alliance for TB Drug Development (TB Alliance)	Senior Vice President, Research and Development
Firdausi Qadri	International Centre for Diarrhoeal Disease and Research (icddr,b)	Emeritus Scientist and Acting Senior Director, Infectious Diseases Division
John Reeder	World Health Organization: Special Programme for Research and Training in Tropical Diseases (WHO/TDR)	Director
Nelson Sewankambo	Makerere University College of Health Sciences	Principal (Head)
Wendy Taylor	United States Agency for International Development (USAID)	Director, Center for Accelerating Innovation and Impact
Tim Wells	Medicines for Malaria Venture (MMV)	Chief Scientific Officer

ADDITIONAL EXPERT	ORGANISATION	TITLE
Matthew Albert	Institut Pasteur Inserm U818	Head of the Laboratory of Dendritic Cell Immunobiology Director of Research
Darragh Duffy	Institut Pasteur	Research Manager, Immunology Department
Arnaud Fontanet	Institut Pasteur	Head of the Emerging Diseases Epidemiology Unit
Angela Loyse	St. George's University London	Academic Clinical Lecturer, Infectious Diseases Specialist Registrar
Mathieu Picardeau	Institut Pasteur	Head of the Biology of Spirochetes Unit
Harry Thangaraj	St. George's University London	Director, Access to Pharmaceuticals Project, Infections and Immunity Research Centre, Division of Clinical Sciences

ANNEXE 3

Survey respondent list

- AbbVie
- Aeras
- American Leprosy Missions (ALM)
- amfAR, The Foundation for AIDS Research*
- Anacor Pharmaceuticals
- Apopo VZW
- Argentinian Ministry of Science, Technology and Productive Innovation (MINCYT)
- Argentinian National Council for Scientific and Technical Research (CONICET)
- Arisan Therapeutics
- Atomo Diagnostics
- Australian Commonwealth Scientific and Industrial Research Organisation (CSIRO)
- Australian Department of Foreign Affairs and Trade (DFAT)
- Australian Department of Industry
- Australian National Health and Medical Research Council (NHMRC)
- Australian Research Council (ARC)*
- Austrian Leprosy Relief Association (ALRA)
- Barcelona Institute for Global Health (ISGlobal)
- BASF SE
- Bayer CropScience
- Baylor College of Medicine
- Becton, Dickinson and Company (BD)
- Belgian Ministry of Foreign Affairs and the Belgian Development Cooperation (DGDC)
- Bernhard Nocht Institute for Tropical Medicine (BNI)
- Bill & Melinda Gates Foundation
- Biocan Diagnostics, Inc
- Biological E Ltd
- Bioneer
- Biovac Institute
- Brazilian Development Bank (BNDES)
- Brazilian Foundation for Support of Scientific and Technological Research in the State of Santa Catarina (FAPESC)
- Brazilian Foundation to Support Scientific and Technological Development Cearense (FUNCAP)
- Brazilian Innovation Agency (FINEP)
- Brazilian Ministry of Health: Department of Science and Technology (DECIT)
- Brazilian Research Support Foundation of the State of Bahia (FAPESB)
- Brazilian Research Support Foundation of the State of Minas Gerais (FAPEMIG)
- Canadian Department of Foreign Affairs, Trade and Development (Global Affairs Canada)*
- Canadian Institutes of Health Research (CIHR)
- Carlos III Health Institute
- Cebu Leprosy and Tuberculosis Research Foundation (CLTRF)
- Centre for the AIDS Programme of Research in South Africa (CAPRISA)*
- Cepheid
- Chilean National Commission for Scientific and Technological Research (CONICYT)
- Chilean National Fund for Scientific and Technological Development (FONDECYT)
- Colombian Department for Science, Technology and Innovation (Colciencias)
- CONRAD
- CSL Ltd
- Cuban Center for Genetic Engineering and Biotechnology (CIGB)*
- Damien Foundation (DFB)
- Danish Ministry of Foreign Affairs and the Danish International Development Agency (DANIDA)
- Defence Materials Technology Centre (DMTC)
- DesignMedix, Inc.
- Drugs for Neglected Diseases initiative (DNDi)
- Dutch Ministry of Foreign Affairs - Directorate General of Development Cooperation (DGIS)
- Dutch Organisation for Scientific Research (NWO)
- Eisai Co., Ltd.
- Emergent Biosolutions
- European & Developing Countries Clinical Trials

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

Partnership (EDCTP)
- European Commission including the Directorate-General for Research and Innovation
- European Vaccine Initiative (EVI)
- FAIRMED - Health for the Poorest
- Fast-track Diagnostics Ltd
- Fio Corporation
- Fondation Mérieux
- 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)
- Fundació La Caixa
- Gavi, the Vaccine Alliance (previously the Global Alliance for Vaccines and Immunizations)
- GeoVax Labs, Inc.
- 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 Health Innovative Technology Fund (GHIT Fund)
- Global Solutions for Infectious Diseases
- GSK Bio
- Hawaii Biotech, Inc.
- Health Research Council of New Zealand (HRC)
- Hebron Farmacêutica Ltd
- Hospital Vall d'Hebron
- ImQuest Biosciences*
- 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 Science and Technology (DST)
- Indian Ministry of Health & Family Welfare
- Innovative Medicines Initiative (IMI)#
- Innovative Vector Control Consortium (IVCC)
- Institut Pasteur
- Institute of Tropical Medicine Antwerp/Prince Leopold Institute of Tropical Medicine (ITM)
- Integral Molecular
- International AIDS Vaccine Initiative (IAVI)
- International Centre for Genetic Engineering and Biotechnology (ICGEB), India
- 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)*
- Johnson & Johnson
- Kineta
- KNCV Tuberculosis Foundation
- Laboratório Farmacêutico do Estado de Pernambuco (LAFEPE)
- Lepra India - Blue Peter Public Health & Research Centre (BPHRC)
- Leprosy Research Initiative (LRI)
- Liverpool School of Tropical Medicine (LSTM)
- Mahidol University*
- Mapp Biopharmaceutical
- Max Planck Society - Max Planck Institute for Infection Biology (MPIIB)
- Médecins Sans Frontières (MSF)
- Medicines for Malaria Venture (MMV)
- Mexican National Council of Science and Technology (CONACYT)
- Mexican National Institute of Public Health, Instituto Nacional de Salud Publica (INSP)

- MSD (Merck)
- Mymetics
- Novartis
- Ontario HIV Treatment Network*
- Osel*
- Otsuka Pharmaceutical Co. Ltd
- Ouro Fino
- PATH including the Malaria Vaccine Initiaive (MVI)
- Pfizer
- Population Council
- Public Health Agency of Canada (PHAC)*
- Public Health England
- 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
- Sanofi
- Sasakawa Memorial Health Foundation (SMHF)
- Science Foundation Ireland
- Serum Institute of India
- Shionogi & Co., Ltd.
- Sidaction*
- Sigma-Tau
- South Africa Medical Research Council (MRC)*
- South African Department of Science and Technology (DST)
- Spanish AIDS Research Institute (Institut de Recerca de la Sida) (IrsiCaixa)*
- Spanish Ministry of Foreign Affairs and Cooperation for Development (MAEC) and the Agency of International Cooperation for Development (AECID)
- State of Sao Paulo Research Foundation (FAPESP)^
- Statens Serum Institute (SSI)
- Strategic Research Council, Academy of Finland
- Sumagen Co. Ltd.*
- 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 Crop Protection AG
- Takeda Pharmaceutical Company
- TB Alliance
- Thailand Government Pharmaceutical Organisation (GPO)
- 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)
- UK Medical Research Council (MRC)
- University of Dundee
- University of Georgia (UGA)
- University of Nebraska Medical Center
- University of North Carolina
- University of Pittsburgh
- University of Siena
- US Agency for International Development (USAID)
- US Biomedical Advanced Research and Development Authority (BARDA)#
- US Centers for Disease Control (CDC)
- US Department of Defense (DOD) including the US Army Medical Research Institute of Infectious Diseases (USAMRIID), the US Naval Medical Research Center (NMRC) 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)
- US Veterans Health Administration*

* Denotes organisations where data was only received via the HIV Vaccines and Microbicides Resource Tracking Working Group
^ FAPESP participated in the survey but data was received too late to be included in the analysis
# Funding data taken from publicly available sources

- Worcester Polytechnic Institute (WPI)
- World Bank
- World Health Organization: Special Programme for Research and Training in Tropical Diseases (WHO/TDR)
- Zalgen Labs

ANNEXE 4

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