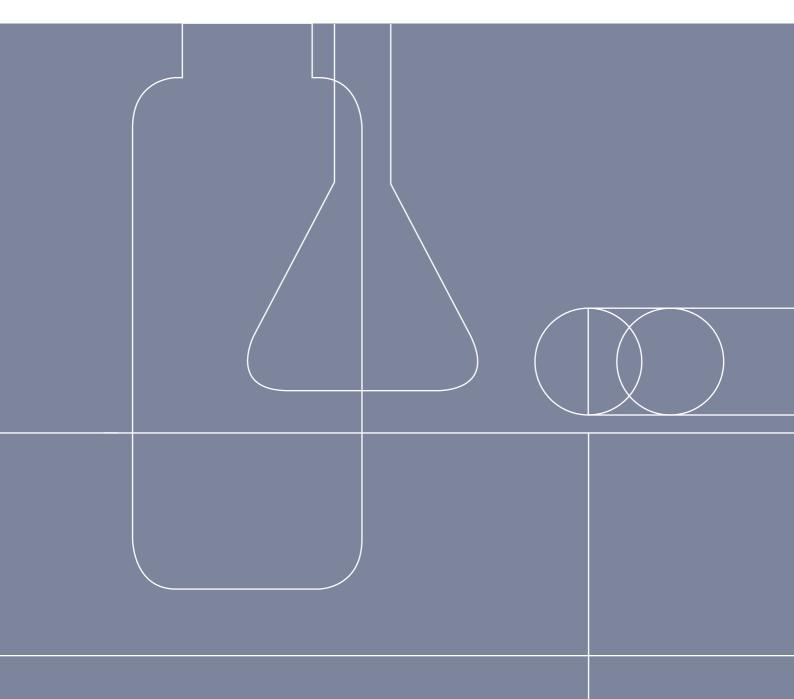


# NEGLECTED DISEASE RESEARCH AND DEVELOPMENT: THE STATUS QUO WON'T GET US THERE



## **ACKNOWLEDGEMENTS**

This is the fifteenth in a series of annual reports published as part of the G-FINDER project. We are 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 for neglected diseases. The patience and engagement of the participating government and multilateral agencies, academic and research institutions, product development partnerships, philanthropic institutions and pharmaceutical and biotechnology companies have made this project possible.

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# NEGLECTED DISEASE RESEARCH AND DEVELOPMENT: THE STATUS QUO WON'T GET US THERE

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## INTRODUCTION

### The G-FINDER report

Each year since 2007, G-FINDER has provided policy-makers, donors, researchers and industry with a comprehensive analysis of global investment into research and development of new products to prevent, diagnose, control or cure neglected diseases in developing countries, making it the gold standard in tracking and reporting global funding for neglected disease R&D.

This year's report, the fifteenth overall, focuses on investments made in participants' 2021 financial year ('FY2021'). While this report does not include some of the graphs incorporated in reports prior to 2020, the full suite of graphs and tables provided in previous editions can be created using our online data portal: https://gfinderdata.policycuresresearch.org/

This year's report contains an overview of neglected disease funding, measured in 2021 US dollars, including:

- · figures for individual diseases and product categories;
- analysis of public, philanthropic and (anonymised, aggregated) private neglected disease funders;
- details of the flow of funds to product development partnerships, other intermediaries and directly to researchers and developers; and
- a discussion of this year's key findings and how they fit with longer term trends, including the ongoing impact of COVID-19 on funding for neglected diseases.

Participation in the G-FINDER survey remained relatively consistent between this year and last, with the exception of missing 2021 funding data from the Indian Council of Medical Research and Biotechnology Industry Research Assistance Council (BIRAC). The disease areas for which headline funding totals are potentially misleading due to this missing data, along with any other minor survey participation effects, are highlighted throughout the report. In these cases, 'participation-adjusted' figures – which measure changes in funding from a consistent set of survey participants – are presented as an attempt to estimate the 'true' change between 2020 and 2021.

### What types of funding does G-FINDER include?

### DEFINING NEGLECTED DISEASES

The scope of the G-FINDER survey is determined in consultation with an Advisory Committee made up of a broad cross-section of international experts in neglected diseases and product development. The basis of this determination is the three-stage filter outlined in Figure 1. As this filter is applied not only at the overarching disease level but also at the product level, not all product areas are included for all of the diseases in the G-FINDER scope, and some are included only where they meet additional conditions designed to identify products targeting low- and middle-income countries (LMICs).

Multi-disease investments judged to have a sufficient connection with fighting neglected disease, including platform technologies (adjuvants & immunomodulators, diagnostic platforms, and drug-, biologic- and vaccine-related platforms), multi-disease vector control R&D and core funding to neglected-disease-focused organisations are captured in our 'non-disease-specific' funding category.

Figure 1. Identifying neglected diseases

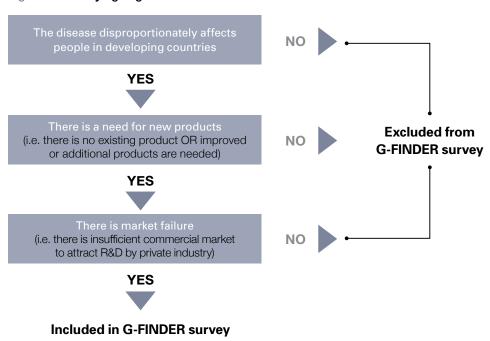


Table 1 offers a complete breakdown of which disease and product combinations are included in our funding totals.

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

		-03	arch	_	_	Diagnostics Microbicides product		
156356		Basic reser	orugs ,	Vaccines ,	Biologics	nagnostre	vicropicio	ectoricts
	`	,		Vae V	000	) · ·	Mis	DI S
HIV/AIDS		Restricted	Restricted	~	Restricted	~	~	-
Tuberculosis		~	~	~	~	~	-	-
Malaria	P. falciparum	~	~	~	~	~	-	~
	P. vivax	~	_	_	_	_	-	_
	Multiple / other malaria strains	~	~	~	_	~	-	_
Diarrhoeal diseases	Shigella	~	Restricted	~	Restricted	~	-	-
	Cholera	~	Restricted	~	Restricted	~	-	-
	Rotavirus	Restricted	-	Restricted	-	-	-	-
	Cryptosporidiosis	~	Restricted	~	Restricted	~	-	-
	Enterotoxigenic E. coli (ETEC)	Restricted	-	~	-	~	-	-
	Enteroaggregative E. coli (EAEC)	-	-	~	-	~	-	-
	Giardiasis	-	-	-	-	~	-	-
	Multiple diarrhoeal diseases	~	Restricted	~	Restricted	~	-	-
Kinetoplastid diseases	Leishmaniasis	~	~	~	~	~	-	-
	Chagas' disease	~	~	~	~	~	-	~
	Sleeping sickness (HAT)	~	~	~	~	~	-	~
	Multiple kinetoplastid diseases	~	~	~	~	~	-	~
Helminth infections (worms & flukes)	Schistosomiasis (bilharziasis)	~	~	~	~	~	-	~
	Onchocerciasis (river blindness)	~	~	~	-	~	-	~
	Lymphatic filariasis (elephantiasis)	~	~	-	-	~	-	~
	Tapeworm (taeniasis / cysticercosis)	~	~	-	-	~	-	~
	Hookworm (ancylostomiasis & necatoriasis)	~	~	~	-	-	-	-
	Whipworm (trichuriasis)	~	~	-	-	-	-	-
	Strongyloidiasis & other intestinal roundworms	~	~	~	-	~	-	-
	Roundworm (ascariasis)	~	~	-	-	-	-	-
	Multiple helminth infections	~	~	~	-	~	-	~
Dengue		~	~	-	~	~	-	~
Salmonella infections	Typhoid and paratyphoid fever (S. Typhi, S. Paratyphi A)	~	~	~	~	~	-	-
	Non-typhoidal S. enterica (NTS)	~	~	~	~	~	-	-
	Multiple Salmonella infections	~	~	~	~	~	-	-
Bacterial pneumonia & meningitis	S. pneumoniae	Restricted	-	Restricted	-	~	-	-
	N. meningitidis	Restricted	-	Restricted	-	~	-	-
	Both S. pneumoniae and N. meningitidis	Restricted	-	-	-	~	-	-
Snakebite envenoming		Restricted	Restricted	-	Restricted	Restricted	-	-
Hepatitis C		-	Restricted	~	-	~	-	-
Hepatitis B		Restricted	Restricted	-	Restricted	~	-	-
Cryptococcal meningitis		-	~	-	~	-	-	-
Rheumatic fever		-	-	~	-	-	-	-
Leprosy		~	~	~	~	~	-	-
Histoplasmosis		~	~	-	-	~	-	-
Scabies		Restricted	~	-	-	~	-	-
Mycetoma		~	~	-	-	~	-	-
Trachoma		-	-	~	-	~	-	-
Buruli ulcer		~	~	~	-	~	-	-
Leptospirosis		-	-	-	-	Restricted	-	-

Inve	stment applicable	to more than one n	eglected disease, o	or to more than one	global health are	ea*
	P	latform technologie	es			Core funding of a
Vaccine-related platform technologies			Adjuvants & immunomodulators	Biologics-related platform technologies	Multi-disease vector control	multi-disease R&D organisation
Restricted	Restricted	Restricted	Restricted	Restricted	~	~

#### TYPES OF RESEARCH INCLUDED

Funding included in G-FINDER covers the spectrum from basic research to post-registration studies of new products. We break these activities down into the broad categories of basic & early-stage research, and clinical or field development & post-registration studies:

- Basic & early-stage research, including:
  - Basic research
  - Discovery and pre-clinical development
- Clinical or field development & post-registration studies, including:
  - · Baseline epidemiology in preparation for product trials
  - Clinical development and field evaluation
  - Post-registration studies of new products, including Phase IV/pharmacovigilance, and operational research for diagnostics

The purpose of G-FINDER is to track and analyse global investment in the research and development of new health technologies for neglected diseases; it is not intended to capture investment in the entire spectrum of neglected disease research. This means that significant and important investments in health systems and operational/implementation research and sociological, behavioural and epidemiological research not related to the development of new health technologies are not included in these funding totals. Similarly, funding for health programme delivery, advocacy, routine disease surveillance programmes, community education and general capacity building to address neglected diseases falls outside the scope of G-FINDER.

For a detailed breakdown of the diseases, products and activities included, please see our neglected disease R&D scope:

https://gfinder.policycuresresearch.org/staticContent/pdf/G-FINDER\_ND\_R%26D\_scope.pdf.

#### CHANGES TO THE LIST OF NEGLECTED DISEASES

The G-FINDER scope is reviewed annually. Unlike last year, when a number of new diseases and product areas were included for the first time, the only substantive change to this year's survey scope was to create a standalone category for biologics-related platform technologies, funding for which had previously been captured under other platform categories. While recent changes to the survey scope have had limited impact on our headline measures of global funding, please take care when examining overall totals from significantly earlier in the survey's history, since some changes may reflect the gradual expansion in our survey's scope.

A more detailed history of the G-FINDER survey's scope is available on our website:

www.policycuresresearch.org/rd-needs-for-global-health/

#### INFLATION ADJUSTMENTS AND AGGREGATION OF INDUSTRY DATA

Funding data is adjusted for inflation and converted to US dollars (US\$) to eliminate artefactual effects caused by inflation and exchange rate fluctuations.

All pharmaceutical industry funding data is aggregated and anonymised for confidentiality purposes, with a distinction made between multinational pharmaceutical companies ('MNCs') and small pharmaceutical and biotechnology firms ('SMEs').

### FUNDING FOR EMERGING INFECTIOUS DISEASES AND SEXUAL & REPRODUCTIVE HEALTH

For the last several years, the G-FINDER survey has been expanded to gather data about funding for R&D targeting emerging infectious diseases and sexual & reproductive health issues. This data and an analysis of the related R&D funding trends are not included in this G-FINDER neglected disease report, but are covered instead in our ongoing series of companion reports (see https://www.policycuresresearch.org/analysis). However, all available neglected disease, emerging infectious disease and sexual & reproductive health survey data (now including FY2021 figures) are available now via the G-FINDER data portal (https://gfinderdata.policycuresresearch.org/).

#### SUPPLEMENTARY MATERIALS

Details on the survey methodology and data validation are included in Annexure B www.policycuresresearch.org/g-finder

All of the data behind the G-FINDER report is available through the online data portal at <a href="https://gfinderdata.policycuresresearch.org/">https://gfinderdata.policycuresresearch.org/</a>

The data portal now includes, for the first time, the ability to examine 'indirect funding' provided by intermediary organisations like Product Development Partnerships (PDPs) using the 'Funding Flows' switch on the filters tab.

Figures in this report, however, continue to include funding provided to intermediary organisations only and, to avoid double counting, exclude the funding they distribute.

Table 2. Disease and product R&D funding 2021 (US\$ millions)

80 a e a	Basic resear	ch	:nes	dics	ostics	vicrobicide	ector control	Inspecified	,
80 2	Basic 1	Drugs ,	Jaccines	3iologics r	Diagnostics	Micros V	produe	Jusper	Total
HIV/AIDS	216.75	278.97	703.52	78.56	20.82	60.02		107.14	1,465.7
Tuberculosis	193.50	371.11	71.27	5.26	68.96			12.82	722.9
Malaria	166.34	254.57	117.96	5.87	15.55		54.85	10.86	626.0
P. falciparum	86.01	75.07	95.54	2.95	6.95		12.21	3.51	282.2
P. vivax	12.21	28.38	9.97	0.34	3.42		0.61	0.15	55.0
Multiple / other malaria strains	68.13	151.12	12.45	2.58	5.18		42.03	7.20	288.6
Diarrhoeal diseases	43.43	12.16	69.93	2.87	2.18			5.45	136.0
Shigella	9.63	1.96	33.14	1.87	0.62			-	47.2
Cholera	19.82	0.87	5.04	1.00	0.36			-	27.0
Rotavirus	1.47		19.17					-	20.6
Cryptosporidiosis	8.54	9.26	1.01	-	0.08			-	18.9
Enterotoxigenic E. coli (ETEC)	0.61		8.86		0.08			-	9.5
Enteroaggregative E. coli (EAEC)			-		0.04			-	0.0
Giardiasis					-				
Multiple diarrhoeal diseases	3.36	0.06	2.70	-	1.00			5.45	12.
Kinetoplastid diseases	44.78	79.09	3.30	0.21	2.79		-	0.16	130.3
Leishmaniasis	18.49	20.53	1.18	-	0.20			0.02	40.4
Chagas' disease	6.45	26.25	2.05	0.21	2.34		-	0.14	37.4
Sleeping sickness (HAT)	17.40	12.41	0.08	-	0.25		-	-	30.
Multiple kinetoplastid diseases	2.44	19.90	-	-	-		-	< 0.01	22.3
Helminth infections (worms & flukes)	41.13	26.30	6.76	0.24	8.39		0.54	2.63	86.0
Schistosomiasis (bilharziasis)	13.03	4.37	5.20	0.24	1.89		0.51	0.36	25.6
Onchocerciasis (river blindness)	2.72	12.55	0.80		1.94		0.01	-	18.0
Lymphatic filariasis (elephantiasis)	5.17	1.92			1.80		0.01	1.37	10.2
Tapeworm (taeniasis / cysticercosis)	5.36	0.59			0.71		-	0.85	7.5
Hookworm (ancylostomiasis & necatoriasis)	2.32	1.15	0.74					-	4.5
Whipworm (trichuriasis)	2.53	0.31						-	2.8
Strongyloidiasis & other intestinal roundworms	2.34	0.32	0.02		0.12			-	2.8
Roundworm (ascariasis)	1.40	0.45						-	1.8
Multiple helminth infections	6.26	4.65	-		1.92		-	0.05	12.8
Dengue	25.55	35.85		2.52	8.62		5.54	0.06	78.
Salmonella infections	34.18	2.67	32.54	-	1.49			0.25	71.
Typhoid and paratyphoid fever (S. Typhi, S. Paratyphi A)	23.27	2.48	25.79	-	1.33			0.23	53.
Non-typhoidal S. enterica (NTS)	4.68	-	3.94	-	-			-	8.6
Multiple Salmonella infections	6.23	0.20	2.81	-	0.16			0.01	9.
Bacterial pneumonia & meningitis	4.82		57.78		0.54			0.58	63.
S. pneumoniae	3.45		49.71		0.05			0.58	53.
N. meningitidis	1.37		8.07		0.11			-	9.5
Both S. pneumoniae and N. meningitidis	<0.01				0.38			-	0.3

ase of	cea	ch		•	*iCS	. side	ector control		
piecase or R80 area	Basic resear	Drugs ,	Vaccines	Biologics	Diagnostics	Microbicide	products	inspecified	iotal
Snakebite envenoming	0.66	7.73		7.59	0.85			0.99	17.82
Hepatitis C		5.37	7.72		3.08			0.03	16.20
Hepatitis B	3.27	2.04		6.51	1.69			2.36	15.87
Cryptococcal meningitis		13.58		0.74				-	14.32
Rheumatic fever			9.20						9.20
Leprosy	3.78	2.07	0.59	-	0.31			0.10	6.85
Histoplasmosis	3.48	0.10			0.01			-	3.59
Scabies	0.72	0.88			-			0.36	1.96
Mycetoma	0.44	0.36			-			-	0.80
Trachoma			0.32		0.36			-	0.68
Buruli ulcer	0.43	-	0.03		0.16			-	0.62
Leptospirosis					0.03				0.03
Platform technologies									145.62
Vaccine-related platform technologies									51.46
General diagnostic platforms & multi-disease diagnostics									45.34
Drug-related platform technologies									20.97
Adjuvants and immunomodulators									16.55
Biologics-related platform technologies									11.31
Multi-disease vector control									75.05
Core funding of a multi-disease R&D organisation									378.09
Other R&D									69.97
Total R&D funding									4,136.72

- No reported funding

Category not included in G-FINDER

# OVERVIEW OF NEGLECTED DISEASE R&D FUNDING

Global funding for basic research and product development for neglected diseases in 2021 was \$4,137m, a drop of \$44m (-1.1%) from 2020.

Most of the fall was due to a small net drop in survey participation, particularly the absence of funding data from India's ICMR and BIRAC, who together provided nearly \$64m in 2020. Adjusting for differences in participation, the true drop in global funding was less than \$10m (-0.2%), leaving it basically unchanged in real terms, and roughly 4% below the peak in global funding between 2018 and 2019.



Figure 2. Total R&D funding for neglected diseases 2007-2021

Several areas were disproportionately affected by the absence of Indian data, particularly leptospirosis and leprosy, since the missing Indian funders respectively accounted for 98% and 36% of each disease's 2020 funding. We have therefore avoided analysing shifts in leptospirosis funding and considered changes in leprosy on a participation-adjusted basis, using only data from organisations for which both 2020 and 2021 data is available.

Last year saw the depreciation of most currencies against the US dollar. Since we aggregate grants made in different currencies using current year (2021) exchange rates, this reduced the value we attributed funding denominated in other currencies, even though their actual purchasing power may not have fallen. A combination of rising inflation and depreciation against the US dollar contributed roughly \$28m to the measured decline in overall funding – nearly two-thirds of the headline fall.

Three diseases – HIV/AIDS, tuberculosis, and malaria – again received the largest shares of funding, accounting for just over two-thirds of reported global investment. Funding for HIV/AIDS increased (up \$39m, 2.7%) while malaria saw a substantial decrease (down \$38m, -5.7%) and funding for tuberculosis remained basically unchanged (down \$0.2m, -<0.1%).

Just three other diseases saw meaningful increases in funding – snakebite envenoming, cryptococcal meningitis and scabies – alongside a further rise in non-disease-specific R&D – a seventh consecutive year of growth – leaving multi-disease funding up 5.6% with a new record total of \$669m, and at 16% of global funding.

Funding for the WHO neglected tropical diseases (NTDs) covered by the G-FINDER survey totalled \$323m, down \$37m (-10%) from 2020, marking two years of decline from their peak in 2019 following a decade of relative stagnation.

Table 3. R&D funding by disease 2012-2021^

and area	5\$ millio	ns)								2	027% 04
80	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
HIV/AIDS	1,365	1,245	1,262	1,199	1,294	1,390	1,556	1,571	1,427	1,466	35
Tuberculosis	610	626	646	647	655	679	732	755	723	723	17
Malaria	652	604	652	640	665	714	729	677	664	626	15
Diarrhoeal diseases	189	224	196	181	170	181	194	182	160	136	3.3
Kinetoplastid diseases	156	141	169	141	161	166	173	174	162	130	3.2
Helminth infections (worms & flukes)	102	103	101	87	83	96	104	103	86	86	2.1
Dengue	83	78	92	100	121	88	84	85	80	78	1.9
Salmonella infections	63	73	74	77	104	91	99	85	80	71	1.7
Bacterial pneumonia & meningitis	124	114	85	105	105	83	97	74	71	64	1.5
Snakebite envenoming							8.5	13	16	18	0.4
Hepatitis C		53	51	38	32	16	51	12	17	16	0.4
Hepatitis B							11	10	17	16	0.4
Cryptococcal meningitis		3.4	6.3	5.7	6.4	13	8.8	8.4	7.3	14	0.3
Rheumatic fever	1.6	1.2	1.9	3.0	2.0	1.9	2.1	15	17	9.2	0.2
Leprosy	15	13	11	12	12	12	9.7	10	8.6	6.8	0.2
Histoplasmosis									4.2	3.6	<0.1
Scabies									1.3	2.0	<0.1
Mycetoma							0.7	1.0	0.8	0.8	<0.1
Trachoma	2.3	2.5	1.5	1.3	2.5	3.0	2.1	2.0	2.0	0.7	<0.1
Buruli ulcer	6.8	7.2	4.2	2.1	3.1	4.7	2.8	3.0	2.6	0.6	<0.1
Leptospirosis		0.4	1.4	1.4	2.6	3.5	1.8	2.0	1.4	<0.1	<0.1
Platform technologies	56	50	26	41	84	57	73	101	130	146	3.5
Vaccine-related platform technologies	1.1	5.1	2.8	5.3	18	3.8	16	35	49	51	1.2
General diagnostic platforms & multi- disease diagnostics	19	19	11	18	43	31	34	36	48	45	1.1
Drug-related platform technologies	4.6	1.9	2.7	4.0	3.7	7.1	2.4	5.9	7.9	21	0.5
Adjuvants and immunomodulators	31	24	9.5	14	20	15	21	24	25	17	0.4
Biologics-related platform technologies										11	0.3
Multi-disease vector control					21	31	44	68	67	75	1.8
Core funding of a multi-disease R&D organisation	118	128	118	156	177	308	357	349	377	378	9.1
Other R&D	126	83	43	52	39	46	70	42	59	70	1.7
Total R&D funding	3,670	3,551	3,540	3,490	3,741	3,983	4,407	4,342	4,181	4,137	100

Hepatitis C, cryptococcal meningitis and leptospirosis were added to G-FINDER in 2013. Multi-disease vector control products were added in 2017; the 2016 total was added retrospectively, and likely understates true funding. Mycetoma, snakebite envenoming and hepatitis B were added in 2018. Histoplasmosis and scabies were added in 2020. Biologics-related platform technologies were moved to a separate category in 2021.

<sup>^</sup> 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, Steptococcus pneumoniae R&D is often targeted at both pneumonia and meningitis.

# HIV/AIDS

**47M** DALYS **849K** DEATHS IN 2019

Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$1,466m	35%	+2.7%		Public Philanthropic Private	Basic & early Late Unspecified

Global funding for HIV/AIDS basic research and product development totalled \$1,466m in 2021. Although only a slight increase from 2020 (up \$39m, 2.7%), this was a heartening correction following last year's record fall, and leaves funding safely above its ten-year average. Investment from industry rose by 47% (up \$70m) to \$220m (15% of total funding) to just above its previous, 2018, peak. The Gates Foundation also saw its HIV funding rebound, by 11% (up \$14m). These gains helped to offset further falls in funding from Unitaid (down \$10m, -49%) and record low funding from the EC (down \$10m, -90%) and the French ANRS (down \$6.9m, -60%).

Thanks to the increases from industry and the Gates Foundation, HIV/AIDS drug R&D increased by just over half (up \$96m, 53%), pushing it to a new record high of \$279m. This lifted drug funding to well over double its historical average and extended the strong growth since 2016, when drug funding totalled just \$58m. A large portion of the overall funding increase from industry went to post-registration studies for a newly registered long-acting injectable. The Gates Foundation's sharply increased drug disbursements (up by 466%, \$41m), came largely in the form of \$39m in new funding for islatravir in the Phase III IMPOWER study for women and adolescent girls in sub-Saharan Africa.

Although vaccine R&D investment dropped by only 4.6% (down \$34m), this was enough to take it to its lowest level on record. Vaccine funding from the Gates Foundation fell by a quarter (down \$22m, -25%) as it concluded long running grants to the Fred Hutchinson Cancer Research Center (down \$11m, -61%) and Duke University (down \$6.0m, -90%). The US NIH also cut vaccine funding by \$13m (-2.6%), mostly in early-stage research. These drops outweighed modest increases in vaccine funding from industry (up \$6.7m, 9.8%), mostly for clinical development, and in both internal funding and external contracts from the US DOD (up \$5.5m, 21%).



The South African Health Products Regulatory Authority was the first to approve a '4-in-1' fixed-dose combination for paediatric HIV in June 2022.¹ The single, easy-to-use granule-filled capsule is taste-masked and can be sprinkled into the child's food. IAVI, NIAID and Moderna commenced Phase I trials in March 2022 of three mRNA-based vaccines leveraging COVID-19-tested technologies.²

**Unmet R&D needs:** There is currently no vaccine against HIV, thanks to the challenge posed by the virus' genetic elasticity. All Phase III candidates so far have failed to demonstrate efficacy, with the most recent Phase III trial (Mosaico) discontinued in January 2023 after disappointing interim results.<sup>3</sup> Passive immunisation with biologics such as monoclonal antibodies (mAbs) remain promising, with WHO and IAVI publishing preferred product characteristics to guide R&D.<sup>4</sup> AMP mAb trials demonstrated proof of concept, though revealed that one monoclonal antibody alone is insufficient.<sup>5</sup> Microbicides – preventive tools designed to block transmission of HIV through the vaginal or rectal mucosa – have shown promise as a complementary tool, with the dapivirine vaginal ring included in WHO's prequalification list in 2020.<sup>6</sup> Current methods for early diagnosis are often not adapted to, or suitable for, developing countries, especially for early infant diagnosis. However, there is progress towards robust, point-of-care diagnostics, culminating in the recent WHO prequalification of several promising candidates.<sup>7</sup>

Investment in microbicides sank to \$60m, (down \$48m, -44%) a record low which continued its steady decline from a peak of \$291m in 2008. Investment from the bellwether public funders of microbicide R&D fell by half: USAID funding was down \$9.4m (-51%) and the NIH down \$39m (-49%). The NIH's cuts fell largely on their external funding (down \$41m, -60%), across both early- and late-stage development.

HIV diagnostics R&D funding fell for the third consecutive year after its peak in 2018, dropping to \$21m (down \$12m, -37%). This was driven by an 82% (\$9.7m) drop in funding from Unitaid, as it wrapped up a long running grant to CHAI for point-of-care diagnostics operational research in sub-Saharan Africa.

Biologics R&D fell only slightly (by \$2.0m, -2.5%) and continued to be almost entirely funded by just two organisations: the US NIH with 76% of the total (\$59m) and the Gates Foundation with 21% (\$17m). NIH funding jumped by 40% (up \$17m), much of which went to clinical development (up \$8.1m, 21%), while Gates' investment in early-stage biologics development dropped by 68% (down \$19m).

LMIC-specific HIV basic research fell by \$14m (-6.2%) almost mirroring the reduction in NIH funding (down \$15m, -7.2%). This fall, alongside the near-cessation of long-term basic research funding from the French ANRS (down \$2.6m -99.7%) overshadowed a 56% increase in basic research from the Gates Foundation (up \$4.1m).

Clinical development & post-registration studies received the largest share of HIV/AIDS R&D funding (\$679m, 46%), with an overall increase of \$71m (12%). This was mostly thanks to increased clinical development funding from industry (up \$68m, 47%) and the Gates Foundation (up \$36m, 96%) – the top two funders of HIV clinical development since 2014 – with both focusing on late-stage drug development. Even the \$70m headline increase likely understates the true growth in clinical development, since 2021 also saw \$39m in new NIH funding for a combination of drug and biologic trials not formally allocated to clinical development.

Basic & early-stage research, meanwhile, dropped by \$80m (-12%) as early-stage research across all products declined alongside investment in basic research, perhaps signalling the increasing maturity of the new wave of LMIC-specific products in the HIV pipeline.

Although three-quarters of 2021's HIV/AIDS R&D funding came from the public sector (\$1,096m, 75%), this also represented a record low (down \$41m, -3.6%). Public funding from HICs decreased by \$27m (-2.4%) largely due to reduced funding from three organisations: the EC (down \$10m, -90%), French ANRS (down \$6.9m, -60%) and USAID (down \$7.5m, -14%). Multilateral investment fell by close to half (down \$11m, -47%), thanks to reduced funding from Unitaid. LMIC public funding dropped by more than a third (down \$2.7m, -39%) partly due to a \$1.3m drop from the South African DSI, but mostly due to the absence of data from Indian ICMR, which had provided \$1.8m in 2020.

Philanthropic funding rose by \$9.3m (6.7%) as the Gates Foundation – which accounts for 97% of philanthropic funding – increased its disbursements by \$14m (11%). This was enough to offset smaller decreases from several other philanthropic funders.

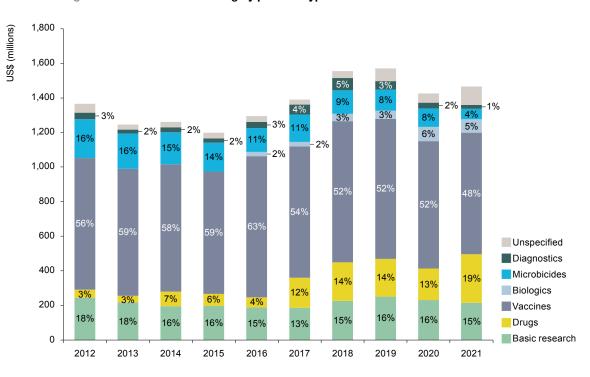


Figure 3. HIV/AIDS R&D funding by product type 2012-2021

Table 4. Top HIV/AIDS R&D funders 2021

'gel	JS\$ (millio	ns)								2	021% of total
Funder	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
US NIH	870	783	811	799	841	813	953	1,021	962	962	66
Aggregate industry	25	18	52	63	96	166	222	201	150	220	15
Gates Foundation	142	139	127	124	148	151	143	159	131	146	9.9
USAID*	83	75	67	66	54	69	52	43	51	44	3.0
US DOD	60	64	71	32	42	40	25	21	31	32	2.2
Unitaid	-	0.8	7.9	6.0	5.1	37	56	27	21	11	0.7
Dutch DGIS	4.2	8.3	6.8	1.4	10	13	6.4	6.3	2.3	8.5	0.6
Inserm	14	14	12	13	12	11	6.7	8.3	5.6	7.4	0.5
French ANRS	11	12	4.8	4.8	5.5	7.6	7.9	14	12	4.7	0.3
German BMBF	1.8	2.4	2.2	4.3	6.8	7.6	11	3.7	2.9	4.4	0.3
South African DSI	4.6	4.7	2.1	2.1	3.1	3.1	3.7	4.2	3.8	2.5	0.2
Canadian CIHR	8.9	9.2	7.3	7.3	6.6	6.8	9.1	6.3	6.3	2.2	0.2
Subtotal of top 12^	1,284	1,170	1,211	1,153	1,255	1,342	1,514	1,531	1,391	1,444	98
Disease total	1,365	1,245	1,262	1,199	1,294	1,390	1,556	1,571	1,427	1,466	100

<sup>^</sup> Subtotals for 2012-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

<sup>\*</sup> USAID and overall HIV vaccine funding is understated by \$3.7m and microbicide funding by \$4.8m as additional funding data was received after G-FINDER analysis concluded

<sup>-</sup> No reported funding

### **TUBERCULOSIS**

**47M** DALYS **1.2M** DEATHS IN 2019

Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$723m	17%	-<0.1		Public Philanthropic Private	Basic & early Late Unspecified

Global funding for tuberculosis basic research and product development was \$723m in 2021. This was essentially unchanged from the previous year (down \$0.2m, -<0.1%) even with the absence of Indian funding data; and left funding more than \$100m above its total from a decade ago. Once we adjust for participation, TB funding actually increased a little (up \$13m, 1.9%), leaving it close to a record high. To avoid focusing on purely artefactual changes, the figures below mostly include only changes from funders for whom comparable data is available in both 2020 and 2021.

Other than the temporarily-absent Indian ICMR, the top ten funders were unchanged from last year. Top funders' overall (participation-adjusted) funding rose (up \$16m, 2.5%), growth that was dampened somewhat by a net reduction of \$2.6m across the 55 ongoing funders outside the top ten.

The most significant funding growth was from Unitaid and industry. Industry increased its investment by 23% (\$20m) and Unitaid's funding jumped by \$17m to \$28m (up 139%). Both increases focused almost exclusively on drugs, and mostly on their clinical development, helping to take drug clinical development to a record high of \$155m in 2021 – though, with recent drug approvals all conditional on further clinical studies, funding for post-registration studies continued to slump, to a four-year low.

These increases were partly offset however, by big reductions from the US NIH, the Gates Foundation, and the UK FCDO. The NIH – the top TB R&D funder since 2012 – saw a second-consecutive drop in funding (down a further \$11m, -3.7%) from 2019's record high, falling mostly on early-stage vaccine research. Funding from the Gates Foundation fell \$6.4m (-5.2%), mostly in diagnostics R&D (down \$4.3m, -30%), while the UK FCDO – whose investment has been directed exclusively to drug R&D since 2019 – cut its funding for the third year running, with its 2021 funding slashed by over a third (down \$5.4m, -38%).



BioNTech's BNT164, the first mRNA-based TB vaccine, entered clinical trials in December 2022<sup>8</sup> – testimony to the flow-on benefits of the unprecedented technological innovations during the development of COVID-19 vaccines. A Phase II trial for drug-sensitive TB is investigating an all-new regimen of Otsuka's investigational compound, OPC-167832, with recently approved bedaquiline and delamanid.<sup>9</sup>

**Unmet R&D needs:** A new TB vaccine, which is effective across all ages and safe for pregnant and lactating women, is critical for achieving targets set by the WHO's End TB Strategy. However, TB vaccine R&D is lagging on most fronts – the number of candidates in late clinical development is unchanged, and most are non-inactivated/attenuated vaccines targeting the same antigen, no new evidence on efficacy since the publication of M72/AS01E's clinical trial results in 2019 and the exclusion of pregnant women, a high-risk group, from clinical trials. A more diverse early-stage pipeline is urgently needed to safeguard against the potential failure of the current clinical candidates. In recent years, the WHO has endorsed several new tools, including molecular tests for diagnosing TB. However, research gaps still exist, including non-sputum-based tests for diagnosing paediatric TB, true point-of-care molecular tests and tools for screening and triage. 12,13

Drug R&D received more than half of global TB funding in 2021, as it has every year since 2018. This is up from around a third of the total over the first three years of the G-FINDER survey, when there was less *overall* funding and it was more focused on basic research. A little over a quarter of 2021 funding went to basic research, which fell by \$6.7m (-3.4%) due to sharp reductions in funding from the German BMG (down \$4.5m, 93%) – one of the main contributors to TB basic research over the last decade – and the Indian DBT (down \$2.2m, -70%). There were smaller reductions from the US NIH, Wellcome and the Gates Foundation, the latter having cut its TB basic research funding every year for the last five years.

Funding for vaccines slumped by \$7.6m to \$71m, leaving vaccines with less than 10% of total funding – a record low. The fall was driven mostly by continuing reductions in funding from the NIH (down \$9.4m, -24%) from its record high in 2019, as well as by decreases in the number of active funders, down from a peak of 22 early in the decade to just nine in 2021.

The drop in vaccine R&D funding reflects a relatively stagnant R&D pipeline, with no significant new clinical candidates since 2015. There are few late-stage and almost no preclinical candidates set to enter clinical trials. Due to the slow-to-emerge nature of TB infection, complex trial protocols for testing multiple use cases, and the need to demonstrate prevention of disease rather than prevention of infection, clinical development of TB vaccines progresses only slowly. Though one candidate, the Gates MRI-funded M72/AS01E is ready to begin Phase III trials and another, H56:IC31, is scheduled to do so in 2025, the TB vaccine pipeline has not been advancing sufficiently to attract significant investment.

Diagnostics R&D funding has been relatively stable over the last five years, at just under a tenth of total funding, but fell \$1.4m (-2.1%) in 2021, as reduced funding from the Gates Foundation was only partly offset by increases from the US CDC and Unitaid.

Conversely, funding for biologics has experienced wild swings, peaking at \$11m in 2008 and sinking to just \$0.2m in 2011 and 2015. In 2021, biologics funding jumped more than tenfold, from \$0.4m to \$5.3m – driven by a suite of US NIH-funded early-stage studies – though it still accounted for less than 1% of total funding.

More than half of total TB funding in 2021 went to basic & early-stage research (\$404m, 57%), and a little over a quarter to clinical development & post-registration studies (\$187m, 26%) – the latter an increase of more than \$30m thanks to the increased drug development funding provided by industry and Unitaid.

As in previous years, most funding for TB R&D came from HIC public organisations, though their share of global funding dropped three percentage points due to both a \$15m fall in their funding and big increases from multilaterals and industry. Growth from Unitaid – the sole multilateral funder of TB R&D – took multilateral funding to a five-year high. The share of private sector funding rebounded from a near-record low in 2020, rising three percentage points to 15% – driven by an additional \$21m from MNCs. Despite consecutive declines in their funding, philanthropic organisations continued to provide the second largest share of overall funding, with 19% of the global total.

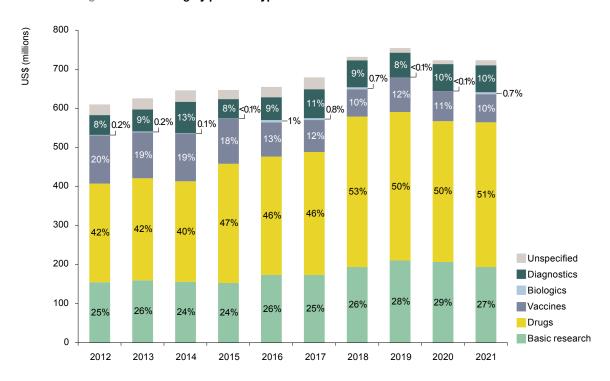


Figure 4. TB funding by product type 2012-2021

Table 5. Top TB R&D funders 2021

,	JS\$ (millic	ius)								7	021% of total
Funder	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
US NIH	207	192	218	226	238	263	291	332	310	299	41
Gates Foundation	118	146	153	147	113	99	110	124	124	117	16
Aggregate industry	152	124	115	114	104	110	110	93	89	112	15
EC	12	21	17	28	23	18	12	11	35	42	5.9
Unitaid	0.4	2.3	0.5	6.8	37	13	14	16	12	28	3.9
German BMBF	5.4	5.5	6.6	7.4	10	18	17	25	16	17	2.3
US CDC	-	-	17	10	9.6	16	16	14	15	13	1.8
Wellcome	13	14	13	11	9.9	10	11	13	11	10	1.4
UK FCDO	1.6	14	15	13	8.5	15	26	19	14	8.9	1.2
UK MRC	15	12	11	7.9	10	9.5	8.5	12	11	7.0	1.0
US DOD	1.3	2.1	0.5	0.4	0.3	<0.1	2.5	6.1	5.8	6.0	0.8
German BMG	3.8	4.0	4.2	4.4	4.6	4.7	4.9	5.0	5.3	5.1	0.7
Subtotal of top 12^	556	560	592	595	595	605	655	689	658	666	92
Disease total	610	626	646	647	655	679	732	755	723	723	100

<sup>^</sup> Subtotals for 2012-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

<sup>-</sup> No reported funding

## MALARIA

**46M** DALYS **643K** DEATHS IN 2019

Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$626m	15%	-5.7%	<b></b>	Public Philanthropic Private	Basic & early Late Unspecified

Global funding for malaria basic research and product development was \$626m in 2021, down \$38m (-5.7%) from 2020. This drop represented the third consecutive year of funding decline since its 2018 peak, taking headline investment to its lowest level since 2013 or, adjusting for long term growth in survey participation, the lowest since 2007 when the G-FINDER survey began.

The decrease was driven by big reductions in funding from industry (down \$11m, -9.0%) and the UK FCDO (down \$18m, -51%), and fell most heavily on R&D targeting multiple and 'other' malaria strains, which dropped by \$67m to \$289m (46% of total funding). In contrast, funding specifically targeting *P. falciparum* rose by 11%, to \$282m (45% of total funding) and funding for *P. vivax* malaria remained unchanged at \$55m (8.8% of the total).

Funding declined across almost all product categories. Vaccine R&D continued its downward trajectory for the fourth year in a row, falling to \$118m (down \$9.1m, -7.2%), though still safely above its record low of \$105m in 2007. However, in a reversal of a trend seen over the past two years, this decrease was largely caused by a fall in funding for early-stage vaccine research, rather than clinical development. Much of the fall in early-stage vaccine funding was due to the Gates Foundation, which reduced its contributions by almost three-quarters (down \$10m, -74%). Despite this, the Gates Foundation remained the third-largest overall funder of malaria vaccine R&D, behind only the US NIH and industry.

While continuing to receive more than a quarter of malaria funding (\$166m), basic research appeared to experience the largest absolute decline in funding in 2021 (down \$21m, -11%). However, this was largely due to the absence of 2021 funding data from the Indian ICMR, which had been the second largest basic research funder in 2020, with contributions of more than \$16m. Adjusting for differences in survey participation, malaria basic research still fell substantially – by \$11m (-6.5%) – attributable mostly to reduced funding from the Australian NHMRC and tapered disbursements from Open Philanthropy, which had made frontloaded payments under its two and three years grants in 2020.



Mosquirix, the only approved vaccine, received WHO prequalification in July 2022. <sup>14</sup> Phase II results for US NIH's CIS43LS monoclonal antibody demonstrated six months protection against *Plasmodium falciparum* after a single dose. <sup>15,16</sup> MMV and Novartis announced a Phase III efficacy trial of ganaplacide/lumefantrine-SDF combination for 2023, the first novel non-artemisinin-based therapy to enter regulatory trials. <sup>17</sup>

**Unmet R&D needs:** There remains a clear need for a more efficacious vaccine and vaccines that can protect against *P. vivax* and placental malaria, and/or block transmission. New drugs are needed in response to emerging resistance and to meet the needs of key populations, as well as for chemoprotection, and – ideally – to meet the goal of a single-dose treatment. In addition to small molecule drugs, monoclonal antibodies (mAbs) are being investigated, though large-scale administration is not yet suited to low-resource settings. There is an urgent need to develop new rapid diagnostic tests in response to emerging *pfhrp2/3* gene deletion in malaria parasites, <sup>18</sup> as well as more sensitive diagnostics to identify non-*falciparum* species, distinguish malaria from other febrile illnesses, detect asymptomatic cases, and diagnose G6PD enzyme deficiency. Next-generation vector control products are needed in response to emerging pyrethroid resistance, including genetic approaches to reduce mosquito populations or block parasite transmission, and endectocides for malaria transmission control. <sup>19</sup>

After receiving \$68m, 10% of funding – its highest ever share – in 2020, vector control product (VCP) R&D fell by just under a fifth to \$55m in 2021. The Gates Foundation and the UK FCDO, which collectively accounted for 80% of VCP funding in 2020, saw their respective funding totals decrease by \$12m (-27%) and \$3.6m (-33%). However, this was partially offset by a rise in funding from Open Philanthropy, which disbursed \$10m to the University of California, Davis to progress a gene drive application designed to reduce the ability of mosquitoes to transmit malaria.

Diagnostics R&D received only 2.5% of total malaria funding in 2021, its lowest share since 2013. Since its sustained peak at over \$30m a year between 2017 and 2019, diagnostics funding has now declined by close to half, dropping to \$16m. The rate of decline slowed in 2021, thanks to a doubling of Gates Foundation funding (up \$3.5m, 110%) and a slight increase from the US NIH (up \$1.2m, 21%). This was offset by a \$6.2m fall in funding from the UK's DHSC and FCDO, with the latter concluding four years of funding to PATH amid substantial declines in its funding to a wide range of neglected diseases.

Only R&D for therapeutics bucked the overall downward trend, with drug R&D rising by \$9.9m (4.1%) and biologics by \$0.4m (7.0%), leaving both with their largest share of overall malaria funding of the last decade. The increase in drug funding was mostly thanks to Unitaid, which more than doubled last year's record contributions to hit a new peak of \$23m (up \$14m, 169%).

In contrast to other product areas, industry remained the top funder of drug R&D, having contributed 38% (\$895m) of all drug R&D funding over the previous 10 years. However, its contributions fell slightly in 2021, to \$75m (29% of total drug R&D funding). The largest decreases were in its funding for drug clinical development, which has trended downwards from a peak of \$81m in 2018 to \$31m in 2021.

Even with the fall in industry's drug development funding, 2021 saw an increase in clinical development funding, both for drugs (up \$5.9m, 8.8%) and overall (up \$7.2m, 4.6%). A shift towards clinical development for vaccines offset the sharp drop for vector control development and pushed the overall share of clinical development back up to 26%, broadly in line with its recent average.

Despite a \$23m drop in contributions from the HIC public sector, it continued to provide a narrow majority (52%) of global malaria funding in 2021. This was largely thanks to the US NIH – the top funder of malaria R&D – whose funding remained stable at \$189m. Philanthropic funding fell slightly, due to reduced funding from the Gates Foundation – still the second largest overall funder – followed by aggregate industry, which remained the third largest funder even after an \$11m drop in funding. Record funding from Unitaid drove multilaterals' share of funding to nearly 4.0%, its highest level ever, while – after adjusting for a lack of Indian funding data – low-and middle-income (LMIC) public funding saw a substantial increase.

Figure 5. Malaria R&D funding by product type 2012-2021

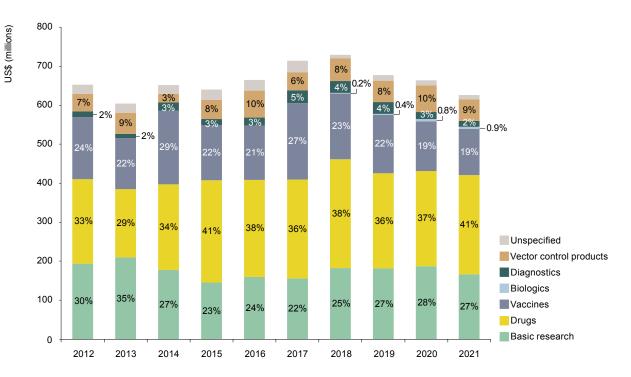


Table 6. Top malaria R&D funders 2021

	JS\$ (millio	nsl									021% of tot
Funder	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	9.
US NIH	198	161	172	178	186	189	184	179	188	189	30
Gates Foundation	155	147	166	135	141	114	135	130	134	127	20
Aggregate industry	120	86	133	159	155	150	176	129	118	108	17
US DOD	14	28	21	38	40	42	49	45	39	34	5.4
Unitaid	-	6.5	9.4	8.8	4.3	4.3	2.9	7.7	9.4	25	4.0
Wellcome	30	27	24	19	16	16	18	20	21	19	3.0
UK FCDO	6.4	28	20	19	14	41	35	37	35	17	2.7
Open Philanthropy						8.5	4.6	3.8	10	14	2.3
Australian NHMRC	17	13	12	3.7	3.8	4.8	11	12	15	13	2.1
EC	16	24	24	16	10	13	12	12	11	10	1.6
UK MRC	17	17	15	9.1	12	14	9.9	11	10	10	1.6
German BMBF	3.0	3.2	3.8	6.7	7.9	8.0	5.5	7.6	8.1	9.0	1.4
Subtotal of top 12^	601	554	611	603	614	636	665	612	608	574	92
Disease total	652	604	652	640	665	714	729	677	664	626	100

<sup>^</sup> Subtotals for 2012-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

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.

<sup>-</sup> No reported funding

## DIARRHOEAL DISEASES

**46M** DALYS **1.0M** DEATHS IN 2019

Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$136m	3.3%	-15%	<b>^</b>	Public Philanthropic Private	Basic & early Late Unspecified

Overall funding for diarrhoeal diseases decreased for the third consecutive year, falling to \$136m (down \$24m, -15% from 2020) – its lowest total ever.

Shigella again received the most funding of any diarrhoeal disease, with \$47m (35% of the total). Cholera funding dropped (by \$11m), as did funding to rotavirus – down \$15m and a total of \$38m since 2018. Together, these three diseases accounted for 70% of diarrhoeal disease funding. Cryptosporidiosis received 14%, a record high despite a slight (\$1.6m) decline to \$19m. Funding for multiple diarrhoeal diseases saw its eighth consecutive fall, slumping to \$13m (9.0%); *E. coli* funding increased again, by \$1.0m (to \$9.6m, 7.0%), while no funding was reported for giardiasis, for the third year running.

Funding for **Shigella**-related diarrhoeal disease rose (up \$5.0m, 13%) and – like most areas of diarrhoeal disease R&D – continued to be dominated by the US NIH and the Gates Foundation. *Shigella* funding from industry fell slightly (down \$0.8m, -8.2%), a pattern repeated across several diarrhoeal diseases. This was offset by an increase in *Shigella* vaccine funding (up \$5.8m) due to new investment from the NIH (up \$4.5m) – primarily to the vaccine and treatment evaluation units at Emory University – and the Gates Foundation (up \$5.1m).

The biggest fall was in funding for **rotavirus**, which fell by over \$15m (-43%) due to a \$17m (-89%) fall in MNC investment – the sharpest of several cuts in industry funding. These cuts concentrated entirely on vaccine R&D, following the completed development of a novel liquid formulation of Rotarix, which had driven the sharp increase in rotavirus vaccine funding in 2018. These decreases overshadowed the first ever substantial funding for rotavirus basic research.

A major contributor to the fall in funding for **cholera**, as well as for **multiple diarrhoeal diseases**, was the absence of funding from the UK FCDO, down from a total of \$1.9m in 2020. Basic research for cholera also dropped, by \$9.6m – although half of this reflects a lack of data from the Indian ICMR.

The long-term decline in funding for multiple diarrhoeal diseases from its 2013 peak of \$75m is felt across all product areas, with vaccine funding having dropped by nearly \$30m (-92%), basic research by \$13m (-79%) and drug funding by \$12m (-99%) since 2013.

pipeline spotlight Beijing Zhifei Lvzhu's live attenuated *Shigella* vaccine entered a Phase III trial in December 2021.<sup>20</sup> NIAID initiated a Phase II *Shigella* human challenge study of another live attenuated candidate, WRSs2.<sup>21,22</sup> In November 2022, Maxvax Biotechnology began Phase II trials of its trivalent rotavirus vaccine, only the second sub-unit vaccine to reach late-stage development.<sup>23</sup>

**Unmet R&D needs:** Approved vaccines against diarrhoeal diseases are sometimes ineffective or unsuitable for infants. New multivalent vaccines suitable for infants and with longer-term protection in high-burden settings are urgently needed. Such next-generation candidates for rotavirus include non-replicating parenteral vaccines, the most advanced being PATH's trivalent NRRV (P2-VP8) candidate, undergoing Phase III trials. Other potential candidates remain in preclinical development, except for Mitsubishi Tanabe's VLP rotavirus vaccine, MT 5625, which has progressed to Phase I development. Oral rehydration therapy and zinc supplementation are the mainstay of management in LMICs but are insufficient in many cases. Safe, effective, and affordable pathogen-specific drugs are also needed. The therapeutic pipeline currently includes both small molecule drugs and biologics, with only a few candidates in early-stage clinical development. Let Likewise, rapid diagnostic tests capable of differentiating between different diarrhoeal diseases, as well as diagnosing multiple diseases, are required; however, only one candidate, RLDT, is in late-stage development.

Table 7. Diarrhoeal disease R&D funding 2021 (US\$ millions)^

Disease	asic resear	on on	Jaccines (	giologics (	Diagnostics	Jnspecified T	iotal c	Vo.
Shigella	9.6	2.0	33	1.9	0.6	-	47	35
Cholera	20	0.9	5.0	1.0	0.4	-	27	20
Rotavirus	1.5		19			-	21	15
Cryptosporidiosis	8.5	9.3	1.0	-	<0.1	-	19	14
Enterotoxigenic E. coli (ETEC)	0.6		8.9		<0.1	-	10	7.0
Enteroaggregative E. coli (EAEC)			-		<0.1	-	<0.1	<0.1
Giardiasis					-		-	-
Multiple diarrhoeal diseases	3.4	<0.1	2.7	-	1.0	5.4	13	9.2
Total	43	12	70	2.9	2.2	5.4	136	100

<sup>^</sup> Strict eligibility conditions on private sector drug and vaccine investments for some pathogens mean direct comparisons between product totals can be misleading.

Category not included in G-FINDER

Table 8. Top diarrhoeal disease R&D funders 2021

	JS\$ (millio	nsl									021 % of total
Funder	2012	2013	2014	2015	2016	2017	2018	2019	2020	2 2021	Qu'
US NIH	63	54	50	43	43	44	48	47	58	60	44
Gates Foundation	45	58	47	45	54	51	47	46	27	31	23
Aggregate industry	34	50	44	38	34	38	52	51	41	23	17
Wellcome	3.9	2.9	5.0	4.1	2.9	3.7	8.2	8.2	9.6	6.5	4.7
US DOD	9.8	12	11	8.0	6.5	9.2	7.7	8.9	5.0	4.5	3.3
EC	3.2	3.5	3.5	3.4	0.6	2.2	3.2	3.6	3.7	3.8	2.8
German DFG	0.7	0.5	0.3	1.1	0.8	1.3	-			1.6	1.2
Swiss SNSF	0.6	1.4	0.2	-	0.4	0.3	0.3	0.3	0.4	1.2	0.9
UK MRC	1.0	1.8	1.6	1.1	1.0	0.9	0.3	1.7	2.1	1.1	0.8
Open Philanthropy						-	-	-	1.0	1.0	0.7
Institut Pasteur	4.3	4.2	4.3	4.1	4.4	4.5	2.4	3.0	1.6	0.9	0.7
German BMBF	-	-	-	-	-	-	-	0.1	<0.1	0.5	0.3
Subtotal of top 12^	183	218	193	175	164	173	189	179	158	134	99
Disease total	189	224	196	181	170	181	194	182	160	136	100

 $<sup>^{\</sup>wedge}$  Subtotals for 2012-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021. 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

<sup>-</sup> No reported funding

### **KINETOPLASTIDS**

1.0M DALYS 16K DEATHS IN 2019

Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$130m	3.2%	-20%	<b>~</b>	Public Philanthropic Private	■ Basic & early ■ Late Unspecified

Kinetoplastid diseases received \$127m in R&D funding in 2021, representing a steep \$30m (-19%) reduction, following cuts from all 12 top funders. This took funding to its lowest level ever, \$11m below its previous low in 2015.

After declines in funding across all kinetoplastid diseases, leishmaniasis continued to receive the largest share of funding (\$40m, 31%), narrowly ahead of Chagas' disease (\$37m, 29%). The remainder went to sleeping sickness (\$30m, 23%) and multiple kinetoplastid R&D, which received a record low of \$22m (17%) after experiencing the largest decline in 2021 funding.

**Leishmaniasis** funding has more than halved since its \$82m peak in 2009. It dropped by \$8.4m (-17%) in 2021 alone, though the absence of data from the Indian ICMR accounted for around half of this drop. Most leishmaniasis funding continued to go to basic research (45% of the total) and drug R&D (51%), though drug funding fell sharply (down \$2.9m, -12%) – driven by a drop in clinical development funding from industry, and from the US DOD, which terminated development of a topical antileishmanial cream. Vaccine R&D funding also experienced a (proportionally steeper) fall, halving to \$1.2m.

**Chagas' disease** and **sleeping sickness** experienced similar drops in funding, with respective falls of \$4.4m (-11%) and \$4.3m (-13%). Both were headlined by big cuts from the US NIH – primarily impacting basic research – and smaller cuts by industry. MNCs reduced drug clinical development for both pathogens, though drug R&D still received a record 70% of overall Chagas' disease funding. Funding for sleeping sickness diagnostics also fell by three-quarters to \$0.3m, as three relatively consistent contributors ceased diagnostic funding in 2021.

Funding targeting **multiple kinetoplastid diseases** experienced a significant fall of \$15m (-39%). This was almost entirely due to a \$14m reduction in drug R&D funding from the UK FCDO, though it remained the top funder of multiple kinetoplastid R&D with \$7.3m. With remaining funding split exclusively between drug R&D (\$20m, 89%) and basic research (\$2.4m, 11%), vector control R&D funding fell to zero. Indeed, there was no vector control funding for any kinetoplastid disease, for the first time since 2014.

Public (HIC) funders continued to account for around 60% of total kinetoplastid disease funding, over half of which was contributed by the US NIH. Industry accounted for 24%, and philanthropic funders' share rose slightly, to 14%.



In November 2022, DND*i* and Novartis initiated a Phase II safety and efficacy trial of oral LXE408 as a monotherapy for treating visceral leishmaniasis.<sup>29</sup> A Phase II/III trial of acoziborole as a single dose cure for adult Human African trypanosomiasis (HAT) completed recruitment, while the paediatric trial launched in July 2022.<sup>30</sup>

**Unmet R&D needs:** Kinetoplastid diseases (Chagas' disease, leishmaniasis and HAT) lack approved vaccines, and current development efforts are in their early stages.<sup>31</sup> Chagas', however, has a relatively full preclinical pipeline<sup>32</sup> and leishmaniasis a candidate in Phase II trials. Many gaps remain with respect to diagnosis: HAT requires a point-of-care test for *T.b. rhodesiense* (r-HAT), simpler confirmatory tests, tests of cure and high-volume testing on dried blood samples as endemic countries move towards surveillance and/or post-elimination maintenance.<sup>33</sup> The existing cutaneous leishmaniasis diagnostic, CL *Detect*, failed to demonstrate satisfactory standalone accuracy in various endemic settings,<sup>34-36</sup> underlining the importance of novel diagnostic tools, while Chagas' needs tests of cure and for congenital infection.<sup>37</sup> Improved and safer drugs are needed, particularly for r-HAT,<sup>38</sup> pregnant women infected with Chagas',<sup>39</sup> and oral drug regimens in leishmaniasis.<sup>40</sup> Biologics and therapeutic vaccines are of particular interest for Chagas', but still lack either a mature candidate or approved product.

Table 9. Kinetoplastid disease R&D funding 2021 (US\$ millions)

Die	ease	Basic reseat	orugs ,	Jaccines F	giologics r	Diagnostics	products	Inspecified	rotal o	10
L	eishmaniasis	18	21	1.2	-	0.2		<0.1	40	31
C	Chagas' disease	6.5	26	2.0	0.2	2.3	-	0.1	37	29
S	Sleeping sickness (HAT)	17	12	<0.1	-	0.3	-	-	30	23
	Multiple kinetoplastid liseases	2.4	20	-	-	-	-	<0.1	22	17
T	<sup>-</sup> otal	45	79	3.3	0.2	2.8	-	0.2	130	100

No reported funding

Table 10. Top kinetoplastid disease R&D funders 2021

	JS\$ (millio	nsl									021% of total
Funder	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	, 
US NIH	59	52	47	40	45	47	44	46	43	41	31
Aggregate industry	20	18	21	22	16	18	39	44	35	31	24
Wellcome	12	11	14	14	14	10	11	11	11	11	8.1
UK FCDO	10	9.3	14	14	15	25	24	22	21	7.3	5.6
Gates Foundation	10	10	22	3.1	15	11	8.6	5.3	6.5	5.2	4.0
EC	6.4	4.2	12	16	13	6.2	3.6	3.4	4.9	4.6	3.5
Dutch DGIS	2.6	5.1	4.2	0.9	5.1	4.0	4.6	3.9	1.9	4.5	3.5
German BMBF	6.1	4.6	6.1	3.5	1.9	3.3	3.0	3.3	7.1	4.3	3.3
UK MRC	1.6	2.3	3.2	2.6	3.5	3.5	3.7	4.3	3.8	3.0	2.3
German DFG	3.4	2.3	4.4	1.7	2.0	2.9	1.5			2.6	2.0
Brazilian FAPESP				1.6	2.7	2.4	2.7	3.7	2.4	2.3	1.8
Swiss SNSF	<0.1	1.8	2.4	1.2	1.8	2.1	2.1	3.3	3.0	2.1	1.6
Subtotal of top 12^	141	127	154	128	140	145	151	155	145	118	90
Disease total	156	141	169	141	161	166	173	174	162	130	100

 $<sup>^{\</sup>wedge}$  Subtotals for 2012-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

Category not included in G-FINDER

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.

# HELMINTH INFECTIONS (WORMS AND FLUKES)



Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$86.0m	2.1%	+0.2%		Public Philanthropic Private	Basic & early Late Unspecified

Global funding for helminth R&D was \$86m in 2021, almost unchanged following 2020's sharp (\$17m) decline. Adjusting for changes in participation, funding actually rose very slightly (by \$1.4m, 1.7%).

Shares of funding across different helminths remained relatively stable. Schistosomiasis again received the largest share (\$26m, 31%). Most of the remainder went to onchocerciasis (\$18m, 22%), followed by multiple helminth infections (\$13m, 14%) and lymphatic filariasis – which dropped to \$10m (11%) because of missing funder data.

In 2021, over half of **schistosomiasis** funding went to basic research, a record 91% of which came from the US NIH. Encouragingly, there was continued growth in funding for clinical development of vaccines, drugs and diagnostics, which has collectively risen from \$1.4m in 2018 to \$7.0m in 2021.

Participation-adjusted funding for **onchocerciasis** fell slightly (down \$0.5m, -2.8%), due to ongoing reductions in industry's drug clinical development, which has fallen steadily since 2018 (down \$12m, -72%). This year's further decline, though, was partly offset by increased funding from the Gates Foundation to DNDi, which is developing emodepside and flubentylosin in collaboration with Bayer and AbbVie, respectively.

Participation-adjusted funding targeting **multiple helminth infections** rebounded by \$1.8m (18%), after a large drop in 2020. The largest increase was for drug R&D, which received \$4.4m (up \$1.3m, 44%); though diagnostics saw proportionately faster growth (up \$1.2m, 154%).

While headline **lymphatic filariasis** funding continued to decline, for the fifth consecutive year, much of this drop was due to the absence of Indian ICMR data. Participation-adjusted funding fell only slightly (by \$0.7m, -8.7%), largely due to falls in industry funding of early-stage drug R&D (down \$0.9m, -69%). Overall, just \$0.2m of its funding was for clinical development, consistent with the two previous years.

Collectively, **tapeworm, hookworm, whipworm, strongyloidiasis** and **roundworm** received the remaining 22% (\$19m) of helminth funding. The NIH provided 89% of the overall funding across the latter four – and two-thirds for tapeworm – mostly split between basic research (\$7.7m, 74%) and drugs (\$2.1m, 21%).

In fact, across all helminth infections, the NIH accounted for half of the global total, with other public HIC funders accounting for almost another quarter. The next largest share was from philanthropic organisations (\$14m, 17%), while the private sector, mostly MNCs, contributed \$6.7m (7.8%), their funding nearly 75% below its 2018 peak.



In May 2022, NIAID initiated a Phase I trial of SchistoShield®, a schistosomiasis investigational vaccine based on a new, never before trialled antigen, Sm-p80.41 The Paediatric Praziquantel Consortium reported successful results from a pivotal Phase III trial of oro-dispersible praziquantel and has submitted a Letter of Intent to the EMA.42

**Unmet R&D needs:** Preventive chemotherapy in the form of mass drug administration or targeting specific groups such as preschool and school-aged children is the only medical countermeasure available for the control and elimination of helminthic diseases. Only one vaccine candidate, rSh28GST/Alhydrogel, targeting schistosomiasis, has ever reached an efficacy trial. Current vaccine development efforts are concentrated on hookworm, onchocerciasis and schistosomiasis, with most candidates either in pre-clinical development or human safety studies. The heavy reliance on preventive therapeutic agents, often as a monotherapy, has the potential to cause drug resistance. New therapies are urgently needed to counteract the future threat of resistance and overcome the shortcomings of current therapies, including child-friendly formulations and macrofillaricidal agents for onchocerciasis. The current therapeutic pipeline includes emodepside<sup>43</sup> and oxfendazole<sup>44,45</sup> for onchocerciasis, oxantel pamoate<sup>46,47</sup> for trichuriasis, tribendimidine for hookworm and TylAMac<sup>48</sup> for filariasis. Diagnosis remains reliant on stool/urine microscopy, underlining the need for rapid, point-of-care, molecular diagnostic tests which can detect resistance.

Table 11. Helminth R&D funding 2021 (US\$ millions)

Disease F	Basic resear	orugs \	Vaccines F	giologics [	Diagnostics	ector contro	unspecified	iotal o	10
Schistosomiasis (bilharziasis)	13	4.4	5.2	0.2	1.9	0.5	0.4	26	30
Onchocerciasis (river blindness)	2.7	13	0.8		1.9	<0.1	-	18	21
Lymphatic filariasis (elephantiasis)	5.2	1.9			1.8	<0.1	1.4	10	12
Tapeworm (taeniasis / cysticercosis)	5.4	0.6			0.7	-	0.9	7.5	8.7
Hookworm (ancylostomiasis & necatoriasis)	2.3	1.2	0.7				-	4.2	4.9
Whipworm (trichuriasis)	2.5	0.3					-	2.8	3.3
Strongyloidiasis & other intestinal roundworms	2.3	0.3	<0.1		0.1		-	2.8	3.3
Roundworm (ascariasis)	1.4	0.4					-	1.8	2.1
Multiple helminth infections	6.3	4.6	-		1.9	-	<0.1	13	15
Total	41	26	6.8	0.2	8.4	0.5	2.6	86	100

<sup>-</sup> No reported funding

Table 12. Top helminth R&D funders 2021

,	JS\$ (millio	ns)								0	021% of total
Funder	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
US NIH	42	33	33	32	35	42	39	44	41	43	50
Gates Foundation	22	25	27	20	20	15	18	9.9	8.9	12	14
Aggregate industry	4.6	9.4	14	13	8.9	11	23	16	8.8	6.7	7.8
German DFG	2.9	3.2	-	2.3	1.6	1.6	2.5	5.0	3.3	4.6	5.3
EC	8.1	7.9	7.5	5.4	3.9	3.4	1.2	2.2	4.1	4.2	4.9
German BMBF	1.2	0.7	0.3	0.3	0.1	4.0	3.7	5.6	2.9	3.5	4.1
Medicines Development for Global Health						3.2	1.2	2.3	2.5	2.4	2.8
Wellcome	6.2	7.5	4.9	4.0	3.9	3.6	2.8	2.3	1.6	1.6	1.8
Swiss SNSF	0.5	0.3	0.4	0.2	0.8	0.5	0.8	0.6	0.7	1.4	1.6
US DOD	-	-	-	-	0.6	-	-	1.3	1.3	1.2	1.4
The Task Force for Global Health		0.1			<0.1	0.5	1.4	1.0	0.3	0.8	0.9
UK MRC	2.3	2.0	2.8	1.4	1.2	0.8	1.5	1.6	0.7	0.4	0.5
Subtotal of top 12^	96	99	98	85	81	91	98	97	81	83	96
Disease total	102	103	101	87	83	96	104	103	86	86	100

<sup>^</sup> Subtotals for 2012-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

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.

Category not included in G-FINDER

<sup>-</sup> No reported funding

### **DENGUE**

2.4M DALYS 36K DEATHS IN 2019

Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$78.1m	1.9%	-2.6%		Public Philanthropic Private	■ Basic & early ■ Late Unspecified

Global funding for dengue basic research and product development was \$78m in 2021, a drop of \$2.1m (-2.6%). A little over half of the fall was due to net changes in survey participation, particularly the absence of Indian data. Even this slight fall left funding nearly \$43m below its 2016 peak, taking it to its lowest level since 2010.

As in all previous years, the US NIH (\$32m, 41%) and industry (\$28m, 36%) were the largest funders of dengue R&D. The overall fall in dengue funding resulted from sizeable reductions in funding from the Gates Foundation (down \$5.0m, -58%) – which fell to its lowest level since 2012 – and a much smaller fall from the US NIH (down \$1.1m, -3.2%). However, these drops were largely offset by a record high \$28m in industry funding (up \$6.9m, 33%), with multiple MNCs increasing their spending. Rising MNC funding, alongside cuts in spending from the NIH, took industry's share of global funding to a record 36%, with HIC public funding falling to a record low 52%.

Increased funding from industry helped push drug R&D to a record high \$36m (up \$11m, 46%), nearly three-quarters of which came from the private sector; although a near-doubling of the NIH's drug R&D (to \$8.1m) also contributed to the increase. The rise in industry drug funding was thanks to the progression of two different candidates through the pipeline, following completion of their preclinical studies in 2020: with J&J's JNJ-1802 reaching Phase II in 2022 and Novartis' EYU688 entering Phase I. This progress also contributed to record-high funding for clinical development, which rose to \$37m in 2021, \$10m above its previous high in 2019, marking a shift in the historical focus of dengue R&D from basic & early stage (71% of the pre-2021 total) towards clinical development (a record high 47% in 2021, from its previous average of 10%).

Aside from an increase in drug R&D and relatively stable diagnostics funding, all other dengue product areas experienced drops in funding. There were sharp reductions in funding for vector control products (down \$5.2m, -49%), basic research (down \$4.2m, -14% after adjusting for participation) and biologics (down to a record low \$2.1m, -45%), as an NIH-backed Phase I clinical trial of a monoclonal antibody candidate concluded in July 2021.



VIS 513, a broadly neutralising monoclonal antibody (mAb) developed by Visterra<sup>49</sup> that targets the E protein, present across all dengue serotypes, has progressed to Phase II clinical development and has been sub-licenced for further development by Serum Institute of India. Janssen's JNJ-1802, a direct-acting antiviral, commenced a Phase II human challenge study in collaboration with NIAID.<sup>50</sup>

**Unmet R&D needs:** Currently, no curative therapy is available for managing dengue fever. Effective therapeutic options are needed, including direct-acting antivirals and mAbs. Several such candidates are currently in early-stage clinical development, including Novartis' EYU 688 and Atea's AT-752.51,52 Point-of-care serological tests are already available but have many drawbacks.53 There is a pressing need for diagnostics that can function across the entire disease spectrum, distinguish dengue from other febrile illnesses, and for RDTs for serostatus screening. New and improved vector control products targeting the *Aedes* mosquito, including adulticidal oviposition traps and space spray insecticides, are needed, as well as biological control tools such as *Wolbachia* and genetic manipulation (with field experiments currently ongoing across Asia and Latin America). Dengue's prevalence in high- and upper-middle-income countries has attracted commercially focused industry investment in vaccine R&D; this category has therefore been excluded from the G-FINDER scope.

US\$ (millions)

Figure 6. Dengue R&D funding by product type 2012-2021

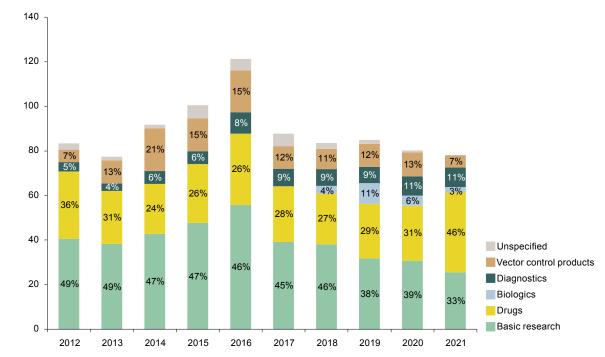


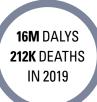
Table 13. Top dengue R&D funders 2021

-ger	5\$ millio	uel								2	021 % of to
under	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
US NIH	49	39	45	51	64	49	40	37	33	32	41
Aggregate industry	9.5	8.3	8.6	16	19	14	20	22	21	28	36
US DOD	0.7	1.4	0.2	1.1	1.9	3.9	3.3	3.7	5.6	4.8	6.2
Gates Foundation	1.0	11	17	8.0	14	5.1	4.7	7.0	8.7	3.7	4.7
Wellcome	5.2	3.7	6.6	6.2	6.1	3.7	2.9	2.7	2.7	2.6	3.3
Bio Manguinhos	-		-							1.2	1.5
Singapore Ministry of Health										1.0	1.3
Australian NHMRC	3.0	1.7	3.2	0.7	0.8	0.4	1.1	1.0	0.9	0.9	1.2
Thai National Science & Technology Agency	<0.1	0.1	0.2	0.1	0.1	0.1	<0.1	<0.1	0.8	0.8	1.1
Philippine Council for Health Research & Development							-		0.6	0.4	0.5
Inserm	-	-	-	3.7	1.2	0.7	0.2	0.4	0.4	0.4	0.5
EC	2.1	2.8	2.7	2.8	2.7	0.1	-	<0.1	0.2	0.3	0.4
Subtotal of top 12^	80	75	91	97	118	84	81	82	78	76	97
Disease total	83	78	92	100	121	88	84	85	80	78	100

 $<sup>^{\</sup>wedge}$  Subtotals for 2012-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021. 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

# SALMONELLA INFECTIONS



Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$71.1m	1.7%	-11%		Public Philanthropic Private	Basic & early Late Unspecified

Funding for Salmonella R&D dropped by \$8.4m (-11%) in 2021, continuing a downward trend from all three top funders, that has seen funding decrease by \$28m since 2018.

Funding to typhoid & paratyphoid fever dropped by \$7.4m in 2021, and by a total of \$22m since 2018, though it still received 75% of overall investment. Funding allocated to multiple *Salmonella* infections fell by a third (\$4.5m), while funding for non-typhoidal *S. enterica* (NTS) remained largely unchanged in real terms (and in line with its average over the last decade) despite the headline increase of \$3.5m, which was only due to new survey participants.

The overall drop in Salmonella funding was felt across all product areas, although most heavily in basic research (down \$3.9m, -10%) and vaccines (down \$2.3m, -6.7%), which together account for nearly all Salmonella funding (94%). The drop in vaccine funding was entirely for typhoid & paratyphoid fever (down \$5.1m), offset somewhat by smaller increases in vaccine funding for NTS and multiple Salmonella infections. Investment in Salmonella basic research has fallen every year since 2018, primarily due to reduced funding from the Gates Foundation. Drug funding dropped slightly, and remained almost entirely funded by the US NIH and focused on early-stage research for typhoid & paratyphoid fevers and multiple Salmonella infections.

Investment from Salmonella's two largest funders remained stable, with the US NIH providing 41% of the total, followed by industry with 19%. Although industry funding remained largely unchanged, this simply maintains the much lower level of funding post 2018, when, following the completed development of a typhoid conjugate vaccine (TCV), it dropped by \$18m. Investment from the Gates Foundation, the third largest funder, reduced by \$8.4m (-43%), due to the wrap-up of its support to IVI for the development of a low-cost typhoid conjugate vaccine, Vi-DT, which completed Phase III trials in 2021

Over two-thirds of all *Salmonella* funding was for basic & early-stage research, up ten percentage points thanks to an influx of early-stage vaccine funding (up \$6.4m, 176% between years), mostly from industry. A similarly-sized fall in industry's late-stage vaccine development saw clinical development funding fall by over a quarter to 27% of total funding).



A new typhoid conjugate vaccine (Vi-DT) completed a Phase III trial in 2021. Vi-DT was found to be immunologically non-inferior to the control, Typbar TCV. Three new vaccine candidates entered clinical trials in 2022; two combination vaccines targeting NTS and typhoid, and a first-in-human trial of typhoid and paratyphoid bivalent vaccine (TYP03/04).<sup>54-56</sup>

**Unmet R&D needs:** Typhoid can be successfully treated with available antibiotics. However, multidrugresistant (MDR) and extensively drug-resistant (XDR) strains of *S. typhi*, the causative agent of typhoid, have emerged and are spreading rapidly. The emergence of the XDR strain is especially alarming as it is resistant to almost all the available therapeutic options. There is an urgent need for a next generation of antibiotics that are effective against resistant strains. Current pipeline candidates include several broadspectrum antibiotics with the potential to be effective against drug-resistant strains of *S. typhi*, but most are in the pre-clinical stage of development. The WHO recommends typhoid conjugate vaccines (TCVs) as the preferred vaccine for use in *Salmonella* prophylaxis in endemic regions. Two such TCVs – Typbar TCV<sup>57</sup> and TYPHIBEV<sup>58</sup> are currently pre-qualified by the WHO.

Table 14. Salmonella R&D funding 2021 (US\$ millions)

(	jisease F	3asic reseat	urugs V	accines	Diagnostics	Juspecified	otal o	10
	Typhoid and paratyphoid fever (S. Typhi, S. Paratyphi A)	23	2.5	26	1.3	0.2	53	75
	Non-typhoidal S. enterica (NTS)	4.7	-	3.9	-	-	8.6	12
	Multiple Salmonella infections	6.2	0.2	2.8	0.2	<0.1	9.4	13
	Total	34	2.7	33	1.5	0.2	71	100

<sup>-</sup> No reported funding

Table 15. Top Salmonella R&D funders 2021

,	JS\$ (millio	ua)								2	021% of total
Funder	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
US NIH	38	36	34	32	44	34	38	38	29	29	41
Aggregate industry	5.0	11	18	16	27	26	28	10	13	13	19
Gates Foundation	6.0	11	7.8	14	14	17	17	20	19	11	15
Wellcome	5.6	5.2	4.1	3.7	3.3	2.7	2.6	4.0	5.7	5.8	8.2
EC	0.2	-	<0.1	<0.1	0.2	0.6	0.9	1.2	2.6	2.6	3.6
German DFG	1.0	1.4	2.1	0.5	2.0	1.8	2.3			1.9	2.7
CARB-X									-	1.5	2.1
UK MRC	1.3	1.5	2.0	2.5	2.3	2.0	2.6	2.4	1.2	1.2	1.7
Gavi	0.2	0.2		0.3	-	-	-	0.3	0.5	1.2	1.7
Swiss SNSF	0.7	-	0.9	0.5	0.7	0.8	0.4	0.6	1.1	0.8	1.1
UK DHSC						-	-	<0.1	-	0.7	1.0
UK NHS							-	0.2	0.5	0.5	0.7
Subtotal of top 12^	61	72	73	76	101	89	96	82	78	70	98
Disease total	63	73	74	77	104	91	99	85	80	71	100

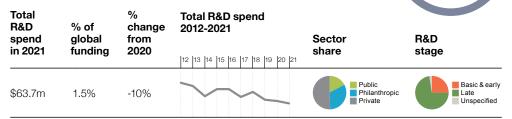
<sup>^</sup> Subtotals for 2012-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

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.

<sup>-</sup> No reported funding

# BACTERIAL PNEUMONIA & MENINGITIS

**65M** DALYS **1.2M** DEATHS IN 2017



Global funding for bacterial pneumonia & meningitis R&D totalled \$64m in 2021, its third consecutive decline (down \$6.9m, 9.8%), which took it to its lowest level since 2007. The drop was even larger – down \$8.6m (-12%) – when adjusted for rising survey participation. The reduction fell exclusively on pneumonia, which still received a near-record 87% of funding, whilst meningitis and R&D targeting both diseases rebounded a little from their record lows last year.

Industry (\$32m, 51%) and the Gates Foundation (\$17m, 26%) – the bellwethers of bacterial pneumonia & meningitis R&D – together accounted for over three-quarters of total funding. Both, however, reported lower funding in 2021 – a 22% (\$4.8m) drop from the Gates Foundation and 8.0% (\$2.8m) from industry – leaving them well below their historical averages. The Gates Foundation's decline drove philanthropic funding to its lowest point since 2014.

As always, **S. pneumoniae** received the largest share of funding (\$54m, 84%), well above the historical average of 75% despite a decrease of \$9.7m (-15%). The drop came from several funders, most prominently the Gates Foundation (down \$5.7m, -27%) and industry (down \$1.4m, -4.8%). The Gates Foundation reported reduced disbursements to industry for early-stage pneumococcal vaccine R&D (down \$7.9m, -64%) as a grant to create a paediatric vaccine for Gavi was closed out. All of industry's pneumococcal investment went to vaccines, almost entirely for clinical development & post-registration studies (\$27m, 94%) as very little early-stage R&D from industry is LMIC-specific.

**N. meningitidis** R&D investment rose from a historic low in 2020 to \$9.5m in 2021 (up \$2.7m, 39%), securing a 15% share of total bacterial pneumonia & meningitis R&D funding. The vast majority of the increase in meningitis R&D funding was for vaccines (up \$2.3m, 39%), mostly for clinical development. Much of the headline increase was due to changes in survey participation, with a true underlying increase of less than \$0.5m (7.2%) which was thanks to a near doubling of UK FCDO and Gates funding (up \$1.1m and \$0.5m, respectively) partly offset by a drop from LMIC-based SMEs (down \$1.4m, -28%).

Essentially all funding targeting **both pneumonia & meningitis** came from the Gates Foundation (\$0.4m, 98%) – via renewed funding under an ongoing diagnostics R&D grant – which replaced the UK MRC as the only substantial funder in this area.



NmCV-5, a pentavalent meningococcal vaccine co-developed by PATH and Serum Institute of India, already proven to be safe, well-tolerated, and capable of producing strong immune responses to all five serogroups has entered a pivotal Phase III trial, specifically designed to generate optimal evidence for a WHO pre-qualification.<sup>59</sup>

**Unmet R&D needs:** Pneumococcal conjugate vaccines (PCVs) are highly effective and have been rolled out in LMICs with favourable results with support from Gavi. However, they are typically expensive to manufacture. There is a need for low-cost candidates that offer broader protection for children against serotypes predominant in LMICs, as gains from existing PCVs are threatened by serotype replacement. Two potential approaches – non-conjugate protein-and whole-cell-based vaccines, both potentially offering broader protection and cheaper manufacturing cost, are being explored; but majority of candidates remain in preclinical development. The introduction of the MenAfriVac monovalent conjugate meningitis A vaccine culminated in a drastic reduction in meningitis A infection across the African continent, but other serogroups have become more prominent, creating the need for low-cost polyvalent vaccine candidates. Rapid diagnostic tests that can detect serogroups to guide vaccine response and multi-pathogen point-of-care tests to guide case management in both epidemic and endemic settings are also needed.

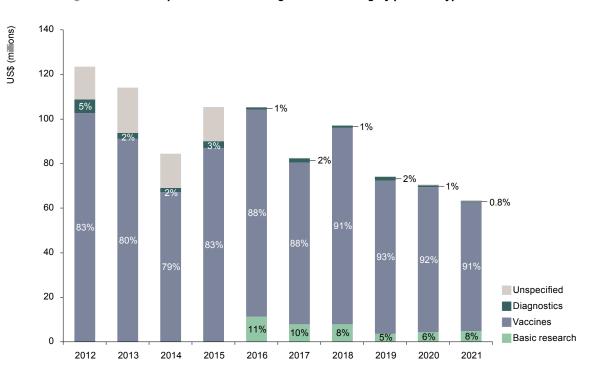


Figure 7. Bacterial pneumonia & meningitis R&D funding by product type 2012-2021

Table 16. Top bacterial pneumonia & meningitis R&D funders 2021

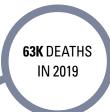
	JS\$ (millio	nsl									021 % of total
Funder	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	,9/
Aggregate industry	46	55	55	41	63	39	45	24	35	32	51
Gates Foundation	48	16	6.1	38	22	27	33	31	22	17	26
US NIH	9.8	7.2	2.5	1.4	3.8	2.5	2.5	1.3	3.3	3.3	5.1
Bio Manguinhos	0.1		0.3							2.3	3.6
UK FCDO	0.1	0.9	2.0	-	3.3	1.0	6.6	8.0	1.0	2.1	3.2
Gavi	6.1	12		7.1	5.3	5.3	2.9	3.2	2.4	2.0	3.1
Wellcome	3.5	2.0	2.1	1.2	1.0	0.4	<0.1	0.4	1.9	1.6	2.4
German DFG	0.4	2.8	3.0	1.9	2.5	2.6	2.9			1.1	1.8
Australian NHMRC	1.7	0.4	-	0.3	0.4	0.5	0.4	0.6	1.3	0.9	1.4
Institut Pasteur	0.6	0.3	0.3	0.5	0.7	2.0	0.8	1.3	0.3	0.4	0.6
UK MRC	0.3	0.6	0.6	0.9	1.9	1.2	0.9	1.8	1.8	0.4	0.6
Swedish Research Council	-	-	-	-	-		-	-	-	0.2	0.4
Subtotal of top 12^	123	114	84	105	104	82	97	74	71	63	99
Disease total	124	114	85	105	105	83	97	74	71	64	100

<sup>^</sup> Subtotals for 2012-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

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.

<sup>-</sup> No reported funding

# SNAKEBITE ENVENOMING



Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$17.8m	0.4%	+8.5%		Public Philanthropic Private	Basic & early Late Unspecified

Funding for snakebite envenoming (SBE) increased by \$1.4m (8.5%) in 2021, to \$18m. This was a smaller rise than in previous years, and partly reflects increased survey participation. Funding for SBE has grown every year since its 2018 inclusion in the survey, making it the only WHO NTD to enjoy robust funding growth.

Drugs and biologics (each with 43% of the total) received the bulk of overall investment, with 99% of drug R&D funding provided by the US DOD and Wellcome – also the top two overall funders in 2021. Both supported Ophirex's Phase II clinical trial of oral varespladib, the most advanced drug candidate currently in clinical development.

Overall biologics funding remained stable, though industry investment rebounded to \$1.5m – up from just \$55k – due to renewed investment from Inosan, the Mexican SME responsible for virtually all reported industry funding. Three other organisations provided at least \$1m for early-stage biologics R&D: Wellcome (\$1.5m), the EC (\$1.4m) and the US NIH (\$1.3m).

There was a significant drop in funding from UK FCDO, which had been the major funder of biologics over the last two years. Its funding – for IAVI's pre-clinical mAb project – dropped from \$4.3m in 2020 to \$0.6 in 2021. A new stream of biologics funding from Wellcome to IAVI covered some of the resulting shortfall, but raises questions about the project's long-term future, and that of the SBE pipeline generally, following the scheduled conclusion of Wellcome's funding in 2026.

There was another slight reduction in diagnostics R&D funding in 2021 (down \$0.1m to \$0.9m), leaving the UK DHSC as the lone funder, and the field still exclusively focused on early-stage research. This decline, and the lack of an advanced pipeline, may reflect a shift away from species identification – the main role for SBE diagnostics – in favour of broad-spectrum therapeutics.

While most funding since 2018 is from HIC public funders and philanthropic organisations, nearly 10% of global SBE funding has been provided by the LMIC public sector, including several public funders based in Brazil, Argentina, and India. This gives SBE the third largest share of LMIC funding among the G-FINDER neglected diseases over that period, although inconsistent survey participation from some of these funders means that the true LMIC funding share is likely even higher.



In early 2022, researchers from the Liverpool School of Tropical Medicine and Kenya Medical Research Institute, with funding from Wellcome, initiated a Phase I clinical trial of Unithiol<sup>64</sup> – a chelating agent which is routinely used to treat heavy metal poisoning – repurposed for treatment of snakebite.

**Unmet R&D needs:** Antibody-based antivenoms are the mainstay of snakebite envenomation treatment. These are effective, life-saving products if administered at the right time, in the correct dose, and for the right species. However, manufacturing immunobiologicals is expensive and complex, requiring harvesting and purifying immune-rich plasma from hyper-immunised large animals. The production of quality antivenom is hampered by the lack of a universal regulatory framework and appropriate reference standards, and geographical variations in the venom pool. Conventional anti-venoms are liquid or freezedried formulations requiring skilled professionals for administration, making them inappropriate in resource-limited settings. There is an urgent need to develop next-generation antivenom products that are safe, effective, geography-appropriate or polyvalent, and affordable for the low-income settings where they are most needed. The current research efforts include recombinantly expressed human antibodies and antibody fragments and small molecule therapeutics (SMT), including oral formulations. One such SMT – varespladib-methyl, is currently in a Phase II clinical trial.

Figure 8. Snakebite envenoming R&D funding by product type 2018-2021

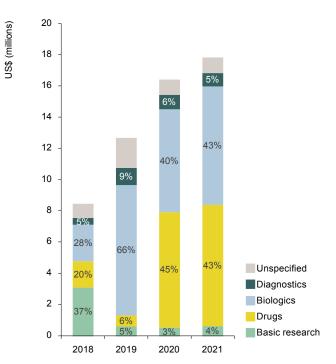


Table 17. Top snakebite envenoming R&D funders 2021

26t .	JS\$ (millio	ns)		7	027 % 04,	total
Funder	2018	2019	2020	2021		
US DOD	1.4	0.5	4.9	5.1	28	
Wellcome	0.3	0.4	2.7	4.4	25	
Aggregate industry	0.7	1.6	<0.1	1.5	8.6	
EC	-	-	0.6	1.4	8.1	
US NIH	0.1	0.2	0.2	1.3	7.5	
UK DHSC	0.3	1.0	0.9	0.9	4.8	
Center for Production and Research of Immunobiology		-	0.1	0.7	4.2	
UK FCDO	0.8	6.0	4.3	0.6	3.4	
Argentinian MINCYT	<0.1			0.5	3.1	
Brazilian FAPESP	0.3	0.2	0.2	0.3	1.9	
UKRI			<0.1	0.3	1.5	
UK NHS	1.3	0.9	0.9	0.2	1.2	
Subtotal of top 12^	7.4	13	16	17	97	
Disease total	8.5	13	16	18	100	

 $<sup>^{\</sup>wedge}$  Subtotals for 2018-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

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.

<sup>-</sup> No reported funding

### **HEPATITIS C**



Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$16.2m	0.4%	-6.5%	<b>-</b>	Public Philanthropic Private	Basic & early Late Unspecified

Global funding for hepatitis C R&D totalled \$16m in 2021, a decrease of 6.5% (\$1.1m), leaving funding well below its industry-driven peak in 2018.

This drop was mostly due to big cuts from Unitaid and MSF, who between them had accounted for more than 60% of 2020's funding – and less than 20% in 2021. Unitaid, following a three-year period over which they had provided \$12m for diagnostics R&D, reported no diagnostics funding in 2021, as the FIND-led HEAD-Started project wound up. This muted the impact of record diagnostic funding from the US NIH (up \$1.8m, 172%), and left overall diagnostics funding at just \$3.1m (down \$3.6m, -54%).

MSF's decrease fell largely on its drug R&D (down \$2.3m, -77%) as the Storm-C clinical trial results were published and conditional approval granted in Malaysia to the sofosbuvir/ravidasvir drug combination – the latter representing the first hepatitis C drug developed largely via South-South collaboration. This resulted in overall drug investment falling by a third (down \$2.7m, -33%).

These reductions from Unitaid and MSF were partly offset by \$6.6m in new NIH funding for early-stage vaccine R&D, along with the aforementioned \$1.8m increase in its diagnostics funding – both reaching record highs. This brought contributions from the US NIH to their highest level since 2013, with 85% of its 2021 funding coming via new programmes.

As a result of these shifts, vaccine R&D received the largest share of hepatitis C funding for the first time ever (\$7.7m, 48%), while investment in clinical development fell across all three product areas, reaching record lows in both amount and share (\$2.2m, 13% of the total).

Overall, the US NIH and Unitaid were the top two funders of hepatitis C R&D for the third year running, jointly responsible for 83% of global funding. Thanks to these two funders, and the Thai GPO – this year's only substantial LMIC public funder – the vast majority of hepatitis C R&D funding was from the public sector (\$15m, 91%). Reductions in funding from MSF and Wellcome drove philanthropic funding down by 61% (down \$2.4m), following three years of robust growth. Industry funding remained close to zero, following a peak in 2018 when it reached \$36m, with just one vaccine-focused MNC reporting any funding in the last two years.



A preventive vaccine based on E1/E2 glycoproteins induced broadly neutralising antibodies against all HCV genotypes in mice. 66 Glecaprevir and pibrentasvir combinations are currently in Phase III trials for acute hepatitis C infections and for paediatric populations. 67,68

**Unmet R&D needs:** Direct-acting antiviral (DAA) drugs are more effective, require a shorter duration of treatment, and have fewer side effects than previous interferon- and ribavirin-based treatments, and have revolutionised the treatment of hepatitis C. However, DAA-based regimens are expensive, and access remains limited in LMICs.<sup>69</sup> More research is also needed to assess DAA-based regimens in developing country populations, adolescents, children under 12, and pregnant or breastfeeding women. Despite extensive research efforts, the virus' genetic diversity and limited infection models have meant that no protective vaccine yet exists, with many candidates not maturing beyond preclinical and early clinical development.<sup>70</sup> A broadly reactive vaccine would prevent incidence of new infections and ideally elicit an antibody and cross-reactive T-cell response. There is also a need for HCV diagnostic tests that are affordable and simple to use in developing country contexts, especially tests for treatment monitoring, screening and tests of cure.<sup>71</sup>

Figure 9. Hepatitis C R&D funding by product type 2013-2021

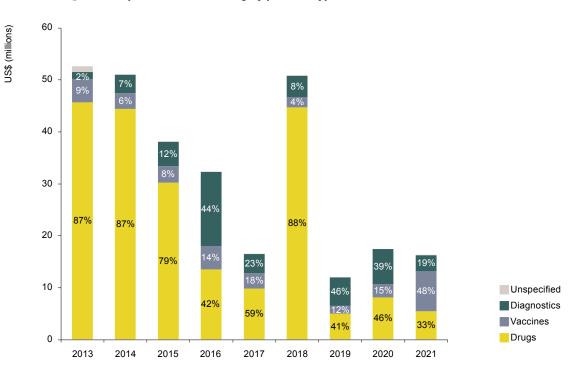


Table 18. Top hepatitis C R&D funders 2021

,	15\$ millo	ns)							o	021 % of tot
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	
US NIH	12	7.4	5.2	4.7	3.7	2.9	4.1	3.8	11	68
Unitaid	-	-	-	6.4	-	3.0	3.3	7.8	2.4	15
Wellcome	<0.1	<0.1	<0.1	<0.1	-	0.8	1.0	0.9	0.8	5.0
MSF	-	-	-	-	0.5	4.6	1.7	3.0	0.7	4.3
Thai GPO	<0.1	<0.1	0.3	0.1	0.3	0.5		1.0	0.4	2.4
French ANRS	2.1	10	4.7	5.2	2.5	1.6	0.8	-	0.3	1.6
Australian NHMRC	0.3	0.2	-	-	0.1	0.3	0.2	0.3	0.3	1.6
Canadian CIHR	-	-	-	0.6	0.1	<0.1	<0.1	0.1	0.1	0.7
Korean HIDI								0.1	0.1	0.6
UK MRC	0.4	0.4	0.4	0.4	0.3	0.4	<0.1	-	<0.1	0.5
Aggregate industry	31	29	24	11	8.1	36	-	<0.1	<0.1	<0.1
Argentinian CONICET	<0.1	-	-	-	-	-	-		<0.1	<0.1
Subtotal of top 12^	52	51	38	32	16	51	12	17	16	100
Disease total	53	51	38	32	16	51	12	17	16	100

<sup>^</sup> Subtotals for 2013-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

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.

<sup>-</sup> No reported funding

## **HEPATITIS B**

17M DALYS 510K DEATHS IN 2019

Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$15.9m	0.4%	-8.1%	5	Public Philanthropic	Basic & early Late Unspecified

Overall funding for hepatitis B R&D was \$16m in 2021, dropping 8.1% (down \$1.4m) from \$17m in 2020 – though still comfortably above the record low of \$10m in 2019.

A portion of the headline fall is due to an absence of 2021 Indian ICMR data, which provided \$0.9m in 2020, and to the depreciation of the Euro against the dollar, which slightly depressed the measured value of consistent EC funding. These factors together explain more than three-quarters of the drop in headline funding.

Alongside the fall in overall funding, the number of individual hepatitis B funders also fell sharply, from a peak of 22 organisations last year to a record low of 12 in 2021. Contributions from 2020's major funders held fairly steadily, with the US NIH providing \$5.9m (up \$0.6m, 11%), the EC \$4.8m (down \$0.1m, -2.5%, but constant in EUR terms) and Inserm \$2.4m (up \$0.2m, 72%). This left these three funders responsible for more than 80% of 2021's funding, up from 72% in 2020. Open Philanthropy, the fourth largest funder in 2020, did not provide any funding in 2021 following its \$1.0m standalone grant for hepatitis B drug development in 2020, likely intended to cover several years; leaving Wellcome – with \$0.5m, 2.9% of the total – as the only philanthropic donor.

Hepatitis B funding again largely went to LMIC-targeted biologics R&D, which received \$6.5m (41% of the total). This was followed by basic research – down slightly – with \$3.3m (21%), with remaining funding split fairly equally between drugs (\$2.0m, 13%) and diagnostics (\$1.7m, 11%).

Diagnostics R&D was the only area to receive additional funding in 2021, increasing by nearly \$1m to \$1.7m, due to growth in a single grant from the US DOD for rapid point-of-care diagnostics. The slight fall in overall funding landed mostly on basic research, while clinical development was essentially steady at \$3.5m, still significantly higher than prior to 2020, when the EC first began supporting the development of the TherVacB and IP-cure-B projects for the development of novel biologics to cure hepatitis B.

Investment from HIC public sources provided the vast majority of hepatitis B funding, contributing just under \$15m of the \$16m total. After record-low investment of just \$0.1m in 2020, industry reported no LMIC-focused hepatitis B R&D at all in 2021.



Vir Biotechnology's VIR-2218 (a small interfering ribonucleic acid) and VIR-3434 (a monoclonal antibody) in combination with pegylated interferon-α<sup>72</sup> and GSK's bepirovirsen (an antisense oligonucleotide)<sup>73,74</sup> recently showed promising results for seroclearance and hepatitis B surface antibody production, a feature not observed in current treatments. Both treatments belong to the novel post-transcription inhibitor class.<sup>75</sup>

**Unmet R&D needs:** An effective vaccine against HBV exists and has been included in 185 countries' national infant immunisation schedules. Current nucleos(t)ide analogues are safe, well tolerated and halt transmission; but life-long treatment is needed to avoid relapse. New therapies are aimed at a functional cure – sustained undetectable viraemia with or without antibody production – with multiple drugs and biologic combinations in clinical development. Tools to diagnose and treat HBV remain sub-optimal as standard serological assays detecting HBV surface antigen (HBsAg) are compromised by HIV/HCV coinfection, low HBsAG titres, and S gene mutations/variants. None of the available molecular tests are prequalified by WHO, and there is a need for low-cost, point-of-care molecular diagnostics that can quantify viral load, for confirmation of diagnosis, treatment monitoring, detection of drug resistance, and treatment initiation to prevent mother-to-child transmission. Epidemiological research in LMICs is needed to inform approaches to screening, monitoring and treatment, and advance understanding of drug and vaccine escape mutations.

US\$ (millions)

Figure 10. Hepatitis B R&D funding by product type 2018-2021

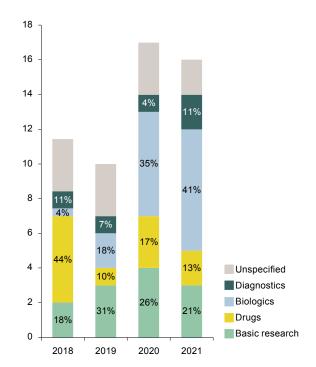


Table 19. Top hepatitis B R&D funders 2021

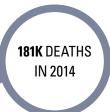
,	15\$ Imilio	nsl		0	1021 % of total
Funder	2018	2019	2020	2021	
US NIH	3.7	3.7	5.3	5.9	37
EC	-	-	5.0	4.8	30
Inserm	1.8	2.4	2.2	2.4	15
US DOD	-	-	0.4	1.4	9.0
Thai GPO	<0.1		0.3	0.5	3.3
Wellcome	-	0.5	0.5	0.5	2.9
Australian Centre for HIV and Hepatitis Virology		<0.1	0.1	0.1	0.6
South African MRC	-	<0.1	<0.1	<0.1	0.6
Chilean FONDECYT	-	<0.1	<0.1	<0.1	0.5
Indian Department of Science and Technology	-	<0.1	0.1	<0.1	0.4
Japan Society for the Promotion of Science (JSPS)	-	-	<0.1	<0.1	0.1
Brazilian FAPERO	<0.1		<0.1	<0.1	<0.1
Subtotal of top 12^	11	10	17	16	100
Disease total	11	10	17	16	100

<sup>^</sup> Subtotals for 2018-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

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.

<sup>-</sup> No reported funding

# CRYPTOCOCCAL MENINGITIS



Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$14.3m	0.3%	+97%		Public Philanthropic Private	Basic & early Late Unspecified

Cryptococcal meningitis drug and biologics R&D funding in 2021 totalled \$14m, a significant increase (up \$7.0m, 97%) from 2020, and a record high.

The entirety of this increase was due to newly-reported funding from a single SME – captured in our survey for the first time this year – but reflecting a genuine, recent industry-led surge in research interest into cryptococcal R&D.

Besides this influx of private sector funding, overall contributions from ongoing survey participants were almost unchanged, with a substantial drop in funding from the US NIH (down \$1.7m, -25%) – the top funder every year prior to 2021 – almost entirely offset by the resumption of funding from the UK MRC (\$1.6m).

Drug R&D continued to receive the lion's share of total funding – a record \$14m, 95% of the 2021 total – buoyed by the significant new private sector funding. The remaining \$0.7m (5.2%) went to biologics – the only other product included in our scope. This was also a record high, thanks in large part to the first ever biologics R&D investment from the NIH (\$0.7m), albeit one which came alongside a substantial fall in its funding for drug R&D (down \$2.4m, -36%).

Overall clinical development funding saw a substantial increase (up \$1.1m, 53%), thanks to resumed investment from the UK MRC, which is supporting Phase III trials of the fluconazole plus flucytosine combination drug regime in Tanzania and South Africa as part of the EFFECT trial. The EC also began a new stream of funding, its first ever for cryptococcal meningitis, supporting an early-stage drug target identification study.

The new funding from industry went to a mix of preclinical and clinical development of MAT2203, on oral formulation of amphotericin B, with 2021 work focused on Phase II trials.

The recent swell in industry funding meant that the private sector (50% of total funding) narrowly displaced HIC public funders (48%) as the largest source of funding in 2021. The small remaining funding came mostly from the philanthropic sector, with just \$5k – a record low – from LMIC governments.



A pivotal Phase III trial of Matinas BioPharma's MAT2203, an orally administered lipid-crystal nano-particle formulation of amphotericin B – with support from the US NIH – is expected to start in early 2023 following the drug meeting all its endpoints in the EnACT Phase II trial.<sup>79,80</sup>

**Unmet R&D needs:** Antifungal medications used for treating cryptococcal meningitis are effective, but poorly suited for use in developing countries. Amphotericin B is expensive and requires administration at a hospital, and flucytosine – another repurposed antifungal – requires careful blood monitoring. As a result, most developing countries resort to fluconazole use, which is only partially effective. <sup>81</sup> Notwithstanding the AMBITION-cm findings, <sup>82</sup> there remains a need for affordable, efficacious oral drugs, adapted for resource-poor settings. New antifungal agents, repurposed drugs and immunotherapies targeting various biochemical processes are in different stages of development, with many candidates showing promising activity against cryptococcal meningitis. <sup>83</sup> One such candidate, Mycovia Pharmaceutical's VT 1598, is in an ongoing Phase I trial. Monoclonal antibodies and immunomodulators alone or in combination with antifungal agents have been investigated, but there are currently no biological candidates in clinical trials. <sup>84,85</sup>

US\$ (millions)

Figure 11. Cryptococcal meningitis R&D funding by product type 2013-2021

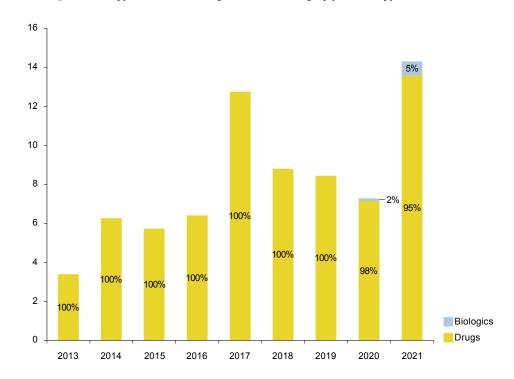


Table 20. Cryptococcal meningitis R&D funders 2021

۱ اهر	15\$ (millio	uel							2	021 % of tota
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	
Aggregate industry	-	-	-	-	-	-	-	-	7.1	50
US NIH	1.6	4.7	3.4	4.8	7.9	5.5	7.7	6.8	5.1	36
UK MRC	1.4	1.3	2.2	1.2	1.2	0.6	0.3	-	1.6	11
Wellcome	0.3	<0.1	<0.1	<0.1	0.4	0.5	0.4	0.4	0.4	2.5
EC	-	-	-	-	-	-	-	-	0.1	0.8
Institut Pasteur	-	-	-	-	-	-	-	<0.1	<0.1	0.5
Brazilian FAPESP				<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
Mexican CONACYT	-	-	-	-	-	-		0.1		-
Brazilian FAPEMIG			-	-	-	-	-	<0.1	1	-
Swiss SNSF	-	-	-	-	0.1	0.1	0.1	-	-	-
UK DHSC					1.9	1.2	-	-	-	-
UK FCDO	-	-	-	-	0.9	0.8	-	-	-	-
Disease total	3.4	6.3	5.7	6.4	13	8.8	8.4	7.3	14	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.

<sup>-</sup> No reported funding

### RHEUMATIC FEVER

**10M** DALYS **274K** DEATHS IN 2019

Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$9.2m	0.2%	-45%		■ Public	Basic & early Late Unspecified

Funding for rheumatic fever vaccines – the only product area included in the G-FINDER scope – fell to \$9.2m (-45%) in 2021, down \$7.6m from last year's all-time high of \$17m. This partly undid the effects of 2019's spike in funding, which saw contributions leap from a relatively consistent total of around \$2m a year to a little under \$15m, thanks to a new stream of funding from Australia's Medical Research Future Fund.

The majority of 2021 funding (82%) went to the Australia-based Telethon Kids Institute, most of it provided by the Medical Research Future Fund. Telethon Kids also received \$5.5m from Open Philanthropy in 2020 – a portion of the 2021 fall reflects Open Philanthropy's frontloaded disbursement of that three-year grant.

A further \$2.2m of the 2021 funding drop is due to the lack of further contributions from CARB-X to Vaxcyte. While CARB-X did not participate in the 2021 survey, its previously reported disbursements exhausted the announced value of the overall grant, meaning the absence of funding in 2021 is likely real, rather than artefactual.

The smallest portion of the overall drop in funding, but potentially the most concerning, is the absence of any funding from the Australian NHMRC (down from \$0.4m in 2020) which had, until now, provided R&D funding every year – totalling more than \$11m and accounting for more than a third of global rheumatic fever funding prior to 2019.

The second largest remaining funder in 2021 was the US NIH, with a \$1.4m, its largest total since 2007. The NIH has been a consistent contributor to rheumatic fever R&D over the life of the G-FINDER project, focusing on early-stage vaccine R&D and providing nearly a quarter of the global total over that time.

In the absence of any further philanthropic funding in 2021, all funding was from public organisations, mostly (82%) in Australia, reflecting the prevalence of rheumatic fever among Australian Indigenous communities. Public funders from three LMICs – Brazil, Argentina, Colombia – also provided funding in 2021, but together represented just 3.2% of the global total.

There has been no industry funding at all in the last seven years, and no substantial private sector funding since 2008/2009, when MNCs invested a little over \$3m over two years in early-stage vaccine research.



Two conjugated peptide vaccines, p\*17-CRM+K4S2-CRM and J8-CRM+K4S2-CRM, commenced a Phase I clinical trial in November 2022 after having successfully completed preclinical studies. The Phase I trial is designed to automatically transition to Phase II if no serious adverse effects are observed.<sup>86</sup>

**Unmet R&D needs:** Prophylactic use of antibiotics is the only preventive measure currently available for preventing rheumatic fever and its associated complications, such as rheumatic heart disease. Such widespread use of antibiotics is potentially vulnerable to and causative of antimicrobial resistance, meaning that a vaccine to prevent rheumatic fever is a much-needed medical countermeasure. Currently, the vaccine development pipeline is mostly at the stage of pre-clinical testing, and only a handful of candidates have undergone human safety trials. These include StreptAnova, the most advanced candidate, which successfully completed a Phase I trial in 2020.<sup>87</sup>

Figure 12. Rheumatic fever R&D funding by product type 2012-2021

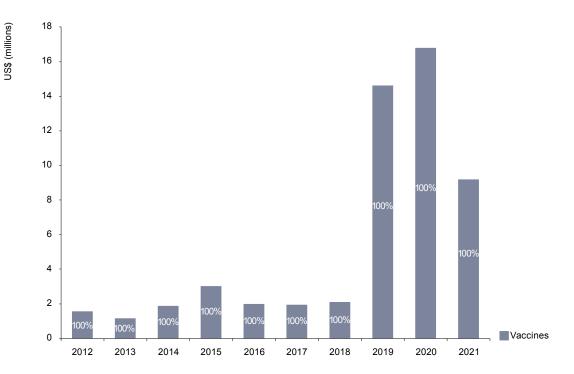


Table 21. Rheumatic fever R&D funders 2021

	15\$ milio	ns)								2	021% of tot
Funder	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
Australian MRFF								12	7.7	7.5	82
US NIH	0.6	0.6	0.6	1.2	1.0	0.9	1.2	1.1	1.0	1.4	15
Colombian Minciencias	-		-	-	-	-	-	-	-	0.3	2.9
Argentinian CONICET	-	-	-	-	-	-	-	-		<0.1	0.2
Brazilian FAPESP					-	-	-	-	<0.1	<0.1	0.2
Australian NHMRC	0.9	0.5	1.1	0.7	0.6	0.9	0.8	1.6	0.4	-	-
Open Philanthropy						-	-	-	5.5	-	-
CARB-X									2.2		-
Health Research Council of New Zealand (HRC)	-	-	-	0.7	0.4	-	0.1	0.1	-	-	-
Brazilian BNDES			-	0.5	-	-	-	-	-	-	-
Austrade					-	0.2	-	-	-		-
Austrian Science Fund (FWF)						-		<0.1			-
Disease total	1.6	1.2	1.9	3.0	2.0	1.9	2.1	15	17	9.2	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

### **LEPROSY**

29K DALYS O DEATHS IN 2019

Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$6.8m	0.2%	-21%	<b>\</b>	Public Philanthropic Private	Basic & early Late Unspecified

Reported funding for leprosy R&D dropped by \$1.8m (-21%) in 2021, falling to \$6.8m. However, this fall in funding was solely due to the near-complete absence of funding data from the Indian ICMR. The ICMR had reported a little over \$3m in leprosy R&D funding in 2020 – 36% of the total – and an average of \$3.6m over the previous decade. If we consider only funders for which data is available in both 2020 and 2021, leprosy R&D funding actually rose by \$0.8m (15%), partially rebounding from last year's fall.

The increase in (participation-adjusted) overall funding was largely thanks to a second consecutive increase in MNC drug funding, which rose by \$0.8m (87%) to \$1.7m. This growth reflects the ramping-up of Phase II trials for Bedaquiline, and helped to offset a second big drop in the UK MRC's basic research funding, which fell to \$60k (down \$123k, -67%) after peaking above \$1m just two years ago.

The combined result of these changes was that, whilst basic research continued to receive a majority of leprosy funding, its (participation-adjusted) share fell to a record low of 55% of the global total. Rising industry funding meant drug R&D received a record high of 32% of global funding (\$2.0m) up from an average of less than 2% over the first ten years of the G-FINDER survey. Vaccine funding – in scope only since 2018 – partly rebounded from last year's fall (up \$0.2m, 39%) as LepVax entered Phase Ib clinical development.

The growth in drug and vaccine development drove a sharp increase in overall clinical development, pushing it to a record high of \$2.5m (41% of the total).

Following a steep decline in 2020, the number of individual funders of leprosy R&D rose by four in 2021, including two first-time funders: Medicines Development for Global Health – an Australia-based non-profit product developer – and the Brazilian FAPESB. Overall, though, leprosy funding has become more concentrated, with the share of funding provided by the three biggest (ongoing) contributors – the US NIH, industry and ALM – rising from 75% to 82%, and the share (and scale) of philanthropic funding continuing its downward trend from a peak of 24% in 2017 to 14% in 2021 – leaving funding landscape increasingly reliant on the private sector maintaining its recently-increased commitments to leprosy R&D.



Phase II clinical evaluation of Bedaquline for therapy and post-exposure prophylaxis is ongoing, while development of the vaccine candidate LepVax has transitioned from Phase Ia to Ib/IIa. AMG 634,80 a compound for the treatment of Erythema Nodosum Leprosum, is being tested for efficacy and safety in a Phase II clinical trial in Nepal.80

**Unmet R&D needs:** Drug regimens used for leprosy treatment, though effective, require 6-24 months of treatment. With surveillance data suggesting emergence of resistance to first-line drugs in high-endemic countries, there is a growing need for drugs with simpler regimens and shorter treatments. WHO's recommendation of single-dose rifampicin as post-exposure prophylaxis constitutes major progress in disease prevention, though we still lack an effective preventive vaccine, with all but one candidate in early-stage development. Leprosy diagnosis is primarily based on clinical criteria and/ or positive microscopy of skin slit specimens. As both methods exhibit suboptimal sensitivity and specificity and rely on individual expertise, novel diagnostic tools are needed. He WHO Diagnostic Technical Advisory Group notes that gaps in the detection of infection, nerve loss function and prediction of future disease need to be addressed. In a proof-of-concept study, a multi-biomarker finger prick point-of-care test showed encouraging results in detecting infection and early-stage disease.

US\$ (millions)

Figure 13. Leprosy R&D funding by product type 2012-2021

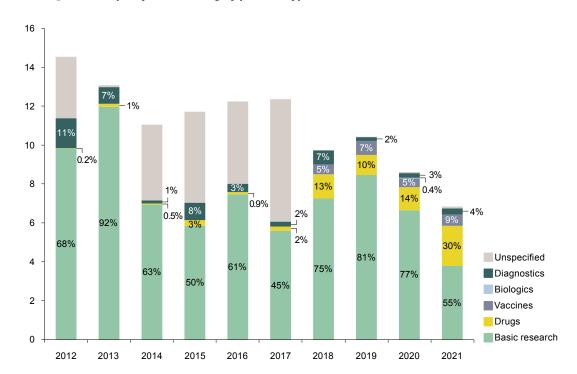


Table 22. Top leprosy R&D funders 2021

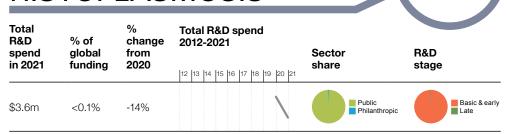
,	JS\$ (millic	ns)								2	021 % of to
under	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
US NIH	11	6.7	6.3	4.8	5.4	2.6	2.5	2.7	3.0	3.0	44
Aggregate industry	-	<0.1	<0.1	0.8	0.4	0.4	1.4	0.5	0.9	1.7	25
ALM	0.4	0.2	<0.1	-	-	0.1	0.6	0.5	0.3	0.4	6.5
German DFG	-	-	-	-	-	-	-			0.3	4.7
Raoul-Follereau Foundation	0.2	0.2	0.2					<0.1		0.2	3.1
effect:hope					0.1	0.7	0.7	0.2	0.2	0.2	2.7
Flemish EWI							<0.1			0.2	2.4
Leprosy Research Initiative				0.6	0.6	0.6	0.3	0.5	0.1	0.1	2.1
Medicines Development for Global Health						-	-	-	-	0.1	1.8
Inserm	-	-	-	-	<0.1	<0.1	<0.1	0.2	<0.1	0.1	1.5
Sasakawa Health Foundation (SHF)	-	-	-	-		-	-	-	<0.1	<0.1	1.1
Institut Pasteur	0.2	0.1	<0.1	0.1	0.1	-	-	-	0.1	<0.1	1.0
Subtotal of top 12^	14	13	11	12	12	12	9.4	10	8.5	6.6	96
Disease total	15	13	11	12	12	12	9.7	10	8.6	6.8	100

 $<sup>^{\</sup>wedge}$  Subtotals for 2012-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

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.

<sup>-</sup> No reported funding

# **HISTOPLASMOSIS**



In 2021, the second year of its inclusion in the G-FINDER report, global funding for histoplasmosis basic research and product development was \$3.6m. This represented less than 0.1% of total funding across all neglected diseases and a modest, but potentially concerning, fall of 14% (\$0.6m) from 2020.

Funding was concentrated almost exclusively on basic research (\$3.5m, 97%), following a slight decline in funding for drug R&D (down \$9k, -8.1% to \$98k), leaving it with just 2.7% of total histoplasmosis funding. There was a near complete absence of diagnostics funding (down \$0.5m to just \$14k), due to the absence of follow-up funding from the US NIH for both of its 2020 diagnostic grants.

As in 2020, only three funders – the US NIH, Brazilian FAPESP and the Fungal Infection Trust – reported disbursing funds for histoplasmosis R&D. Despite its cuts to diagnostic funding, the US NIH continued to dominate the landscape, again providing more than 99% of all funding, with the vast majority (97%) going to basic research and the remaining \$0.1m to early-stage drug R&D. This reliance on a single source of funding leaves the histoplasmosis R&D landscape vulnerable to even small shifts in funding priorities, and this year's 15% fall in NIH investments (down \$0.6m) underlines the urgent need for a more diversified funder base.

The small amount of non-NIH funding came from the Brazilian FAPESP – which continued to provide a little under \$5k for basic research – and the Fungal Infection Trust – a UK-based charity which in 2021 more than doubled its 2020 diagnostic investments (though still totalling just \$15k) for the field evaluation of histoplasma antigen tests. The latter represented both the only diagnostic funding and the only clinical development funding for histoplasmosis in 2021.



To improve the sensitivity of existing real-time quantitative PCR (qPCR) assays, the French Mycoses Study Group has developed a novel assay that amplifies whole nucleic acids of *Histoplasma spp.*<sup>97</sup> Clinical validation showed the test as highly sensitive, and able to perform *Histoplasma* detection from blood and bronchoalveolar lavage fluid.

**Unmet R&D needs:** Timely diagnosis and early start of treatment are critical for histoplasmosis management, as disseminated histoplasmosis is often fatal if left untreated. Clinical guidelines for managing histoplasmosis recommend a year-long treatment with liposomal amphotericin B and itraconazole. Though highly efficacious, the parenteral liposomal amphotericin B is heat unstable, and itraconazole presents significant drug-drug interaction with anti-tubercular and anti-retroviral medications, thus requiring monitoring of its blood concentrations, limiting LMIC use. There is a need for new treatments, preferably oral, with shorter duration, that are safe in combination with other therapies. Most new investigational agents are in early-stage development, with only the triterpenoid antifungal by Scynexis Inc., Ibrexafungerp, undergoing a Phase III trial for histoplasmosis. Current techniques for diagnosing Histoplasma are mainly laboratory-based with inconsistent sensitivity, making them unsuitable in poorresource settings. Highly sensitive and specific point-of-care tests, which are appropriate for LMIC settings are urgently needed – such as antigen-based RDT from MiraVista diagnostics.

Figure 14. Histoplasmosis R&D funding by product type 2020-2021

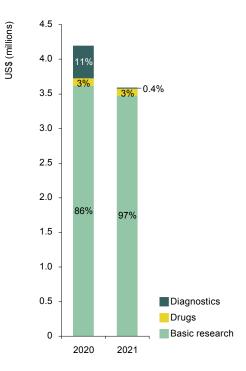


Table 23. Histoplasmosis R&D funders 2021

	under	15\$ millio	(ns)	027% 017	otal
۶	une	2020	2021		
	US NIH	4.2	3.6	99	
	Fungal Infection Trust	<0.1	<0.1	0.6	
	Brazilian FAPESP	<0.1	<0.1	0.1	
	Disease total	4.2	3.6	100	

## **SCABIES**

4.8M DALYS O DEATHS IN 2019

Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$2.0m	<0.1%	+50%	/	Public Philanthropic	Basic & early Late Unspecified

In 2021 – the second year of its inclusion in G-FINDER – scabies R&D funding LMIC-targeted basic research, drugs, and diagnostics rose to \$2.0m, up 50% (\$0.7m) from 2020.

Scabies drug R&D rose by \$0.6m (275%), leaving it with 45% of the overall funding, up from just 18% in 2020. This was largely driven by \$0.6m in new funding from Medicines Development for Global Health (MDGH) for a Phase II dose finding trial of single oral doses of moxidectin. This made MDGH the top funder in 2021, and also represented the only clinical development funding for scabies R&D in 2021. The only other drug investment was \$0.3m in ongoing funding from the Australian NHMRC to the Queensland Institute of Medical Research for early-stage drug R&D (\$0.3m, 29%).

Funding to LMIC-targeted basic research was \$0.7m (37% of the total) almost unchanged from 2020. This included continued investments from the Macquarie Group Foundation (\$0.4m, 61% of the basic research total) as part of the World Scabies program, and from the UK Government (\$0.3m, 39%) via the NIHR Global Health Research Unit on Neglected Tropical Diseases to improve outcomes for scabies infection. As in 2020, there was no reported funding specifically for diagnostics R&D, though a small portion of the NHMRC's funding targets advances in diagnosis alongside treatment and community control.

Contributions from the only three funders in 2020 – the NHMRC, Macquarie Group Foundation and the UK DHSC – remained essentially unchanged in 2021. Also, as in 2020, more than three-quarters (\$1.5m, 77%) of funding in 2021 came from the public sector in Australia and the UK, with the remainder provided by an Australian philanthropic organisation – the Macquarie Group Foundation. This Australia-centric picture of scabies R&D funding may partly reflect limitations in survey participation, but also signals a genuine and ongoing commitment to scabies R&D among funders and researchers in Australia, where scabies is a significant burden in Australian Indigenous communities.



In January 2022, Medicines Development for Global Health completed a Phase II proofof-concept study investigating the effectiveness of moxidectin in eliminating the scabies parasite.<sup>102</sup> Data from the completed trial will inform the dose-confirmatory Phase IIb trial, which is expected to start enrolling its first patient early in 2023.<sup>103</sup>

**Unmet R&D needs:** Due to the cost and limited availability of the most efficacious scabicide (permethrin 5% cream), many LMICs rely on less effective and less well-tolerated alternatives, such as benzyl benzoate and sulphur ointments. <sup>104</sup> Topical treatments often suffer from acceptability and compliance issues. Oral ivermectin, approved in many countries for the treatment of scabies, is highly effective but does not kill scabies eggs, necessitating repeat doses and increasing the difficulty of mass drug administration (MDA). Ivermectin is also contraindicated for children less than 15kg and for pregnant and breastfeeding women. <sup>105</sup> Thus, new oral drugs exhibiting prolonged skin activity, effective against newly hatched eggs, and usable by children and pregnant women are urgently needed. Novel diagnostics, such as molecular tests are at an early stage of development. There is an urgent need to develop point–of–care tests as an alternative to existing clinical examination and as a tool to guide ivermectin-based MDA. <sup>106</sup>

Figure 15. Scabies R&D funding by product type 2020-2021

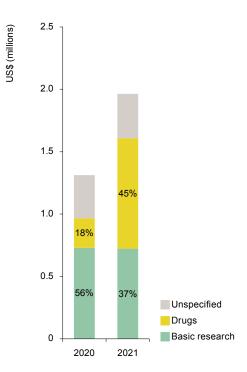


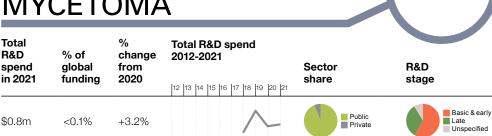
Table 24. Scabies R&D funders 2021

Funder	US\$ Imilli	ons)	027 % 013	iotal
Fulle	2020	2021		
Medicines Development for Global Health	-	0.6	32	
Australian NHMRC	0.6	0.6	31	
Macquarie Group Foundation	0.5	0.4	23	
UK DHSC	0.3	0.2	10	
UK NHS	-	<0.1	3.9	
Disease total	1.3	2.0	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.

<sup>-</sup> No reported funding

## **MYCETOMA**



Overall funding for mycetoma remained stable at \$0.8m in 2021, falling by just \$25k from its 2020 total. Mycetoma funding has remained low since its inclusion in the G-FINDER survey in 2018, reaching the \$1m mark only once - in 2019.

What little funding there was, was split relatively evenly between basic research and drugs, the only two areas with any reported funding. Basic research again received 55% of the total, with the remaining 45% again going to drug R&D. As in previous years, no funding was reported for mycetoma diagnostics, the only other product area included in the G-FINDER scope.

Funding for mycetoma R&D comes overwhelmingly from the HIC public sector, which in previous years has provided all of the reported funding. In 2021, however, we saw the first nontrivial industry funding for mycetoma R&D, with an investment of \$48k for Phase II drug development (6.0% of the global total for mycetoma).

The UK DHSC has been the top funder of mycetoma R&D since 2018, and in 2021 provided \$0.3m (40% of the total). In fact, overall UK government funding made up over half (54%) of 2021 mycetoma funding, all of which was invested in basic research conducted by the University of Sussex's Global Health Research Unit for Neglected Tropical Diseases.

Investment in mycetoma drug R&D was once again dominated by \$0.2m in funding from the Canton of Geneva (60% of drug funding), in line with its contributions in each of the previous two years. Its funding went to DNDi for a Phase II clinical trial of fosravuconazole in Sudan, the first of its kind for mycetoma. The initial tranche of funding for this trial predated mycetoma's 2018 inclusion in the G-FINDER survey, and was uncovered retrospectively: a total of \$2.3m from GHIT, commencing in 2017, to fund the Sudanese trial via a collaboration between DNDi, Eisai and the Mycetoma Research Centre in Sudan. This initial funding from GHIT more than doubles the cumulative value of mycetoma drug R&D funding reported since we began tracking funding in 2018.

A little over half (58%) of mycetoma funding was for basic & early-stage research, and just a third (33%) went to clinical development - though this represented nearly three-quarters of 2021's drug R&D funding.



A clinical trial investigating fosravuconazole, the only drug ever to undergo an efficacy trial for mycetoma treatment, was completed in late 2021. DNDi and its partners have established a strategy for registering fosravuconazole in Sudan for compassionate use in advance of full approval.107

Unmet R&D needs: The current standard treatment for mycetoma has a cure rate of around 30% and comes with serious side effects. More effective, less toxic drugs with shorter duration of treatment are urgently needed.<sup>108</sup> Aside from fosravuconazole, mycetoma drug R&D efforts are at a very early stage, such as DNDi's MycetOs, a screening project to identify new leads, and niclosamide, a repurposed drug which showed potential in in-vitro studies.<sup>109</sup> At present, mycetoma is diagnosed clinically, with identification of causative agents via histology and culture, techniques which require laboratory infrastructure and skilled practitioners. Specific diagnostics, such as PCR-based tests, are available only for research purposes. In 2022, the WHO published a target product profile (TPP) for a rapid test for diagnosis of mycetoma at the primary healthcare level. The TPP aims to facilitate the development of point-of-care tests that diagnose mycetoma and differentiate actinomycetoma and eumycetoma to allow initiation of appropriate treatments.

Figure 16. Mycetoma R&D funding by product type 2018-2021

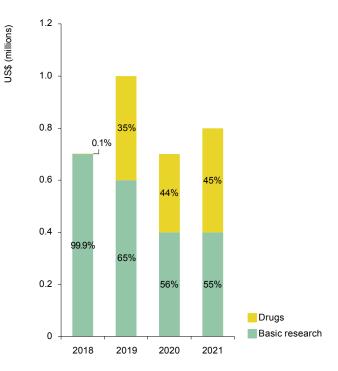


Table 25. Mycetoma R&D funders 2021

, det	15\$ millo	ns)		7	021% of tot	ial
Funder	2018	2019	2020	2021		
UK DHSC	0.5	0.6	0.4	0.3	40	
Canton of Geneva		0.2	0.2	0.2	27	
UK NHS	-	-	-	0.1	14	
US NIH	0.2	0.1	0.1	<0.1	12	
Aggregate industry	<0.1	-	-	<0.1	6.0	
Japan Society for the Promotion of Science (JSPS)	-	-	<0.1	<0.1	1.1	
Disease total	0.7	1.0	0.8	0.8	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.

<sup>-</sup> No reported funding

### **TRACHOMA**



Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$0.7m	<0.1%	-66%	<b>-</b>	■ Public	Basic & early Late Unspecified

Overall funding for trachoma R&D in 2021 fell to a record-low of \$0.7m, just a third of 2020's total of \$2.0m, and well below its previous low of \$1.3m in 2015.

This sudden drop in funding reflects the conclusion of the EC's three-year TracVac project early in 2021. Our estimate of the EC's 2021 funding is based – in the absence of disbursement data – on the pro-rated share of the project budget for the portion falling in 2021. If actual payments were front- or back-loaded, the fall may have arrived earlier or later than these figures suggest. The expiration of EC funding – which totalled \$8.2m and accounted for 83% of all trachoma R&D between 2017 and 2021 – leaves a huge gap in the funding landscape.

There was at least some positive news, with organisations which had seen their funding lapse – the US NIH and the Task Force for Global Health – resuming their contributions in 2021. The NIH had played a significant role in trachoma R&D funding between 2008 and 2016 – providing a total \$12m over that period – and in 2021 resumed funding after a four-year absence, providing \$0.2m for diagnostics R&D. The other returning funder, the Task Force for Global Health, had previously provided a total of \$79k for diagnostics R&D across 2018 and 2019, and contributed a further \$122k in 2021.

Trachoma has just two product areas, diagnostics and vaccines, included in the G-FINDER scope. Vaccine R&D had dominated the trachoma funding landscape for the past decade, but with the conclusion of the TracVac project this year, both diagnostics (\$0.4m, 53%) and vaccine R&D (\$0.3m, 47%) received roughly equal funding.

Nearly half (\$0.3m, 47%) of all 2021 trachoma R&D funding was for early-stage research, with just a fifth (\$0.1m, 18%) for clinical development – all of which was in diagnostic field development. This was the highest total for clinical development since 2016, and the highest for diagnostic field development since 2011.

Over 80% of trachoma funding came from HIC government sources in 2021, just below the 10-year average of 90%, with multilaterals providing the remainder. There has been no philanthropic funding since 2016, and none reported from industry in the last decade.

pipeline spotlight In a study examining samples from different epidemiological settings, two rapid lateral flow assays LFA – latex and LFA – gold, demonstrated promising and comparable results to ELISA immunoassays. Their low cost, lack of instrument requirements, and ease of training and use make these Rapid Diagnostic Tests an appealing option for post-validation surveillance.<sup>110</sup>

**Unmet R&D needs:** An effective vaccine would be a breakthrough development, given that the goal of eliminating trachoma as a public health problem is unlikely to be reached solely through the implementation of the existing SAFE (surgery; antibiotics; facial cleanliness; environmental improvement) strategy. <sup>111</sup> The trachoma vaccine pipeline is at an early stage of development. Only a few candidates have reached beyond the concept stage, such as VD1-MOMP ('TracVac'), designed to target ocular and genital serovars, which was found to be immunogenic in pre-clinical studies. <sup>112</sup>

3.5 - 3.0 - 2.5 - 2.0 - 1.5 - 30% 28% 10% 54% 59% 99% 100% 54% 59% Diagnostics

Figure 17. Trachoma R&D funding by product type 2012-2021

Table 26. Trachoma R&D funders 2021

2014

2015

2016

2017

2018

2019

2020

2021

Funder	15\$ millio	ns)								ว	021% 01.00	ial
Full	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021		
EC	-	-	-	-	-	1.8	2.1	2.0	2.0	0.3	47	
US NIH	1.7	1.7	1.0	1.1	1.5	-	-	-	-	0.2	35	
The Task Force for Global Health							<0.1	<0.1	-	0.1	18	
German DFG	-	0.2	-	-	0.8	1.1	-			-	-	
Institut Pasteur	-	0.1	0.1	-	0.1	0.1	-	-	-	-	-	
Wellcome	0.6	0.5	0.3	0.2	<0.1	-	-	-	-	-	-	
US CDC	-	-	0.1	-	-	-	-	-	-	-	-	
Disease total	2.3	2.5	1.5	1.3	2.5	3.0	2.1	2.0	2.0	0.7	100	

Vaccines

0

2012

2013

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.

<sup>-</sup> No reported funding

### **BURULI ULCER**



Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
\$0.6m	<0.1%	-76%	<b>\</b>	Public Philanthropic	Basic & early Late

Global funding for Buruli ulcer basic research and product development fell to just \$0.6m in 2021, down 76% (\$2.0m) from the previous year after a period of stagnation between 2018 and 2020. This left Buruli ulcer R&D at an alarming all-time low, \$1.5m (70%) below its previous lowest point in 2015.

Basic research received nearly 70% of total funding in 2021, as three key drug development programmes appeared to come to an end: there was no further drug funding from Institut Pasteur (down from \$0.2m in 2020), none from the US NIH (down from \$0.9m in 2020) as its five-year grant for early-stage Buruli ulcer drug R&D ended in 2020, and an end to a stream of private sector funding backing a combination of drug and diagnostic development. The absence of these funders left Wellcome as top funder in 2021, though largely by default: its \$0.2m contribution was essentially unchanged from 2020.

With the Institut Pasteur absent from basic research funding for the first time ever, Wellcome (\$0.2m, 54%) and Inserm (\$0.2m, 35%) were left responsible for the vast majority of basic & early-stage research funding. This was alongside \$44k in new funding from the Raoul-Follereau Foundation – after a year of non-participation – for the evaluation of GPR84 as a potential therapeutic target in *M. ulcerans* infection. The small amount of remaining basic & early-stage research funding – a little over \$33k – was from the Australian NHMRC to the University of Melbourne for vaccine R&D, signalling continuing interest from Australian researchers in Buruli ulcer vaccine development following several small Australian outbreaks.

Clinical development funding received only \$0.2m, which went exclusively to diagnostics, with the Medicor and Anesvad Foundations both providing funding for FIND's rapid diagnostic test evaluation studies.

Just six organisations provided Buruli ulcer funding in 2021, down from a peak of 14 in 2017. With the absence of funding from two previous major public funders – US NIH and Institut Pasteur – the bulk of investment in Buruli ulcer R&D in 2021 came from the philanthropic sector (\$0.4m, 70%). The remainder was provided by the high-income country public sector (\$0.2m, 30%), with no private sector investment reported in 2021.



A Phase II clinical trial of reducing treatment duration via expansion of the standard regimen to include amoxicillin/clavulanate is underway in Benin.<sup>113</sup> A larger study of f-TCL diagnosis conducted in Ghana showed over 80% diagnostic accuracy, suggesting its potential to become an ideal tool for diagnosing Buruli ulcer.<sup>114</sup>

**Unmet R&D needs:** Adoption of IS2404 PCR by national Buruli ulcer (BU) programs has dramatically improved diagnostic and epidemiological accuracy in endemic countries. However, there remains a need for simpler diagnostic tools allowing prompt and accurate diagnosis at the community level. BU-MYCOLAC, the first RDT designed to detect mycolactone, still needs clinical evaluation in endemic settings, <sup>115</sup> while other point-of-care molecular methods like BUD-LAMP require field evaluation. <sup>116</sup> Treatment of BU remains cumbersome – often complicated by paradoxical reactions – and lengthy, making development of new drugs a key priority. Telacebec, Clofazamine and TB47 are stand-alone or combination pipeline candidates – all still in preclinical or early clinical phases, <sup>117-119</sup> highlighting the need for acceleration and diversification of drug R&D. Tools for immunization against BU remain underdeveloped. All vaccine candidates are in early preclinical stages, while the widely available repurposed TB vaccine, BCG, vaccine provides only short-term protection and is no substitute for a targeted BU vaccine. <sup>120</sup>

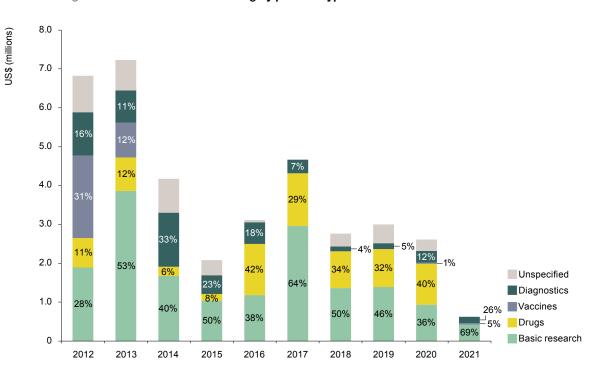


Figure 18. Buruli ulcer R&D funding by product type 2012-2021

Table 27. Buruli ulcer R&D funders 2021

,	15\$ Imilio	ns)								2	021% of total
Funder	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
Wellcome	0.3	0.3	0.2	<0.1	<0.1	0.3	0.3	0.3	0.3	0.2	37
Inserm	-	-	-	-	<0.1	<0.1	0.2	0.1	0.2	0.2	24
Medicor Foundation	0.2	0.2	0.2	0.4	0.1	0.3	<0.1	0.1	0.1	0.1	21
Raoul-Follereau Foundation	0.2	0.2	0.2					<0.1		<0.1	7.0
Australian NHMRC	<0.1	-	0.1	0.1	<0.1	1.4	0.3	0.6	0.3	<0.1	5.4
Anesvad Foundation						0.2			0.2	<0.1	4.6
US NIH	1.2	1.1	-	-	1.2	1.1	0.9	0.9	0.9	-	-
Institut Pasteur	0.4	0.4	0.5	0.5	0.6	0.3	0.1	0.2	0.3	-	-
Aggregate industry	-	-	-	-	-	-	0.3	0.5	0.3	-	-
Japan Society for the Promotion of Science (JSPS)							-	<0.1	<0.1	-	-
ALM	<0.1	0.2	0.2	-	-	-	-	<0.1	<0.1	-	-
Flemish EWI					0.3	0.2	0.2	0.1			-
Disease total	6.8	7.2	4.2	2.1	3.1	4.7	2.8	3.0	2.6	0.6	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

### **LEPTOSPIROSIS**

2.9M DALYS 59K DEATHS IN 2015

Total R&D spend in 2021	% of global funding	% change from 2020	Total R&D spend 2012-2021	Sector share	R&D stage
<\$0.1m	<0.1%	-98%		■ Public	Basic & early

Reported funding for leptospirosis diagnostics R&D – the only product area included in the G-FINDER scope – was just \$33k in 2021. This dramatic fall from 2020's total of \$1.4m is purely the result of an absence of data from the Indian ICMR, which provided 98% of leptospirosis funding in 2020.

As such, we have no reliable estimate for total funding in 2021.

This gap in our data underscores the significant extent to which leptospirosis diagnostics R&D is reliant on the contributions of a single funder – the Indian ICMR – which has seen its share of the global total rise from 47% in 2016, when it began providing funding, to 98% in 2020.



Researchers from Thailand recently reported that a CRISPR-based leptospiral rapid diagnostic assay targeting the lipL32 gene demonstrated acceptable sensitivity and excellent accuracy. The overall performance of the CRISPR-based molecular test was better than the commercial rapid diagnostic test.<sup>121</sup>

**Unmet R&D needs:** Leptospirosis can be effectively treated with antibiotics if diagnosed accurately and timely. Gold standard leptospirosis diagnosis during the acute phase of infection currently involves polymerase chain reaction (PCR) techniques, which require sophisticated laboratory equipment and technical expertise, making it inappropriate for resource-limited settings. There are several leptospirosis diagnostic test kits commercially available. However, the marketed tests have questionable sensitivity and specificity. The recently published Thai-Lepto AKI study revealed that the five leptospirosis RDTs commercially available in Thailand had overall sensitivity ranging from 1.8% to 75% and specificity ranging from 52.3% to 97.7%. This highlights the need for novel, easy-to-use, rapid diagnostic tests to accurately detect leptospirosis infection in LMIC settings.

Figure 19. Leptospirosis R&D funding by product type 2013-2021

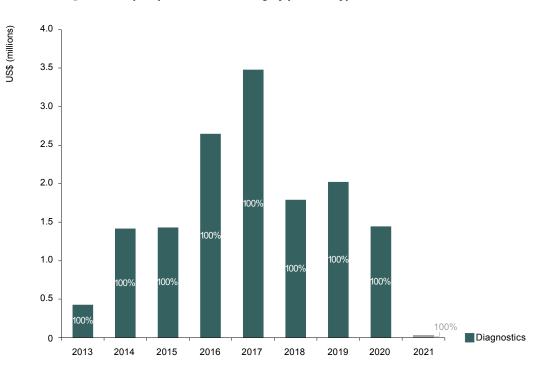


Table 28. Leptospirosis R&D funders 2021

-4e <sup>8</sup> /	US\$ (millio	ns)							2	021 % Of to
Funder	2013	2014	2015	2016	2017	2018	2019	2020*	2021	
Institut Pasteur	0.4	1.0	1.1	1.2	1.9	0.4	0.2	<0.1	<0.1	100
Indian ICMR	-	-	-	1.3	1.4	1.0	1.2	1.4		-
US NIH	-	0.3	0.3	-	-	0.3	0.6	-	-	-
Aggregate industry	-	-	-	-	<0.1	<0.1	-	-	-	-
Inserm	-	-	-	0.2	-	-	-	-	-	-
Colombian Minciencias		<0.1	-	-	-	-	-	-	-	-
plan:g	<0.1	-	-	-	-	-	-			-
Disease total	0.4	1.4	1.4	2.6	3.5	1.8	2.0	1.4	<0.1	100

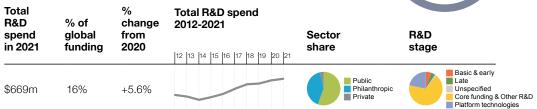
<sup>\*</sup> Data from 2020 represents the most recent accurate funding summary

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

# R&D FOR MORE THAN ONE DISEASE





G-FINDER includes four categories of funding that cannot be allocated to a specific neglected disease: core funding of a multi-disease organisation, platform technologies, multi-disease vector control products, and other R&D.

**Core funding** refers to non-earmarked funding given to organisations that work in multiple disease areas, where the distribution of funding across diseases is not determined by the funder.

**Platform technologies** are tools that can be applied to a range of areas, but which are not yet focused on a particular disease or product. The platform technology category includes vaccine, drug and biologics platforms; adjuvants and immunomodulators; and general diagnostic platforms.

The **multi-disease vector control product** category captures R&D funding for products that target vectors capable of transmitting several different diseases, including fundamental vector control research, biological and chemical VCPs and reservoir targeted vaccines.

The **Other R&D** category captures any remaining grants that cannot be otherwise allocated across individual diseases or other multi-disease categories.

Overall funding for non-disease-specific (NDS) R&D increased again in 2021, rising by \$36m (5.6%). This made 2021 the seventh consecutive year of growth in NDS funding, which has risen from \$188m in 2014 to \$670m in 2021.

Driving the somewhat slower overall growth were increases in all the underlying multi-disease categories, some much larger than others: investments for platform technologies rose by \$15m (12%), Other R&D by \$11m (19%), multi-disease vector control products by \$8.1m (12%) and core funding – still by far the largest single category – by just \$1.2m (0.3%).

The Gates Foundation provided a total of \$196m, making it once again the top funder of non-disease-specific R&D after increasing its funding for a seventh consecutive year, by a further \$23m. As in previous years, over half (53%) of all NDS funding came from the public sector in high-income countries, headlined by the EC, US NIH and US DOD. Most of the remaining funding (41%) came from philanthropic organisations.

#### CORE FUNDING

Core funding of multi-disease R&D organisations was almost unchanged at \$378m, maintaining the 2020 increase – and leaving it with well over half (57%) of all NDS funding.

As in each of the last two years, the top providers of core funding were the EC (\$113m, 30% of the total), the Gates Foundation (\$98m, 26%) and Wellcome (\$48m, 13%). Core funding from the EC rose sharply (up \$22m, 25%) while Gates funding (down \$4.4m, -4.3%) fell slightly. There was a more substantial decline from Wellcome (down \$8.1m, -15%) thanks to the conclusion of a long running funding stream to Mahidol Oxford Tropical Medicine Research Unit in Thailand. This was more than offset by a \$16m rebound in funding to GHIT from the Japanese government – reflecting typical cyclical fluctuations in its disbursements – which brought total Japanese government funding to GHIT to \$25m, nearly half of GHIT's total \$51m in core funding, and making GHIT the second largest core funding recipient.

The single largest recipient of core funding – accounting for nearly a third of the global total – was, once again, the EDCTP. The EDCTP continued to receive almost all of EC's core funding and, including its additional funding from other European government agencies – most prominently the German BMBF with \$8.8m – it received a near-record total of \$124m in 2021.

The most significant contributor to the drop in overall core funding in 2021 was the UK FCDO, whose funding to FIND – the sole recipient of FCDO core funding since 2018 – dropped by \$39m, albeit from the record high it established in 2020. This brought FCDO core funding to its lowest level since 2015. There were also substantial falls across other UK government agencies, including the UK DHSC – which provided no core funding in 2021, after having dropped from a high of \$50m in 2018 to just \$4.8m in 2020 – and the UK MRC, whose core funding also ceased after consistent contributions (averaging \$3.3m) in each of the previous six years.

Almost half of the Gates Foundation's core funding went to PATH (\$43m, 43%), with the stated aim of achieving progression of vaccine candidates through the pipeline, and another \$21m to the Gates Medical Research Institute.

#### PLATFORM TECHNOLOGIES

Platform technologies received \$146m in 2021, accounting for 22% of NDS funding and continuing their upward trend. This was an increase of \$15m over 2020 and marked platform funding's fourth consecutive year of growth.

Funding for drug-related platform technologies – which had historically received the lowest share of funding – increased significantly (up \$13m), almost tripling the total from 2020. The newly introduced standalone category of biologics platforms received \$11m. Funding for biologics platforms was previously captured as part of drug or vaccine platform R&D, but also represents a relatively new area of activity – at least in its application to neglected diseases – meaning the 2021 total is likely to be largely the product of recent funding growth.

Vaccine-related platforms again received the largest share of funding (35% of the platforms total), a slight decrease from 2020, with diagnostic platforms not far behind at 31%. Funding for adjuvants & immunomodulators, previously buoyed by a three-year jump in US NIH funding, decreased by a third (-\$8.1m), as NIH funding returned to pre-2018 levels.

Half of all platform technology funding in 2021 came from the Gates Foundation (\$74m), which increased its funding by \$20m. Nearly half of this funding (49%) was invested in vaccine platforms – meaning 70% of all 2021's vaccine platform R&D was backed by the Gates Foundation. The US DOD, a distant second with 21% of total platform funding, also increased their funding (by \$5.3m). This was offset by a similarly-sized (\$5.8m) decrease in platform funding from the US NIH, the third largest funder with 15% of the total. These three funders accounted for 86% of all platform technology funding.

The EC was the fourth largest funder of platform technology in 2021, their funding having grown by over 200% thanks to several new programmes, including Inno4Vac – a public-private partnership focused on addressing bottlenecks in vaccine development – and another backing the development of nano-pharmaceutical platforms. The Mexican CONACYT – first-time funders in this area – provided \$2.6m for vaccine-related platforms.

Open Philanthropy, which funded over \$18m worth of platform R&D across 2019 and 2020, did not report any new funding in 2021, having front-loaded their disbursements for an ongoing five-year research project on viral diagnostics. The Gates Foundation spread its 2021 platform funding across 54 different product developers, including 28 first-time recipients, none of which received more than \$4.6m. Around half of Gates platform funding went to universities and other research institutions, and most of the remainder to SMEs.

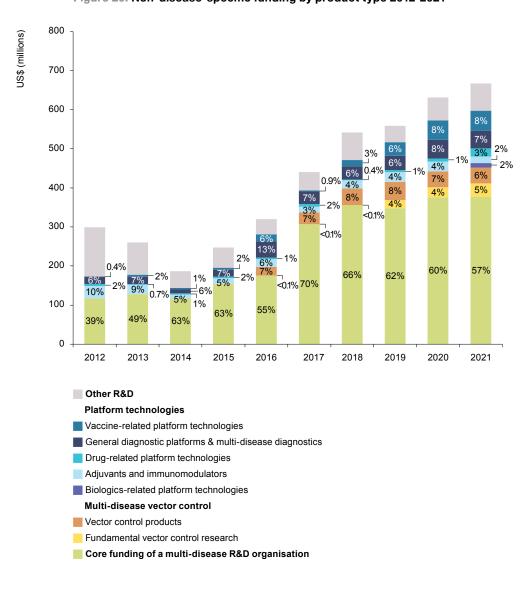


Figure 20. Non-disease-specific funding by product type 2012-2021

#### MULTI-DISEASE VECTOR CONTROL PRODUCTS

Funding for multi-disease vector control products (VCPs) increased to a record-high of \$75m (up \$7.5m), accounting for 11% of total non-disease-specific funding.

Almost half of this funding went to fundamental vector control research (46%), which increased by \$9.1m, building on rapid funding growth since its 2019 inclusion in the G-FINDER scope. Most of the remaining half was split between biological and chemical VCPs, with only minimal funding (just \$60k) for research into reservoir targeted vaccines (RTVs). The latter is the first funding we have seen for RTVs in the multi-disease category, reflecting the difficulty of developing vaccines which can inoculate reservoirs against multiple pathogens. Funding for chemical VCPs rose (by \$4.1m, 26%) while biological VCP spending dropped by \$5.3m (21%), due to the completion of a US NIH project investigating the use of *Wolbachia*-infected mosquitoes for reducing arbovirus transmission in Brazil.

Funding from the US NIH fell by \$6.1m (-19%) from last year's peak, though it remained the biggest funder of multi-disease VCPs, with a little over a third of the 2021 total. The Gates Foundation almost doubled its funding, to \$10m, though it remained a comparatively small share of its overall non-disease-specific funding. Unitaid, which first funded multi-disease VCPs in 2020, increased their funding by \$7.4m (a seven-fold increase) accounting for 11% of multi-disease VCP investment, supporting innovative repellents for mosquitoes. Both the US DOD and Wellcome saw their funding remain relatively stable – for the second year running – as they maintained support for ongoing projects.

#### OTHER R&D

Funding included under the catchall category of 'Other R&D' increased by \$11m to \$70m. Alongside increased 'other R&D' funding from the US NIH (26% of the total), the Gates Foundation (19%) and Wellcome (10%), much of the remaining increase was due to \$7.2m (10% of the total) from the UK DHSC for the Joint Global Health Trials programme, which was not able to be allocated to the individual trials included under the grant.

Table 29. Top non-disease-specific R&D funders 2021 (US\$ millions)

-tunder	Core funding	g Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease Julti-disease	ol afformologie echnologie	5 Other R&D	tal	
, in	Cove	lect 4	ech (	Office	rotal o	10
Gates Foundation	98	10	74	13	196	29
EC	113	3.0	8.5	1.1	126	19
US NIH	6.4	26	21	17	72	11
Wellcome	48	7.9	-	6.9	62	9.3
US DOD	-	7.9	30	4.2	42	6.3
Japanese government (including MOFA and MHLW)	25	-	-	-	25	3.7
Aggregate industry	22	-	-	2.6	24	3.6
German BMBF	12	0.4	0.5	0.5	13	2.0
Korean Ministry of Health & Welfare	8.4				8.4	1.3
Unitaid	-	8.4	-	-	8.4	1.3
UK FCDO	6.7	-	0.5	-	7.3	1.1
UK DHSC	-	-	-	7.2	7.2	1.1
Subtotal of top 12	339	64	135	53	592	88
Non-disease-specific total	378	75	146	70	669	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.

<sup>-</sup> No reported funding

### **NEGLECTED DISEASE FUNDERS**

Global funding for neglected disease basic research and product development totaled \$4,137m in 2021, a headline fall of \$44m, or 1.1%. Nearly fourth-fifths of the reduction (\$35m) was the result of a net dip in survey participation – particularly the absence of most Indian funding data. Higher inflation and the depreciation of most currencies against the US dollar (which we use to aggregate global funding) also depressed the measured total by more than \$25m – although some of this was probably artefactual rather than a genuine fall in buying power. In real terms, then, total funding was almost unchanged from 2020.

Despite a drop in funding from the public sector, it continued to provide nearly two thirds of global investment. High-income country (HIC) governments again provided the vast majority of this public funding (\$2,561m, 95% of public funding and 62% of the global total). The remainder came via public multilateral organisations (\$79m, representing a record-high 2.9% of public funding) and lowand middle-income country (LMIC) governments.

Philanthropic organisations again provided just over a fifth of global funding (\$842m), while private sector funding rose to \$608m, rebounding to 2019 levels and making up nearly 15% of the global total. Multinational pharmaceutical companies ('MNCs') continued to provide most of the private sector R&D funding (\$552m, 91% of the private total) with the remaining \$56m coming from small pharmaceutical & biotechnology firms ('SMEs').

This year's small (\$44m) drop in overall funding was mostly due to a somewhat larger fall in HIC public funding, which decreased by \$70m (-2.7%) to \$2,561m after three years of record and near-record funding. High-income country public funding remains comfortably above its pre-2018 average, but consecutive falls totaling more than \$160m begin to look like cause for concern.

There was better news from the private sector, with MNC's funding rebounding sharply (up \$72m, 15%) following two years of worryingly sharp drops from their 2018 peak. Funding from MNCs is now at its third-highest level in the 15 years covered by the G-FINDER survey, as is philanthropic funding, despite slumping slightly (down \$22m, -2.5%) after a near record high last year. Multilateral funding also enjoyed a banner year, rising by \$22m (39%) and contributing a record 1.9% of global funding and a near-record \$79m.

Funding from SMEs, on the other hand, fell slightly – once we account for their slight increase in survey participation – dropping by \$3.1m (-6.6%) to \$56m. This follows two years of stagnant SME funding at levels far below their previous average. The steep headline fall in LMIC funding, on the other hand, is misleading, and results only from the near-total absence of funding data from India – the top LMIC funder every year since 2008 and provider of nearly three-quarters of 2020's LMIC funding. The LMIC data we do have shows a slight increase in funding among ongoing survey participants (up \$3.1m, 9.7%), though this change is liable to being swamped by any (as yet unknown) 2021 shifts in Indian funding.

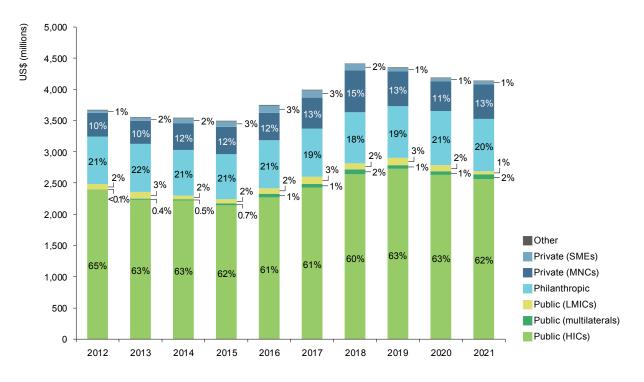


Figure 21. Total R&D funding by sector 2012-2021

### **Public funding**

The public sector invested \$2,685m in neglected disease basic research and product development in 2021. This was a decrease of \$102m (-3.7%) from 2020, and was the second consecutive year in which funding fell from its peak of nearly \$2.9bn in 2019.

As with overall funding, a substantial portion of the drop (43% in the case of public funding) was due to changes in survey participation – mostly the near complete absence of Indian funding data – and a smaller share (about 17%) due to higher inflation and depreciation against the US dollar.

Table 30. Top public R&D funders 2021

,	15\$ (millio	nel									027% 017
Country	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
United States of America	1,883	1,680	1,689	1,624	1,778	1,795	1,935	2,013	1,981	1,963	73
EC	103	123	122	147	88	127	133	133	176	202	7.5
United Kingdom	87	121	127	105	114	216	242	236	205	91	3.4
Germany	59	48	52	58	52	69	74	89	59	86	3.2
Australia	52	26	38	23	35	27	45	58	52	47	1.7
France	57	84	69	69	54	52	45	49	42	27	1.0
Japan	2.8	11	11	14	18	18	34	33	12	26	1.0
Switzerland	18	19	21	23	20	20	18	18	19	25	0.9
Netherlands	17	26	20	6.7	27	27	22	21	12	25	0.9
Brazil	16	13	7.1	7.3	12	8.1	13	13	10	14	0.5
Sweden	17	6.4	6.5	9.1	16	5.0	16	15	13	12	0.5
India	49	58	45	51	59	81	72	80	73	11	0.4
Subtotal of top 12^	2,378	2,230	2,214	2,140	2,276	2,463	2,655	2,756	2,657	2,529	94
Total public funding	2,485	2,355	2,302	2,240	2,415	2,596	2,820	2,898	2,786	2,685	100

<sup>^</sup> Subtotals for 2012-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021

#### FUNDING FROM HIGH-INCOME COUNTRIES

As in previous years, high-income countries (HICs) contributed the vast majority of funding for neglected disease R&D in 2021, together providing a total of \$2,561m (64% of global funding and 95% of the public sector total). While this was a decrease of \$70m (-2.7%) – or \$85m once we account for a slight improvement in survey participation – it still left HIC public funding at its fourth highest ever total, behind only the sustained peak between 2018 and 2020.

The US government (most prominently the NIH, DOD and USAID) remained the largest HIC public sector funder at \$1,963m, accounting for nearly 77% of total high-income public funding. US funding was basically unchanged (down 0.9%) from 2020, and still only a little below its 2019 peak, despite record-low funding from USAID.

The EC¹ became the second largest HIC public funder for the first time since 2015, contributing a record \$202m (7.9% of the total). This shift was the result of both the record funding from the EC (up \$25m, 14%) and a sharp decline in contributions from the UK – which had been the second biggest national funder since 2016. Neglected disease R&D investment by the UK government fell drastically in 2021, dropping by more than half to \$91m (down \$114m, -56%). The fall in UK funding was headlined by significant cuts from the FCDO, which reduced its investment by two-thirds (\$87m) to \$45m. These cuts impacted all the recipients of FCDO funding, especially FIND, which saw its FCDO funding drop by nearly \$40m (85%), albeit from a COVID-driven peak in 2020. Funding from the UK MRC also fell for its second consecutive year, from a peak of \$50m in 2019 to \$31m in 2021 (down \$15m, -32% from 2020). Funding from the UK DHSC also fell, for a third year in a row, to \$10m – leaving it at around a sixth of its 2018 peak, and down \$6.2m (-38%) from 2020 – largely driven by the complete cessation of its funding to the EDCTP.

<sup>&</sup>lt;sup>1</sup> The term 'EC' used here and throughout the report refers to funding from the European Union budget that is managed by the European Commission or related European Union partnerships and initiatives.

Reported funding from Germany rose sharply (up \$27m, 46%), but this mostly reflected the one-year absence of the DFG from the G-FINDER survey in 2020. The participation-adjusted change was a more modest increase of \$7.8m, and suggests German funding has likely experienced three years of relative stability at something close to its 2019 peak of \$89m. A \$16m fall in French funding is likewise exaggerated by changes in participation, with the true drop likely closer to \$8.8m. This is still, however, a record low for France, following substantial cuts from the ANRS, Institut Pasteur and IRD.

Funding from the Japanese Government continued to fluctuate in tandem with its contributions to GHIT – the recipient of 97% of Japan's 2021 funding – which rebounded by \$16m from last year's record low. The Dutch DGIS's funding also bounced back to \$25m (up \$13m, 120%), with the rise mostly dedicated to HIV vaccines, kinetoplastid drugs and TB drugs, via funding to IAVI, DNDi and TB alliance.

In absolute terms the overall reduction in public funding fell most heavily on the 'big three' diseases: HIV (down \$27m, -2.4%), malaria (down \$23m, -6.7%) and TB (down \$15m, -3.4%), along with kinetoplastid diseases (down \$21m, -22%) – the latter a result of cuts from the UK FCDO. However, the diseases with the sharpest proportional reduction in funding from high-income countries were Buruli ulcer (-90%) and trachoma (-72%), as programmes from their 2020 major funders – respectively the NIH and the EC – came to a close. Non-disease-specific funding from high-income countries continued its rise, reaching a new high of \$353m in 2021 (up \$12m, 3.6%).

Reductions in HIC public funding primarily impacted basic & early-stage research (down \$70m, -4.9%), though funding for clinical development & post-registration studies also dropped for a fourth consecutive year, falling to \$574m (down \$18m, -3.0%) – its lowest level since 2015.

#### FUNDING FROM PUBLIC MULTILATERALS

Funding from public multilaterals grew by \$22m (39%) in 2021, a rebound from the previous two years of decline, leaving it just below its 2018 peak. In the last five years, public multilaterals have contributed an average of nearly \$67m, or 1.6% of the global total, a tenfold increase from the \$6.2m a year they contributed over the first five years of the G-FINDER survey.

Most of this ongoing growth, and most of the 2021 increase, is thanks to Unitaid, which began contributing to neglected disease R&D in 2012 and has seen its funding grow from \$0.4m to nearly \$75m in 2021 – now representing 95% of the public multilateral total. Almost all the remaining funding came from either the World Bank (\$1.3m), the Task Force for Global Health (\$0.9m) or CARB-X, whose reported funding dropped by 31% to \$1.5m – likely only because it did not participate in this year's survey, leaving us reliant on partial reporting from its recipients.

Prior to this year, multilateral funders had devoted nearly half of their total funding (46%) to HIV, a little over a quarter (28%) to TB and 15% to malaria. In 2021, their HIV funding fell by nearly half, and their contributions to malaria and TB more than doubled (each up more than \$15m). This left multilateral funding much more concentrated on TB than in the past, and with less of a focus on HIV.

Table 31. Public (HIC and multilaterals) R&D funding by disease 2012-2021^

general control of the control of th	15\$ (millio	ns)								2	021 % of 3
aD a	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
HIV/AIDS	1,142	1,041	1,052	985	1,031	1,056	1,179	1,194	1,130	1,092	41
Tuberculosis	305	307	348	355	400	415	450	485	465	466	18
Malaria	321	322	316	311	336	388	363	368	359	350	13
Kinetoplastid diseases	102	93	103	93	105	114	103	101	98	77	2.9
Diarrhoeal diseases	96	99	94	82	64	73	77	70	74	74	2.8
Helminth infections (worms & flukes)	66	56	51	47	49	62	58	70	62	64	2.4
Dengue	61	51	56	66	76	58	49	45	43	41	1.5
Salmonella infections	45	45	44	43	59	45	49	47	37	39	1.5
Hepatitis B							9.5	7.6	14	15	0.6
Hepatitis C		15	22	14	20	7.2	8.5	8.7	12	14	0.5
Snakebite envenoming							6.5	9.1	12	10	0.4
Rheumatic fever	1.6	1.2	1.7	2.5	2.0	1.9	2.1	15	11	8.9	0.3
Bacterial pneumonia & meningitis	19	29	21	19	13	10	14	14	7.8	8.4	0.3
Cryptococcal meningitis		3.1	6.2	5.6	6.2	12	8.3	8.1	6.8	6.9	0.3
Leprosy	11	6.8	6.5	5.0	6.5	3.8	3.8	4.2	3.5	3.9	0.1
Histoplasmosis									4.2	3.6	0.1
Scabies									0.9	1.5	<0.1
Mycetoma							0.7	1.0	0.8	0.8	<0.1
Trachoma	1.7	2.0	1.2	1.1	2.4	3.0	2.1	2.0	2.0	0.7	<0.1
Buruli ulcer	3.8	4.5	0.8	1.0	2.5	3.8	2.1	2.0	1.8	0.2	<0.1
Leptospirosis		0.4	1.3	1.4	1.4	1.9	0.8	0.8	<0.1	<0.1	<0.1
Platform technologies	30	33	13	18	43	34	40	47	67	65	2.5
General diagnostic platforms & multi- disease diagnostics	8.3	9.5	6.7	13	30	24	21	18	30	33	1.2
Vaccine-related platform technologies	0.5	4.7	1.8	0.8	0.2	0.6	1.1	16	16	12	0.4
Drug-related platform technologies	0.1	-	0.7	0.7	0.7	0.8	1.0	1.2	2.4	9.9	0.4
Adjuvants and immunomodulators	21	18	3.8	3.6	12	8.0	16	12	18	7.6	0.3
Biologics-related platform technologies										3.2	0.1
Multi-disease vector control					14	27	31	41	51	55	2.1
Core funding of a multi-disease R&D organisation	74	73	66	85	69	143	216	218	188	197	7.5
Other R&D	118	65	37	36	24	29	44	26	37	45	1.7
Total public funding (HICs/multilaterals)	2,397	2,246	2,240	2,170	2,326	2,486	2,717	2,785	2,688	2,640	100

Hepatitis C, cryptococcal meningitis and leptospirosis were added to G-FINDER in 2013. Multi-disease vector control products were added in 2017; the 2016 total was added retrospectively, and likely understates true funding. Hepatitis B, mycetoma, and snakebite envenoming were added in 2018. Histoplasmosis and scabies were added in 2020. Biologics-related platform technologies were moved to a separate category in 2021.

<sup>^</sup> Please note that some of the diseases listed are actually groups of diseases, such as the diarrhoeal illnesses and helminth infections.

<sup>-</sup> No reported funding

#### PUBLIC FUNDING FROM LOW- AND MIDDLE-INCOME COUNTRIES

Although our headline figures suggest that there was a substantial drop in funding from LMIC public funders in 2021, this is solely due to the absence of funding data from two key Indian government organisations – the ICMR and BIRAC. Together these organisations provided nearly three-quarters of pre-2021 Indian funding, with India itself accounting for more than 60% of the LMIC total, with more funding than any other LMIC government in every year since it began participating in 2008. Adjusting for this big drop in survey participation, funding actually increased by \$3.1m (9.7%) in 2021. This slight rise in contributions from consistent survey participants was mostly thanks to increased funding from the Indian CSIR and the Brazilian FAPESP, and to near-record funding from Mexican public organisations.

It is difficult – and potentially misleading – to draw strong conclusions about shifts in the allocation of LMIC funding based only on partial, participation-adjusted totals. We *can* say that around half of LMIC funding typically goes to either malaria or TB, and that this will probably retrospectively prove to have been true for 2021, once the relevant Indian funding data becomes available. Of the 2021 Indian funding that was reported – largely from the DBT and CSIR – over half (58%) went to tuberculosis and about a fifth to malaria, broadly in line with these organisations' historical focus, and both slight increases on 2020. Overall funding from these participating Indian organisations rose by 21% (\$2.0m) in 2021, but there was a big drop in their funding to kinetoplastid diseases (down \$1.0m, 79% in 2021), mostly due to the end of multiple early-stage leishmaniasis projects.

Conversely, kinetoplastid diseases, and especially leishmaniasis, received the largest share of (participation adjusted) Brazilian funding (\$3.1m, 29%) after increasing by \$0.5m in 2021. Most of the increase in Brazilian funding, though, was due to record high investment in malaria vaccine R&D, which saw a 25-fold increase (up \$1.4m), helping to offset a \$1.5m drop in Brazilian funding for TB.

The only other meaningful shift in LMIC public funding on a participation-adjusted basis was the big rebound in LMIC platform funding, rising to \$3.0m from \$0.6m in 2020. This was concentrated on vaccine and diagnostic platforms, respectively funded by the South African MRC and Indian DBT, and represented the first diagnostic platform funding from the Indian DBT since 2012. The most substantial (participation-adjusted) drop in LMIC public funding was for HIV, which fell \$0.9m (-18%) to \$4.1m, leaving it well below its long-term average. This was due to 40% reductions from both South African funding organisations, contributing to an 8.7% drop in overall South African public funding.

Funding from Thailand increased by 30%, concentrated in funding for HIV drugs and offsetting a sharp (62%) drop in Thai funding to hepatitis C. The primary source of Mexican funding, the CONACYT, did not participate this year; but reports from its recipients imply a substantial increase in its 2021 contributions. There were also small amounts of 2021 funding reported from the Philippines, Colombia and Mozambique.

Table 32. Public (LMIC) R&D funding by disease 2012-2021^

and area	15\$ (millio	ns)								2	021 % of t
80	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
Tuberculosis	18	33	15	17	25	31	32	31	26	10	22
Malaria	21	19	10	14	15	22	22	24	20	5.8	13
HIV/AIDS	12	20	6.1	6.4	4.6	10	7.4	9.6	7.1	4.3	9.6
Kinetoplastid diseases	12	8.6	8.6	8.4	11	12	9.2	9.8	8.8	4.0	8.9
Dengue	6.3	3.4	3.3	3.9	6.3	7.4	7.0	7.7	5.2	3.3	7.4
Bacterial pneumonia & meningitis	0.2	<0.1	0.3	<0.1	0.6	<0.1	1.7	1.2	1.7	2.5	5.6
Snakebite envenoming							0.8	1.5	1.1	1.8	4.1
Hepatitis B							1.4	2.0	1.5	0.7	1.5
Helminth infections (worms & flukes)	2.9	1.9	2.6	2.1	2.0	3.3	2.5	3.7	3.3	0.6	1.2
Hepatitis C		6.0	0.2	0.8	0.4	0.7	0.8	0.6	1.1	0.4	0.9
Rheumatic fever	-	-	-	0.5	-	-	-	-	<0.1	0.3	0.7
Salmonella infections	0.4	0.6	0.7	0.2	0.6	0.3	2.0	2.5	2.3	0.3	0.6
Diarrhoeal diseases	4.6	5.9	6.0	6.3	8.1	7.9	7.3	5.4	6.7	0.1	0.2
_eprosy	1.9	4.8	4.0	5.3	4.5	6.6	2.5	3.9	3.1	0.1	0.2
Cryptococcal meningitis		-	-	-	<0.1	<0.1	<0.1	<0.1	0.2	<0.1	<0.1
Histoplasmosis									<0.1	<0.1	<0.1
_eptospirosis		-	<0.1	-	1.3	1.4	1.0	1.2	1.4	-	-
Platform technologies	4.9	0.6	0.3	1.4	3.3	1.5	1.2	3.1	1.8	6.9	15
Vaccine-related platform technologies	-	0.4	-	1.3	2.5	0.3	0.2	0.2	0.7	3.7	8.2
General diagnostic platforms & multi- disease diagnostics	0.5	<0.1	<0.1	<0.1	0.7	0.9	0.8	2.4	0.9	1.7	3.8
Drug-related platform technologies	4.3	<0.1	0.2	<0.1	0.1	0.3	0.1	0.5	<0.1	1.4	3.1
Biologics-related platform technologies										0.1	0.3
Adjuvants and immunomodulators	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
Multi-disease vector control					<0.1	1.0	0.3	1.6	1.0	1.3	2.9
Core funding of a multi-disease R&D organisation	-	0.5	0.3	3.0	4.1	2.3	1.7	0.5	0.6	<0.1	0.1
Other R&D	3.5	2.6	3.7	0.2	2.1	1.7	1.7	4.4	6.1	2.4	5.4
Total public funding (LMICs)	88	108	62	70	89	110	103	113	99	45	100

Hepatitis C, cryptococcal meningitis and leptospirosis were added to G-FINDER in 2013. Multi-disease vector control products were added in 2017; the 2016 total was added retrospectively, and likely understates true funding. Hepatitis B and snakebite envenoming were added in 2018. Histoplasmosis was added in 2020. Biologics-related platform technologies were moved to a separate category in 2021.

<sup>^</sup> Please note that some of the diseases listed are actually groups of diseases, such as the diarrhoeal illnesses and helminth infections.

<sup>-</sup> No reported funding

#### PUBLIC FUNDING BY GDP

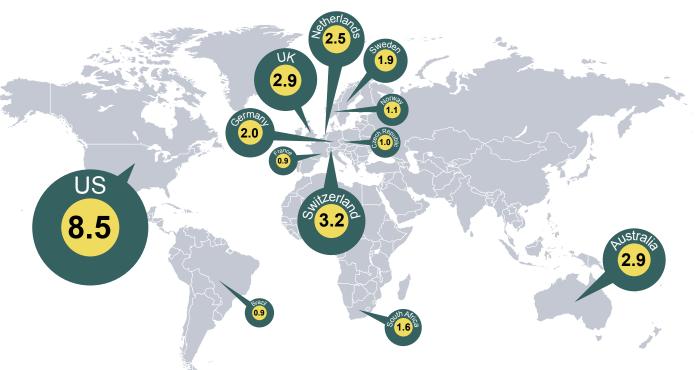
Absolute funding can be a misleading measure of public investment in neglected disease basic research and product development as it can understate the relative contributions of smaller countries and LMICs. For this reason, we also analyse countries' investments in relation to their gross domestic product (GDP).

When analysing by proportion of GDP rather than absolute funding, a slightly different picture of public funding emerges – one which gives greater recognition to the contributions of nations with smaller populations or lower income per head.

The US, though, remains the top public funder by share of GDP, devoting \$8.53 per \$100k of GDP to neglected disease R&D. Though this is down slightly from last year, it is still more than double the next highest share. The US was followed by Switzerland, which provided the eighth most funding in absolute terms, but the second highest share of GDP, at \$3.18 per \$100k. The UK, still narrowly the second largest provider of funding in real terms, fell in these rankings as investment from its biggest funding organisations – the FCDO and MRC – dropped sharply.

Three countries outside the top 12 largest funders appear here when ranked by their contributions relative to GDP: South Africa, Norway and Czech Republic. The absence of most funding data from India (fifth on last year's list) left South Africa – the 16th largest funder but the eighth highest share of GDP – and Brazil – the 10th largest with the 12th highest share – as the only LMICs to rank among the top twelve funders by GDP.

Figure 22. Public R&D funding by GDP 2021^\*
(A value of 10 is equivalent to an investment of 0.01% of GDP)



<sup>^</sup> GDP figures taken from International Monetary Fund (IMF) World Economic Outlook database

<sup>\*</sup> Figure provides value of (US\$ funding / GDP) \* 100,000

### Philanthropic funding

The philanthropic sector provided \$842m of neglected disease R&D funding in 2021, accounting for 20% of the global total. Philanthropic funding dropped substantially (down \$22m), mostly reversing the \$29m increase in 2020 – though it remained comfortably above its average over the previous decade.

As in all previous years, the Gates Foundation was 2021's primary philanthropic funder, contributing 79% of the total. This was its highest share since 2016 – reversing some of the recent diversification in philanthropic funding – and was thanks to both Gates funding's rise to its highest level in more than a decade (up \$11m to \$665m), and to substantial cuts from almost all of 2020's other top philanthropic funders. These cuts were headlined by a \$10m (-7.3%) drop from Wellcome, returning its funding to its 2018-19 levels, along with a 38% decrease from Open Philanthropy and 22% drops in funding from both MSF and Fundació La Caixa. Aside from Gates, only Gavi bucked the overall downward trend, its funding rebounding slightly from last year's record low.

Together, the top three philanthropic funders – Gates, Wellcome and Open Philanthropy – accounted for 96% of all philanthropic funding. The remainder came from 40 other philanthropic organisations, down from an average of 43 over the previous three years. Almost all the major shifts in philanthropic funding were driven by changes from the Gates Foundation. The only major exceptions were substantial falls in core funding from Wellcome, platform technology funding from Open Philanthropy, and hepatitis C funding from MSF.

The increase in overall Gates Foundation funding went to HIV R&D (up \$14m) and non-disease-specific funding (up \$23m) – mainly platform technologies – continuing an ongoing shift towards multi-disease R&D. There were falls in Gates' funding for malaria (down \$7.5m), TB (down \$6.4m) and particularly for *Salmonella* infections (down \$8.4m). The Gates Foundation's funding for bacterial pneumonia & meningitis and dengue also dropped, with the dengue fall driven by steep cuts in VCP spending, as their funding has shifted towards multi-disease VCP.

Wellcome's funding remained dominated by non-disease-specific funding (49% of the total), with another 15% invested in malaria R&D. The majority of Open Philanthropy's investment in 2021 was for malaria R&D (90%), with smaller amounts for diarrhoeal diseases, TB and helminth infections. While Open Philanthropy's actual disbursements dropped by \$10m from 2020, this mostly reflects frontloaded payments for multi-year projects over the preceding two years – particularly a \$5.5m, three-year rheumatic fever grant that was disbursed in full in 2020.

In line with similar overall shifts in global funding, drug R&D received the largest share of philanthropic funding in 2021, with just over a quarter of the total. This represents a change from previous years' focus on vaccine R&D, and comes as a result of a \$47m increase in drug funding – which went mostly to HIV – combined with a \$40m decrease for vaccines, also mostly in HIV. The increase in drug R&D was entirely thanks to new investment from the Gates Foundation, predominantly backing Phase III clinical trials of islatravir for HIV.

In line with recent years, more than half of total philanthropic funding (54%) in 2021 went to academic and other research institutions, while another 22% went to PDPs, a record low. Almost all the remainder (16%) went to industry organisations, with record-high philanthropic funding to MNCs thanks largely to that Gates Foundation investment in Phase III HIV drug trials.

This spike in funding for industry (up \$15m, 13%) contributed to a rebound in philanthropic funding for clinical development & post-registration studies (up \$31m from last year's decade low), though it remained far below its long-term average. Early-stage (down \$47m, -25%) and basic research (down \$9.6m, -12%) both fell to record lows, primarily due to drops in HIV biologics (down \$19m), TB drugs (down \$11m) and malaria vaccines (down \$10m).

Just over a fifth of philanthropic funding was distributed as core funding to multi-disease R&D organisations, the largest recipients of which were PATH, the University of Oxford and the Gates Medical Research Institute.

Table 33. Top philanthropic R&D funders 2021

<u>,</u>	Jes Imilionel								2021 % of total			
Funder	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021		
Gates Foundation	578	597	592	602	625	590	621	654	654	665	79	
Wellcome	138	127	119	92	113	116	127	129	138	128	15	
Open Philanthropy						8.5	4.6	14	26	16	1.9	
MSF	6.2	6.4	5.1	6.7	12	12	18	14	15	11	1.4	
Fundació La Caixa	3.0	3.4		3.9	3.8	5.5	3.5	5.0	5.7	4.5	0.5	
Individual donors and foundations	0.4	0.8	1.0	1.3	1.3	1.7	2.4	1.8	4.8	4.0	0.5	
Gavi	11	21		11	6.5	8.0	3.6	3.9	2.9	3.4	0.4	
Mundo Sano Foundation	<0.1			<0.1	<0.1	0.1	2.0	1.8	3.1	1.5	0.2	
Children's Investment Fund Foundation (CIFF)							-	1.5	1.6	1.1	0.1	
Swedish Heart-Lung Foundation								0.4	0.7	0.8	<0.1	
Anonymous funder							-	0.6	0.3	0.6	<0.1	
All other philanthropic organisations	24	16	11	8.1	6.9	34	29	7.8	12	4.9	0.6	
Total philanthropic funding	760	771	728	725	768	776	811	834	864	842	100	

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

<sup>-</sup> No reported funding

Table 34. Philanthropic R&D funding by disease 2012-2021^

gase or	15\$ (millio	nsl								Q'	021% of
80 a	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
Malaria	190	177	192	155	158	154	168	156	167	162	19
HIV/AIDS	178	165	151	145	162	158	148	166	140	150	18
Tuberculosis	135	161	167	159	125	121	138	145	142	134	16
Diarrhoeal diseases	54	70	52	55	63	62	58	56	37	38	4.6
Bacterial pneumonia & meningitis	58	31	8.3	46	29	33	36	35	26	21	2.4
Kinetoplastid diseases	23	22	37	18	30	22	22	19	20	18	2.2
Salmonella infections	12	16	12	18	17	20	20	25	28	18	2.2
Helminth infections (worms & flukes)	29	36	33	25	24	19	21	12	12	14	1.7
Dengue	6.6	15	24	14	20	8.9	7.6	9.7	11	6.2	0.7
Snakebite envenoming							0.5	0.6	2.9	4.4	0.5
Hepatitis C		0.1	0.1	<0.1	<0.1	0.5	5.4	2.7	3.9	1.5	0.2
Leprosy	1.7	1.3	0.5	0.7	0.8	1.5	2.0	1.7	1.1	1.1	0.1
Hepatitis B							-	0.9	1.4	0.5	<0.1
Scabies									0.5	0.4	<0.1
Buruli ulcer	3.0	2.7	3.4	1.1	0.6	0.9	0.4	0.5	0.6	0.4	<0.1
Cryptococcal meningitis		0.3	<0.1	<0.1	0.1	0.5	0.5	0.4	0.4	0.4	<0.1
Histoplasmosis									<0.1	<0.1	<0.1
Trachoma	0.6	0.5	0.3	0.2	<0.1	-	-	-	-	-	-
Rheumatic fever	-	-	-	-	-	-	-	-	5.5	-	-
Leptospirosis		<0.1	-	-	-	-	-	-	-	-	-
Platform technologies	22	17	13	21	38	22	30	51	62	74	8.8
Vaccine-related platform technologies	0.6	-	0.9	3.2	15	2.9	15	19	33	36	4.3
General diagnostic platforms & multi- disease diagnostics	10	9.3	4.3	4.6	12	6.2	10	15	17	11	1.3
Drug-related platform technologies	0.2	1.8	1.8	3.3	2.8	6.1	1.3	4.2	5.4	9.7	1.2
Adjuvants and immunomodulators	11	5.6	5.7	9.7	7.8	6.5	4.1	12	6.4	8.9	1.1
Biologics-related platform technologies										8.0	<0.1
Multi-disease vector control					7.2	2.4	8.4	22	13	18	2.2
Core funding of a multi-disease R&D organisation	44	48	34	53	83	136	126	120	173	159	19
Other R&D	2.6	8.5	1.5	14	11	14	19	11	15	20	2.4
Total philanthropic funding	760	771	728	725	768	776	811	834	864	842	100

Hepatitis C, cryptococcal meningitis and leptospirosis were added to G-FINDER in 2013. Multi-disease vector control products were added in 2017; the 2016 total was added retrospectively, and likely understates true funding. Hepatitis B and snakebite envenoming were added in 2018. Histoplasmosis and scabies were added in 2020. Biologics-related platform technologies were moved to a separate category in 2021.

<sup>^</sup> Please note that some of the diseases listed are actually groups of diseases, such as the diarrhoeal illnesses and helminth infections.

<sup>-</sup> No reported funding

## Private sector funding

The private sector invested a total of \$608m in neglected disease basic research and product development in 2021, accounting for 15% of global funding. This represented an increase of 15% (\$77m) from 2020. As in all previous years, multinational pharmaceutical companies ('MNCs') were responsible for the vast majority of this funding (\$552m, 91% of private sector investment), with small pharmaceutical and biotechnology firms ('SMEs') contributing the remainder (\$56m, 9.2%).

Investment in 2021 is essentially equal to the totals seen in both 2017 and 2019, reversing last year's sharp fall, though still below what now appears to be a one-off peak in 2018. Most of this year's increase was driven by near-record private sector funding for HIV/AIDS R&D (up \$70m, 47%).

#### MULTINATIONAL PHARMACEUTICAL COMPANIES

Investments from MNCs rose by 15% (up \$72m) to reach the third highest total ever reported. MNC funding for the top three diseases – HIV/AIDS, TB, and malaria – rose by 23% (up \$79m) to total more than three-quarters of MNC investment (\$428m, 78%), safely above the long-term average share for those diseases. MNC funding for the WHO neglected tropical diseases remained relatively stable, rebounding only slightly (up \$1.6m, 2.6%) following a significant fall in 2020 from its 2018-2019 peak.

The main driver of the overall growth in MNC investment was increased support for late-stage drug R&D, particularly for HIV/AIDS and TB. Total funding for HIV/AIDS increased by 46% (up \$69m) to a new record high, thanks mostly to new post-registration studies of a recently registered long-acting injectable. Tuberculosis R&D rebounded from a twelve-year low as funding increased by a quarter (up \$21m, 25%). This was largely a result of near-record MNC funding for late-stage tuberculosis drug development (\$74m, 73%) as investment from a key industry player rebounded further from its record low in 2019. Increased drug investment in three other diseases was also driven by record MNC contributions: dengue (up \$7.2m, 38% increase in total MNC investment), leprosy (up \$0.8m, 87%), and the first nontrivial MNC funding for mycetoma R&D (<\$0.1m). Malaria R&D investment fell for the third consecutive year (down \$10m, -8.8%) from its peak in 2018, with the reduction heavily focused on drug R&D (down \$8.9m, -11%).

MNC investment in diarrhoeal disease R&D fell by half (down \$18m, -50%), with the cuts felt mostly in vaccines (down \$16m, -54%). Funding for late-stage diarrhoeal disease vaccine development almost disappeared (down \$18m, -93%) following the completion of LMIC-based studies for the development of a porcine circovirus-free liquid formulation of Rotarix.

Over two-thirds of 2021 MNC investment went to drug R&D (\$387m, 70%) – an increase of 24% (\$74m) – which lifted it to its highest ever share of funding, and the second highest amount ever. Vaccine investment fell for a third consecutive year to a ten-year low of \$135m (down \$11m, -7.7%), dropping it to a 24% share of MNC investment – well below the historical average of 36%. MNC's diagnostic funding – always a small part of their overall portfolio – more than doubled to a record high of just \$1.3m. This still represented just 0.2% of their total funding, mostly for the clinical evaluation of an Al-based multiple-helminth diagnostic.

A near-record 72% (\$398m) of MNC investment was for clinical development & post-registration studies, with most of the remainder for early-stage research (\$122m, 22%). Funding for late-stage development rebounded from last year's fall (up \$78m, 24%), taking overall clinical development & post-registration studies investment to its second highest amount on record, though still well below the 2018 peak of \$471m.

Table 35. MNC R&D funding 2012-2021^

35 <sup>e</sup> 0 <sup>1</sup>	JS\$ (millic	ins)								7	021 % of tr
section (	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
HIV/AIDS	17	11	45	53	87	151	214	200	148	217	39
Malaria	113	81	128	154	150	148	174	127	117	106	19
Tuberculosis	142	119	106	103	94	94	104	87	84	105	19
Kinetoplastid diseases	19	18	13	17	14	18	39	44	35	31	5.6
Dengue	9.2	8.3	8.4	16	16	13	17	20	19	26	4.7
Diarrhoeal diseases	31	43	34	23	16	29	43	45	35	18	3.2
Bacterial pneumonia & meningitis	40	34	36	13	23	2.1	4.2	4.2	13	10	1.9
Helminth infections (worms & flukes)	3.8	9.3	7.5	12	8.8	10	23	16	8.7	6.7	1.2
Salmonella infections	4.6	4.6	4.2	3.8	4.4	2.2	1.6	1.8	3.9	6.5	1.2
Leprosy	-	<0.1	<0.1	0.8	0.4	0.4	1.3	0.4	0.9	1.7	0.3
Mycetoma							<0.1	-	-	<0.1	<0.1
Hepatitis C		31	29	24	7.5	5.6	36	-	<0.1	<0.1	<0.1
Buruli ulcer	-	-	-	-	-	-	0.3	0.5	0.3	-	-
Rheumatic fever	-	-	0.2	-	-	-	-	-	-	-	-
Multi-disease vector control						-	3.8	3.8	-	-	-
Core funding of a multi-disease R&D organisation	-	4.4	15	15	21	26	14	10	15	22	3.9
Other R&D	1.6	6.4	1.5	0.8	0.7	0.7	4.5	<0.1	0.7	2.5	0.5
Total MNC funding	381	370	429	435	443	501	678	560	480	552	100

Hepatitis C was added to G-FINDER in 2013. Multi-disease vector control products were added in 2017. Mycetoma was added in 2018.

#### SMALL PHARMACEUTICAL & BIOTECHNOLOGY COMPANIES

Small pharmaceutical & biotechnology companies allocate their neglected disease R&D funding very differently to MNCs: combined funding for HIV, TB and malaria accounts for just 20% of their total, reflecting a post-2012 shift away from these diseases. Instead, funding from SMEs has favoured bacterial pneumonia & meningitis, which received 39% of total SME investment in 2021 (\$22m).

SME investment rose by 11% in 2021 (up \$5.5m) to around half its peak in 2016. This headline increase was a result of a new participant, which reported funding for cryptococcal meningitis (\$7.1m) for research efforts that began before 2021 but were captured in our survey for the first time this year. This represented the first SME funding for cryptococcal meningitis captured in the G-FINDER survey, all of which went to drug R&D. Funding from consistent survey participants actually fell slightly (by \$3.1m, -6.6%).

SME funding for tuberculosis (up \$1.7m, 30%) and HIV/AIDS (up \$1.4m, 90%) rose from record lows, with much of the increase directed towards clinical development. SME investment in snakebite envenoming R&D also rebounded from a record low (up \$1.5m, 2,667%), with the additional funding largely focused on early-stage development of biologics.

<sup>^</sup> Please note that some of the diseases listed are actually groups of diseases, such as the diarrhoeal illnesses and helminth infections.

<sup>-</sup> No reported funding

Salmonella R&D investment saw the largest disease-specific decrease, as funding dropped by a quarter (down \$2.3m) – the cuts falling mostly on clinical development of typhoid and paratyphoid vaccines. SME investment in non-disease-specific R&D almost disappeared (down \$2.5m, -98%), following a record high in 2020. Much of the decrease was felt in spending on adjuvants & immunomodulators, alongside a largely artefactual fall in multi-disease vector control funding, driven by the absence of further data from a major 2020 funder.

The majority (67%) of SME funding again went to clinical development & post-registration studies, though it dropped slightly in 2021 (down \$3.3m, -8.1%). Most of the remaining funding went to early-stage research (\$9.2m, 17%).

LMIC-based SMEs continued to provide a clear majority of global SME investment in neglected diseases, as they have since 2013, accounting for two-thirds of SME funding in 2021 (\$37m, 66%) – virtually all of which came from India-based SMEs.

Table 36. SME R&D funding 2012-2021^

adase or	5\$ milic	nsl								2	021 % of
a de la companya de l	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
Bacterial pneumonia & meningitis	6.1	20	20	27	40	37	41	20	22	22	39
Tuberculosis	10	5.7	9.2	11	10	16	6.6	6.4	5.5	7.2	13
Cryptococcal meningitis		-	-	-	-	-	-	-	-	7.1	13
Salmonella infections	0.4	6.7	13	12	23	24	26	8.7	9.1	6.8	12
Diarrhoeal diseases	3.0	7.0	10	15	18	10	8.5	6.1	5.8	5.3	9.6
HIV/AIDS	8.4	7.1	7.1	9.5	8.3	15	8.0	1.6	1.6	3.0	5.4
Dengue	0.3	<0.1	0.2	0.3	2.7	0.6	2.1	2.4	2.1	1.8	3.2
Snakebite envenoming							0.7	1.6	0.1	1.5	2.7
Malaria	6.4	4.9	5.4	5.8	5.8	2.1	2.0	1.9	1.5	1.1	2.0
Kinetoplastid diseases	0.9	0.7	7.5	5.0	1.8	0.2	<0.1	<0.1	<0.1	<0.1	0.1
Helminth infections (worms & flukes)	0.8	<0.1	6.9	0.7	<0.1	0.1	<0.1	0.2	<0.1	<0.1	<0.1
Hepatitis C		-	-	-	3.9	2.5	0.4	-	-	-	-
Hepatitis B							<0.1	-	<0.1	-	-
Leprosy	-	-	-	-	-	-	0.1	<0.1	-	-	-
Leptospirosis		-	-	-	-	<0.1	<0.1	-	-	-	
Multi-disease vector control						0.8	-	-	2.5	-	-
Core funding of a multi-disease R&D organisation	-	1.9	2.1	-	-	-	-	-	1	-	-
Other R&D	<0.1	-	-	-	-	-	-	-	-	<0.1	0.1
Total SME funding	37	54	81	88	114	108	97	49	50	56	100

Hepatitis C, cryptococcal meningitis and leptospirosis were added to G-FINDER in 2013. Multi-disease vector control products were added in 2017. Hepatitis B and snakebite envenoming were added in 2018.

<sup>^</sup> Please note that some of the diseases listed are actually groups of diseases, such as the diarrhoeal illnesses and helminth infections.

<sup>-</sup> No reported funding

## Top funding organisations

As in every previous year, the top three funders of basic research and product development for neglected diseases were the US NIH, the Gates Foundation and industry (which we treat as a single aggregate entity for these purposes). Between them, these three funders provided \$3,034m, or 73% of global funding – nearly tying 2015's record high.

The most heartening change in 2021 was the sharp rebound in industry funding, which had fallen two years in a row from its peak of \$776m in 2018. It rose by \$77m this year, driven by its near-record funding for HIV/AIDS R&D (up \$70m, 47%), returning to its 2019 level of just over \$600m, and ending what had begun to look like a long-term decline.

Funding from the NIH – the top funder in this and every previous year – remained basically unchanged at \$1,761m, just 3.1% below its peak in 2019 and far above its long-term average. The Gates Foundation likewise saw another year of relatively stable above average funding (up \$11m, 1.7%).

There were several shifts among the remaining top 12 funders. The Indian ICMR – the ninth largest funder in 2020 – does not appear this year due to the absence of its 2021 funding data. The UK FCDO – previously the sixth largest – cut its funding by nearly two-thirds (\$87m) in 2021, with big reductions across nearly all of its portfolio, headlined by a \$39m (-85%) cut to core funding, an \$18m (-51%) cut to malaria R&D, and \$14m (-65%) cut for kinetoplastid diseases. The EC – again the fourth largest funder – topped up last year's record funding by a further \$25m (14%), the increase again going mostly to TB and as core funding to the EDCTP.

Funding from Unitaid surged by \$24m (47%) to a near-record high of \$75m, with most of the boost going to TB and malaria, while USAID reduced its contributions to neglected disease R&D for the fourth year running, bringing it to a record-low. This year's reductions focused mostly on its HIV funding, now less than half of its 2010 peak.

Table 37. Top neglected disease R&D funders 2021

	US\$ (millic	insl								c	021% of the
Funder	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	,
US NIH	1,668	1,458	1,460	1,435	1,548	1,533	1,711	1,817	1,767	1,761	43
Gates Foundation	578	597	592	602	625	590	621	654	654	665	16
Aggregate industry	418	424	510	523	557	609	776	609	531	608	15
EC	103	123	122	147	88	127	133	133	176	202	4.9
US DOD	97	116	110	90	124	137	116	114	131	131	3.2
Wellcome	138	127	119	92	113	116	127	129	138	128	3.1
Unitaid	0.4	9.5	18	22	52	54	76	54	51	75	1.8
USAID*	107	92	87	83	92	99	79	67	63	54	1.3
German BMBF	18	17	19	27	34	45	49	52	44	52	1.2
UK FCDO	42	68	74	59	63	115	131	126	132	45	1.1
UK MRC	44	47	46	40	47	46	40	50	46	31	0.8
Australian NHMRC	40	25	29	12	13	12	29	30	30	26	0.6
Subtotal of top 12^	3,304	3,176	3,232	3,189	3,390	3,547	3,937	3,865	3,793	3,778	91
Total R&D funding	3,670	3,551	3,540	3,490	3,741	3,983	4,407	4,342	4,181	4,137	100

<sup>^</sup> Subtotals for 2012-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

<sup>\*</sup> USAID's funding total for 2021 is understated by \$8.5m as additional HIV funding data was provided after G-FINDER analysis concluded.

## **FUNDING FLOWS**

Organisations can invest in neglected disease basic research and product development in two main ways: by funding their own in-house research ('internal investment', also referred to as 'intramural funding' for public sector entities or 'self-funding' when conducted by the private sector); or by giving grants to others ('external investment'). External investment can either be given directly to researchers and developers, or it can be provided to them via product development partnerships (PDPs) and other intermediary organisations.

Some organisations invest only internally (most pharmaceutical companies, for example); others, like Wellcome, only invest externally, without conducting any R&D themselves. There are also organisations, such as the US NIH, which use a mixed model, providing external grants to others as well as intramural funding to their own research programmes.

Different types of funders generally invest in different types of recipients. Government agencies primarily focused on the advancement of science and technology ('S&T agencies'), for example, mainly provide funding to researchers and developers, either directly or via the non-PDP intermediaries ('Other Intermediaries') with which they work closely. An obvious example of the latter is the EC's relationship with the European and Developing Countries Clinical Trials Partnership (EDCTP) – by far the largest of the Other Intermediaries – which accounts for over half of the EC's 2021 funding.

Philanthropic foundations and aid agencies have typically provided of the vast majority of PDP funding, but this share has trended downward, from 94% over the first five years of the G-FINDER survey to 75% in 2021. Instead, the share of PDP funding from S&T agencies has been trending upwards, reaching 19% in 2021, from an average of just 6.1% over the first decade of the G-FINDER survey.

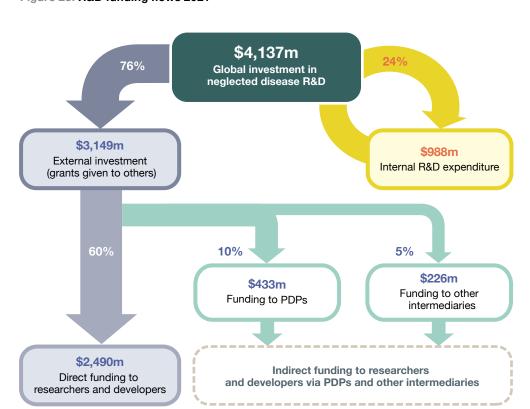


Figure 23. R&D funding flows 2021

### Funding flow trends

A little over three quarters of total investment in neglected disease R&D in 2021 was external funding (\$3,149m, 76%), with the remaining 24% spent internally via public intramural funding and private sector self-funding. These shares were unchanged from 2020 and broadly in line with the distribution observed over the last decade. While these proportions were stable, there were however small decreases in headline amounts for both, with external funding dropping by \$42m (-1.3%) and internal funding by \$2.5m (-0.3%).

Although the volume of internal funding appears relatively similar to 2020, after adjusting for the absence of intramural funding data from the Indian ICMR, it actually increased by a relatively substantial \$46m (5.0%). This participation-adjusted increase is due to a \$70m rise in self-funding from MNCs. This rise was partially balanced by a \$19m decrease in internal funding from HIC public funders, and smaller drops from SMEs and philanthropic funders.

Unlike in 2020, when all areas of external funding declined, the entirety of the 2021 drop in external funding was due to a \$97m fall in funding to PDPs (-18%) – its third consecutive year of decline – which was in turn almost entirely due to an \$87m drop in funding from the UK FCDO. The decline in PDP funding was partly offset by a \$33m (17%) increase for non-PDP intermediaries ('Other Intermediaries') – predominantly from the EC – and a \$22m (0.9%) rise in funding directly to researchers & developers.

The high-income country public sector accounted for most of the drop in external funding (down \$50m), with increases from the EC and German DFG offsetting some of the \$87m drop in funding from the UK FCDO.

Philanthropic external funding also fell – by \$18m – as a result of decreases from Wellcome and Open Philanthropy. This was partly balanced, however, by a \$11m increase from the Gates Foundation – mostly due to increased contributions to the Gates MRI. The overall decline in external philanthropic funding comes after five consecutive years of growth, totalling \$128m between 2015-2020.

Funding from aid agencies dropped significantly in 2021 (down \$81m), their second straight year of decline. The drop in aid agency funding fell almost entirely on PDPs (down \$93m, -40%), while funding from Science and Technology (S&T) agencies increased by \$21m, rebounding slightly from a big drop in 2020, thanks solely to a big increase in the EC's funding to the EDCTP.

### Funding by R&D stage

In 2021, 43% of all funding for neglected disease R&D was invested in basic & early-stage research (\$1,767m), and just under a third in clinical development & post-registration studies (\$1,272m, 31%). The rest was invested in core funding and other R&D (\$448m, 11%), platform technologies (\$146m, 3.5%), and funding which did not specify an R&D stage (\$504m, 12%).

Funding to basic & early-stage research fell by 8.2% (down \$159m), reversing the growth since 2017 and leaving it just above its 2016 level. The fall impacted all products except for vector control, which saw a substantial increase of 35% (up \$9.1m). The largest of the drops were in basic research (down \$77m, -9.0%) and early-stage vaccine R&D (down \$36m, -7.0%) – both of which were driven by reductions from the US NIH and the Gates Foundation. These two still remained the top two funders of basic & early-stage research overall, despite their respective investments in this area falling by \$57m (NIH) and \$50m (Gates).

A pair of artefactual changes also contributed to the headline drop in basic & early-stage research: this year's absence of data from the Indian ICMR (which contributed \$42m in 2020, almost entirely for basic research) outweighed the effects of a resumption in survey participation from the German DFG. Adjusting for differences in participation, the true drop in basic & early-stage research was slightly smaller, at \$133m (-7.1%).

Funding for clinical development & post-registration studies, in contrast, rose by 9.1% in 2021. This was an increase of \$106m, representing a slight rebound from the declines in the preceding two years, following the peak of \$1,532m in 2018. The main drivers of the increase were industry (up \$74m, 21%), the Gates Foundation (up \$38m, 32%) and Unitaid (up \$25m, 86%).

The rise in overall clinical development funding drove increases in investment across all stages of the pipeline, with substantial growth in funding for Phase I, II and III trials and in post-registration studies. The increase was concentrated exclusively in therapeutics, with a spike in drug trial funding (up \$149m, 35%) and a smaller jump for biologics (up \$4.0m, 7.8%), which nonetheless left biologics clinical development at a record high. Investment fell for all other product areas, with the largest proportional drops in clinical development of microbicides (down \$31m, -43%) and diagnostics (down \$6.2m, -12%).

Much of the increase in clinical development from industry and the Gates Foundation went to HIV/AIDS drug R&D (\$62m and \$40m, respectively), as industry initiated post-registration studies for a newly registered long-acting injectable, and the Gates Foundation increased contributions to the Phase III IMPOWER study investigating islatravir in women and adolescent girls in sub-Saharan Africa. Together with Unitaid's record funding for malaria drugs (up \$14m, 221%) and increased late-stage TB drug development (up \$12m, 436%), this resulted in a headline increase of \$149m (35%) in late-stage neglected disease drug R&D, a record high and the first time that late-stage drug R&D received more than vaccines.

Funding for platform technology R&D increased again in 2021, by \$15m (12%), reaching an all-time high following its record growth over the past three years. Much of the increase came via investment in drug-related platforms (up \$13m, 166%) – which reached a new record high – and the newly introduced category of biologics-related platforms (\$11m).

## Funding for product development partnerships

Funding to product development partnerships (PDPs) declined steeply in 2021 (down \$97m, -18%), hitting a record low of \$433m – more than 10% below its previous low in 2016. While some of this fall reflects the shift of funders' contributions to emerging infectious diseases – funding which is not captured in this report – it also represents an acceleration of the longstanding downward trend in funding and support to PDPs as intermediaries for neglected disease R&D.

The decline in 2021 funding was largely the result of big reductions in disbursements to PDPs from the UK FCDO. The FCDO had been the second largest funder of PDPs – behind only the Gates Foundation – in each of the preceding four years, contributing an annual average of \$124m. In 2021, however, its investment fell by two-thirds, to just \$45m (down \$87m, -66%). While this impacted all the FCDO-funded PDPs, reductions fell most heavily on DNDi (down \$14m, -65%), MMV (down \$12m, -55%), and especially FIND – which saw a drop of \$39m (-85%), although this is exaggerated somewhat by their previous year's COVID-driven spike in FCDO funding.

PDP funding from USAID also fell, to \$42m (down \$18m, -30%) – its lowest level on record and well below its peak in 2009. The fall was driven by cuts in its HIV funding to CONRAD and IAVI.<sup>1</sup>

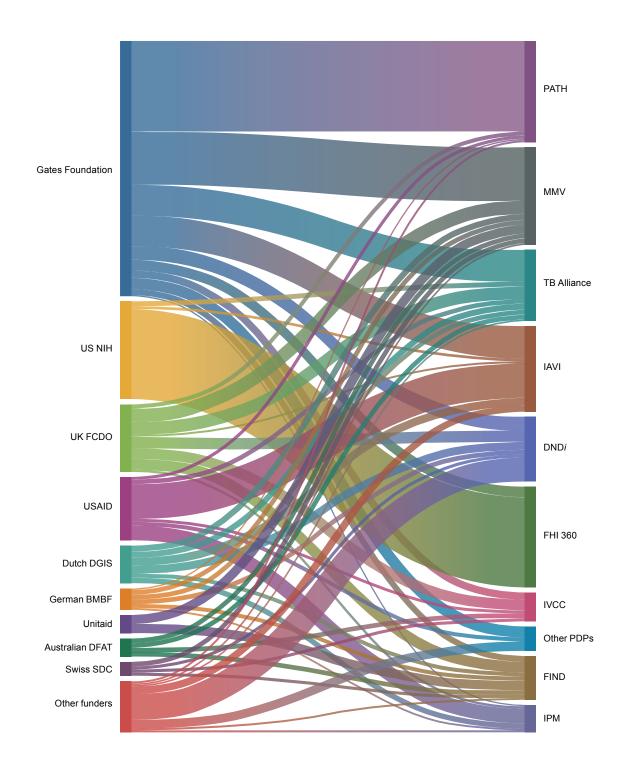
The Gates Foundation remained the top funder of PDPs and accounted for 40% of total PDP funding, however its investment also declined – for the third year in a row – falling to another record low of \$171m (down \$9.1m, -5.1%). This mostly affected IVCC and IVI, with their respective Gates Foundation funding decreasing by \$11m (-68%) and \$7.0m (-60%).

In contrast to the substantial drops in funding from several main funders, the Dutch DGIS increased its yearly disbursements by \$13m (120%). This represented the last of the funding disbursed through its seven-year PDP III Fund – with the PDP IV fund slated to start mid-2022 – and still left Dutch funding only slightly above its average level prior to its sharp drop in 2020. The US NIH's PDP funding also rebounded, following two consecutive years of decline, to hit a new high of \$66m (up \$8.1m, 14%), thanks to an increase in funding to the FHI 360-led HIV Prevention Trials Network (HPTN).

Despite the overall fall in PDP funding from the Gates Foundation, its funding to PATH jumped by \$7.5m (14%) to \$61m, making PATH the highest-funded PDP in 2021. It received a total of \$69m, accounting for 16% of total PDP funding in 2021. FHI 360 was the only other PDP to receive a meaningful boost in funding (up \$10m, 19%), leaving it a close second to PATH with \$67m (another 16% of the global total). Almost all other PDPs saw reductions in their funding, headlined by a \$19m (-31%) drop in funding to DND*i* and the \$36m fall in FIND's disbursements from the FCDO – contributing to FIND's funding received dropping by more than half from last year's record high.

High-income country public funders accounted for more than 90% of the overall decline in PDP funding, though they continued to provide more than half of the 2021 total. Most of the remaining funds were provided by philanthropic funders (44% of total funding), the vast majority of which (91%) was from the Gates Foundation.

Figure 24. PDP funding 2021



## Funding for other intermediaries

Following two consecutive years of decline, funding to non-PDP intermediaries ('Other Intermediaries') rebounded to \$226m in 2021, an increase of \$33m (17%). Although this left funding more than \$20m below its two-year peak between 2018 and 2019, it is still well above its 10-year average.

More than two-thirds of this year's rebound was due to increased funding from the EC. Its funding rose for the fifth year in a row, to \$111m (up \$23m, 25%), leaving it responsible for a record 49% of global funding to Other Intermediaries. Contributions from the EC were more than four times those of the Japanese Government – the next biggest funder – whose actual disbursements to GHIT continued to fluctuate within the structure of its fixed multi-year funding commitment, rising significantly following last year's sharp decline (by \$16m, 173%).

Alongside the substantial rises in funding from these two organisations, there were smaller increases from the Gates Foundation (up \$5.8m, 40%) and the Catalan Department of Health (up \$3.4m, 366%) – both with record highs – as well as from the German BMBF (up \$4.7m, 38%).

In contrast, Unitaid's funding for Other Intermediaries continued to fall, dropping another \$7.1m to \$11m (-39%), which left it at less than one third of its peak in 2018. This reduction from Unitaid fell solely on the HIV/AIDS programme of the Clinton Health Access Initiative (CHAI), whose funding consequently fell sharply, to \$2.1m (down \$10m, -83%). Wellcome's funding to the GHIT fund also fell in 2021 – by more than 60% to \$2.9m – though, as with the rise in the Japanese Government's GHIT funding, this reflects planned cyclical changes tied to a fixed multi-year total. The UK DHSC, which had contributed more than \$100m to the European & Developing Countries Clinical Trials Partnership (EDCTP) from 2017 to 2020, ceased its funding completely in 2021 (down from \$4.8m in 2020 and from \$28m in 2019), following the UK's exit from the European Union. However, the EDCTP continued to receive a small amount of residual UK funding (\$0.9m) under the Joint Global Health Trials programme.

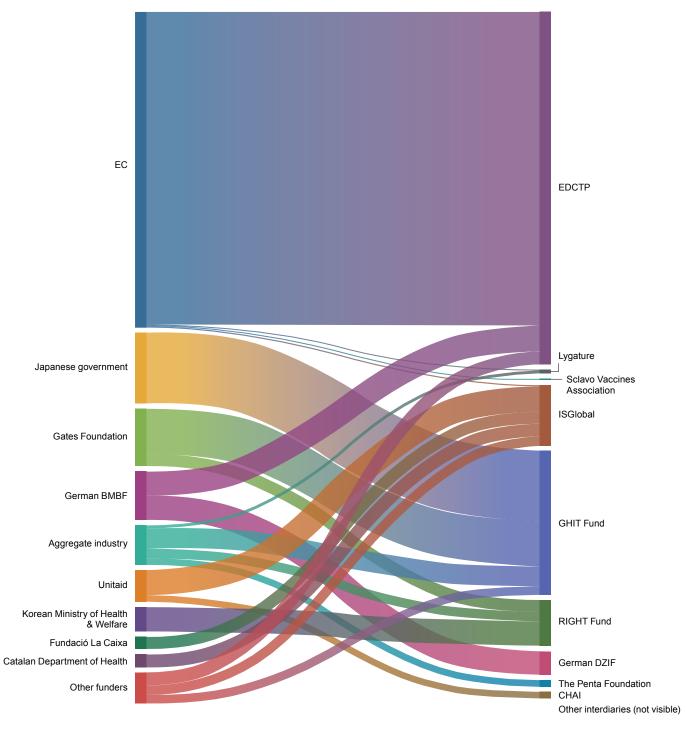
While the EDCTP's funding had fallen in 2020 due to the earlier (and larger) cuts from the UK DHSC, it recovered to \$124m in 2021 (up \$20m, 19%) thanks to record funding from the EC. The EDCTP also received slightly increased funding from individual European countries due to a record \$8.8m contribution from the German BMBF. Overall, the EDCTP received 55% of 2021 funding for Other Intermediaries, and disbursed funds to 205 recipient organisations, targeting 17 different neglected diseases. Roughly mirroring the overall funding landscape, HIV/AIDS, tuberculosis and malaria received the largest shares of funding from the EDCTP, jointly accounting for nearly 60% of its 2021 disbursements.

The GHIT fund was the second largest recipient of Other Intermediary funding, with 23% of the global total. It received 97% of the Japanese government's 2021 neglected disease R&D funding, which drove a substantial rise in GHIT's overall funding, despite the cyclical fall in funding from Wellcome. IsGlobal also experienced a 40% rise in funding (up \$5.9m), including an increase in investment from Unitaid (up \$2.6m, 41%).

Public HIC funders and philanthropic funders accounted for just under 90% of funding to Other Intermediaries. Private (MNC) investment comprised just 6.1% of funding in 2021, most of which went to GHIT and the RIGHT fund.

The vast majority of Other Intermediaries' funding continued to be provided as untied core funding (89% of the 2021 total, up from 85% in 2020) with almost all of the remainder split between malaria (6.1%), HIV (3.0%) and TB (1.2%).

Figure 25. Intermediary funding 2021



## **DISCUSSION**

## Funding for neglected disease R&D was basically unchanged in 2021, and has changed little since 2018

Funding in 2021 sat just 4% below its record high from 2018. The changes we have seen since then were mostly just fluctuations in survey participation and minor expansions in the survey scope.

So global funding has remained essentially flat for three consecutive years. This failure to build on the long-term growth which delivered the 2018 peak has left funding around \$400m lower than had it continued. The failure of global neglected disease R&D to continue its longer-term upward trend is obviously disappointing – albeit less so in the face of a global pandemic. Though we are comforted by the persistence of near record funding, we remain concerned about the potential for post-pandemic backsliding and especially by the failure of funding to reach the most neglected diseases – the WHO neglected tropical diseases – which saw their funding fall again.

Our static overall funding is only good news if it can deliver meaningful improvements to the product landscape. The global response to COVID-19 showed it is possible to develop novel health technologies in a matter of months, given sufficient support from funders. But, under 2021's status quo, no single pathogen is receiving anything close to this level of support; meaning we cannot hope to come close to matching the success enjoyed by COVID R&D.

## COVID-19 has yet to have the disastrous impact on clinical trials and funding that many expected

Following a substantial fall in clinical trial spending in 2020, which some funders directly attributed to COVID-19, we were relieved to see a rebound in industry and trial funding in 2021. The pandemic appears to have had little ongoing impact on the conduct of neglected disease R&D and, so far, mostly not diverted funding towards COVID-19 R&D.

The ongoing absence of a big impact from COVID-19 remains consistent with our prior observation that funding for emerging infectious disease (EID) R&D – which had risen rapidly even prior to COVID – appears to draw from a separate pool of funds from neglected diseases. But, given the enormous observed impact the pandemic had on daily life and most measures of economic activity, it seems surprising that research and development, and particularly clinical trials, were able to continue in 2021 much as they had in 2019. As in other areas of the economy, where actual output dropped even as expenditure remained stable at the height of the pandemic, the lack of impact may reflect fixed funding flows alongside significant underlying disruption to the actual conduct of research.

While it is a relief to see that neglected disease R&D survived the pandemic mostly unscathed – at least on paper – we still lack data on how funding will fare post-pandemic, as governments look to recoup their pandemic spending. We hope for renewed progress, but are concerned cuts to ODA and other areas perceived as inessential might instead tip funding into a period of decline.

#### The worrying decline in clinical development seems to have reversed

Following a substantial fall in clinical trial spending in 2020, which was partly attributable to the challenges in conducting trials during the pandemic, 2021 saw a big rebound (up \$106m, 9.1%). Clinical development returned to slightly below its 2019 level, though still about 17% below its peak in 2018.

Funding for clinical development is typically more variable than other forms of funding. This reflects the cycle of increasing investment required for product development, usually followed by a swift post-registration decline – particularly in the case of LMIC-specific trials. We should therefore expect – and not overreact to – continued fluctuations in clinical development; hopefully alongside a long-term upward trend.

#### Funding to PDPs reached its lowest level ever

The latest in a series of ongoing falls in PDP funding left it nearly 40% below its 2008 peak, a downward trend of more than \$10m a year. The drop in 2021 funding was mostly a result of steep cuts from the UK FCDO; but the longer-term decline from peak PDP funding of more than \$700m to \$433m is largely the result of an ongoing decline in investment from the Gates Foundation (down \$270m, -61%) and USAID (down \$44m, -51%).

Funding to PDPs is one area where there does appear to have been some COVID-related displacement over the last two years. While PDP funding for neglected disease R&D is down, overall funding to PDPs across all three global health areas covered by the G-FINDER survey has grown substantially in each of the last two years – thanks to big increases in funding to PDPs for COVID-19 R&D.

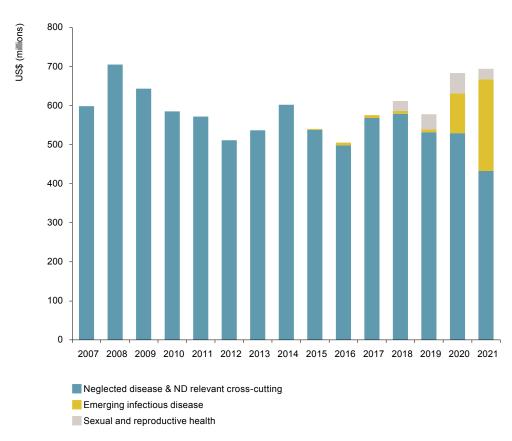


Figure 26. PDP funding by global health area 2007-2021

The trend in funding for individual PDPs with respect to neglected disease R&D is less uniform. Most of the main recipients from 2008 have seen big reductions in funding over the intervening years, including a \$76m (-52%) fall for PATH, a \$52m (-73%) reduction for IPM, together with the wind-up of Aeras and OneWorld Health – respectively the third and eighth-largest PDP recipients in 2008. But some PDPs have seen their funding gradually increase, most notably FHI 360 (up \$38m, 128% since 2008) and DNDi (up \$18m, 76%, despite a sharp drop in 2021).

If the gradual but persistent decline in the share of funding delivered via PDPs represents a conscious change in approach from donors, it raises questions about what this means for the future shape of the R&D landscape, given the central role PDPs have long played in coordinating the distribution of funds for neglected disease R&D. If funders increasingly invest directly with multiple individual product developers and research institutions, or increase their share of 'in-house' R&D, what might this mean for the degree of coordination and efficiency in the ecosystem, and what are the implications of the increased burden on funders that this approach implies?

Funding from the United Kingdom government fell by more than half, with several key contributors slashing their contributions to neglected disease R&D

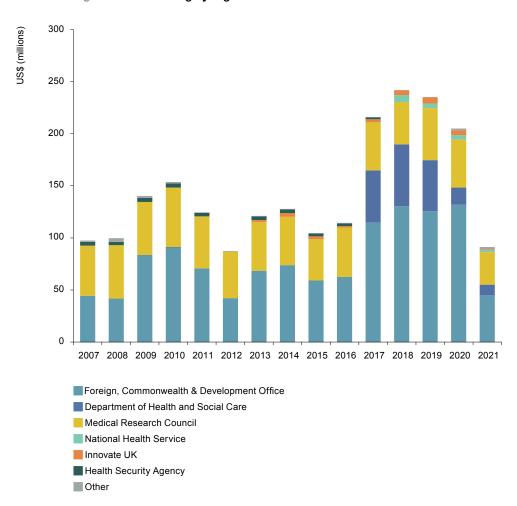


Figure 27. UK funding by organisation 2007-2021

Growth in the UK's public funding played a significant role in the run-up of global funding – particularly a new stream of official development assistance (ODA) funding from the Department of Health and Social Care (DHSC) which began in 2017. Alongside the Foreign, Commonwealth & Development Office (FCDO), which accounts for a little over half of the UK's funding over the life of the G-FINDER survey, ODA from the DHSC gave the UK a record 9% share of global public funding in both 2017 and 2018, far ahead of any country besides the US, and more total funding than the EC and Germany put together.

There was a slight decline in overall UK funding in 2020, driven by a sharp reduction from the UK DHSC. But in 2021, as the UK finalised its exit from the European Union – and in the first year of its reduced, 0.5% of GNI, target for ODA – funding from almost every funding agency tumbled. The falls were headlined by an \$87m (-66%) cut in FCDO funding, but there were substantial drops from the DHSC, the MRC, the NHS, and Innovate UK. In all, UK public funding fell by \$114m – by far the largest-ever year-on-year fall in national funding from any nation outside the US. UK funding to the EDCTP, the biggest recipient of its funding between 2017 and 2019, fell to just \$0.9m, down from a peak of \$52m in 2018.

In the absence of its usual commitments to the EDCTP, there was no shift in the UK's funding programmes towards non-EU recipients, as their funding to LMIC recipients dropped in line with their overall contributions. The UK's funding for COVID, non-COVID EIDs and SRH all saw drops in 2021, implying that the drop in neglected disease funding did not simply represent a reallocation of funding, as appears to be the case with PDPs.

There is room to hope that this rapid, across-the-board fall in UK funding represents a temporary period of realignment as its major donors adjust to Brexit and the (temporary, but still ongoing) fall in ODA spending. But it is hard to forecast substantial growth in global funding absent a renewed commitment from the UK.

## The top funders of neglected disease R&D have remained largely the same for at least the past decade

The sharp drop in UK funding still left it, narrowly, as the second-largest funding nation. But it underlined the degree to which global funding continually depends on the potentially vulnerable budget lines of the dozen biggest funders, especially the US NIH, which provided 43% of global neglected disease funding in 2021.

Collectively, the US NIH, the Gates Foundation and the pharmaceutical industry were the source of almost three quarters (73%) of all global funding for neglected disease R&D in 2021 – the most concentrated funding has been since 2015. The same top ten funders that provided 88% of global funding a decade ago have continued to account for at least 85% of global funding every year since; and funders not active in 2012 accounted for just 2.1% of 2021's funding.

#### The trend towards therapeutics R&D and away from vaccines shows no signs of slowing

2021 marked the first time in the fifteen-year history of the G-FINDER survey that spending on drug R&D exceeded R&D for vaccines.

Over the first five years of the G-FINDER survey, vaccine R&D averaged \$1,334m a year, more than twice the \$640m average for drug R&D. In the four years since global funding peaked in 2018 their shares were much closer – with drug funding just 12% below that for vaccines.

The vast majority of the shift between 2009 – when the gap between drug and vaccine funding peaked at \$850m – and today was due to increases in the proportion of funding going to drug R&D across almost every disease group. The share of TB drug funding rose by 18 percentage points, HIV by 15 and malaria by 11. Many smaller diseases saw even larger shifts, with drugs' share of dengue and leprosy R&D rising by 24 percentage points. The only major exception was Buruli ulcer, which had also seen ongoing growth in its share of drug funding until its sudden cessation in 2020.

The reverse is broadly true of vaccine R&D, with the vast majority (80%) of ongoing disease groups seeing reduced focus on vaccines, an average drop of five percentage points including a fifteen percentage point drop for malaria, ten percentage points for TB and nine for HIV.

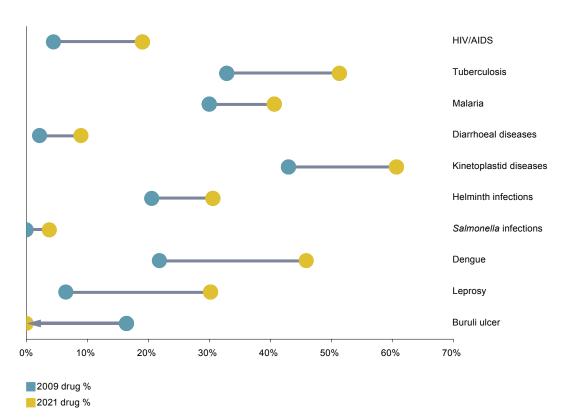


Figure 28. Share of disease funding for drug R&D, 2009 versus 2021

This represents a contrast with the initial global response to COVID-19, which saw more than four times as much funding directed to vaccine R&D as to drugs. It is also inconsistent with rising concerns about anti-microbial resistance, which envision improved vaccines as a key strategy for slowing the development and spread of drug resistant strains.

Some of the shift towards drugs reflects the successes in vaccine development, including new products targeting diarrhoeal disease and typhoid; some represents the result of high-profile failures in vaccine development; and some of it the decisions of individual funders based on the investment opportunities presented to them. But in practice, especially given the higher costs of vaccine trials, it is likely to cause a seismic shift in the distribution of future product registrations, trading prevention for treatment.

## After years of stagnation, funding for the WHO NTDs fell by more than 10%, to their lowest ever share of global funding

Funding for NTDs grew rapidly over the first two years of the G-FINDER survey, rising from \$277m in 2007 to \$390m in 2009. A little over a third of this growth was thanks to increases in survey participation, and about half due to rapid expansion of funding from the US NIH. Global funding for NTDs has since matched that 2009 total only once, in 2019; and in 2021 fell to \$323m, more than \$65m (17%) below its peak, and by far the lowest total since those first two years of the G-FINDER survey.

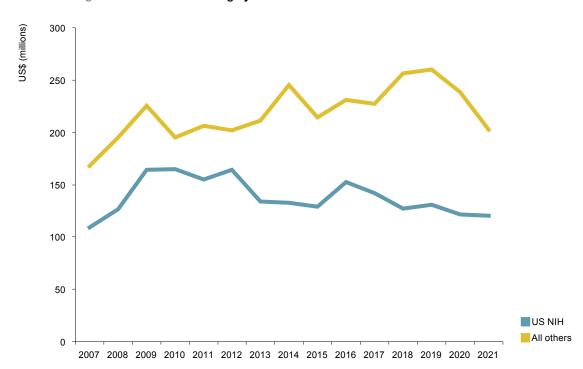


Figure 29. WHO NTD funding by NIH and all others 2007-2021

Since 2009, funding for the WHO NTDs has trended down at a little under \$1m a year, despite the addition of several new diseases. The sharpest downward trend has been for kinetoplastid R&D, which has fallen by an average of \$1.5m (0.8%) every year. There were even steeper proportional declines for leprosy (which lost an average of 2.4% each year), trachoma (9.2%) and especially Buruli ulcer, which has fallen by an average of more than 15% each year.

The steep downward trends in Buruli ulcer and trachoma funding partly reflect the sharp cuts each experienced in 2021: both trachoma and Buruli ulcer saw their (participation-adjusted) funding fall by more than two-thirds, each falling to well under \$1m for the first time. Kinetoplastid funding also reached a record low, while funding for leprosy was at its lowest level since 2007.

Though it has grown slightly over time, industry involvement in these diseases remains minimal (\$69m across all NTDs in 2021) – partly thanks to our deliberate exclusion of products, like dengue vaccines, for which there is a commercial market. The last few years have seen meaningful growth in clinical development funding, which has averaged over \$90m a year over the last four years, up from \$45m over the previous decade. But there remains a clear mismatch between the scale of the unmet R&D needs for these diseases and the amount of funding they can realistically hope to receive. Over the life of the survey, the median annual contribution to each product area for each individual pathogen is less than \$0.8m, far too little to achieve meaningful progress; and the US NIH alone accounts for more than a third of all global NTD funding since 2007.

Funding for R&D provided by intermediaries (which we refer to as 'onward funding') is not included in the G-FINDER report, to avoid double counting it alongside the payments made *to* intermediaries, which *are* included. A substantial share of core funding is ultimately disbursed to NTDs. Though this onward funding for NTDs was also down in 2021 (by \$12m, -22%) the overall trend since 2009 is slightly positive, with disbursements from intermediaries growing by an average of nearly \$0.7m a year. This growth is mostly thanks to the EDCTP, which began providing funding for NTDs in 2016 and in 2021 disbursed a record \$15m – heartening, but not nearly enough to change the overall picture of stagnation and decline.

Funding for NTDs, however it is measured, has been stagnating for more than a decade. We need a new model for attracting R&D funding to replace an existing approach which consistently fails to deliver investment at the scale required, even as global funding rises. Despite slight increases in funding from industry, there remains very little private sector interest, and, as a result, very little actual clinical development. This is partly by design – our definition of 'neglect' *requires* the absence of market incentives for product development. So how, beyond our annual pleas for more public and philanthropic funding, do we close the gap between the \$0.8m a year in existing investment and the kind of funding necessary to advance NTD products through the pipeline?

# ANNEXURE A - ADVISORY COMMITTEE MEMBERS

ADVISORY COMMITTEE MEMBER	ORGANISATION	TITLE					
Dr Ripley Ballou	International AIDS Vaccine Initiative	ADVANCE Program Lead and Principal Investigator					
Professor Balram Bhargava	Indian Council of Medical Research	Former Director General					
Dr François Bompart	Drugs for Neglected Diseases Initiative (DND/)	Access Committee Chair					
Dr Wanderley de Souza	Financiadora de Estudio e Projetos (FINEP)	Former President					
Dr Emily Erbelding	National Institute of Allergy and Infectious Diseases, National Institutes of Health	Director, Division of Microbiology and Infectious Diseases					
Dr Arnuad Fontanet	Institut Pasteur	Head of Emerging Diseases Epidemiology Unit					
Dr Sue Kinn	UK Foreign, Commonwealth & Development Office	Head of Southern Africa Regional Hub for Science, Innovation and Technology					
Dr Jean Lang	Sanofi Pasteur	Associate Vice President					
Dr Firdausi Qadri	International Centre for Diarrhoeal Disease and Research (icddr,b)	Senior Scientist and Head of Immunology					
Dr John Reeder	World Health Organization; Special Programme for Research and Training in Tropical Disease	Director					
Professor Nelson Sewankambo	Makerere University College of Health Sciences	Professor of Internal Medicine					
Dr Soumya Swaminathan	World Health Organization	Chief Scientist					
Wendy Taylor	Jhpiego	Vice President, Technical Leadership and Innovation					
Dr Tim Wells	Medicines for Malaria Venture	Chief Scientific Officer					

## ANNEXURE B - METHODOLOGY

### Survey methodology

#### IDENTIFICATION OF SURVEY PARTICIPANTS

The G-FINDER project aims to survey all key public, private and philanthropic organisations involved in R&D for global health. Although the primary focus is on funders, we also survey key research, intermediary and industry groups to allow us to better track funding flows.

In 2008 (the first year of the project, then focused exclusively on neglected diseases), survey participants were identified through various avenues, including: our own database of contacts; previous surveys covering HIV/AIDS, tuberculosis, and malaria R&D; and research to find previously unknown funding organisations in countries with high R&D expenditure as a percentage of gross domestic product. In the following year we focused on groups and countries that were missing or poorly represented in 2008, developing proactive strategies to both increase the number of survey participants and improve response rates in these areas. Major Indian public agencies involved in funding R&D for neglected diseases were identified and incorporated in our list of participants, and additional diagnostics organisations and small pharmaceutical and biotechnology firms were also included.

Since then we have put in place a number of targeted strategies to further increase survey participation of major public funders and product developers in low- and middle-income countries, including those in South America, Africa and Asia. In addition, each time that a new disease or health issue is added to the survey scope, organisations known to be active in these areas are identified and surveyed.

### DATA COLLECTION

The G-FINDER project operates according to two key principles:

- capturing and analysing data in a manner that is consistent and comparable across all funders and diseases; and
- 2. presenting funding data that is as close as possible to 'real' investment figures.

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

For some organisations with very large datasets, the online survey and equivalent offline reporting tool are difficult to use. The G-FINDER team therefore uses publicly available databases to identify the relevant funding. Information on funding from the US Department of Defense (DOD) is collected using the Defense Technical Information Center's 'DOD investment budget search' tool. Funding from the European Commission (EC) is retrieved from the Community Research and Development Information Service (CORDIS) public database and the Innovative Medicines Initiative's (IMI) online project list. Supplementary data is provided by the EC. Information about R&D projects funded by Innovate UK is extracted from spreadsheets available on its website. For the US National Institutes of Health (NIH), grants are collected using the Research Portfolio Online Reporting Tools (RePORTER) and the Research, Condition and Disease Categorization (RCDC) databases.

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

#### THE SURVEY

Survey participants – funders, intermediaries and product developers – are asked to enter grant-bygrant expenditures incurred or disbursements received during their financial year with the largest overlap with the previous calendar year (which is different from the financial year in many countries). Survey participants are asked to enter details of every global health investment they disbursed or received, including:

- · a specific disease or health issue, from a predefined list
- a product type (e.g. drugs, vaccines, microbicides), from a predefined list
- an R&D stage within the product type (e.g. discovery and pre-clinical, clinical development, Phase IV/pharmacovigilance studies of new products), from a predefined list
- · the name of the funder or recipient of the grant
- · a brief description of the grant
- an internal grant identification number
- · the grant amount

Where survey participants cannot provide data to this level of detail, they are asked to provide the finest possible level of granularity. Where survey participants are not able to allocate the grant to a single disease, five options are available:

- 'Core funding of a multi-disease / issue organisation' such as funding to an organisation working in multiple diseases or sexual & reproductive health issues, where the expenditure per health issue was not known to the funder
- 'Platform technologies', further allocated as investment into diagnostic platforms; adjuvants and immunomodulators; or drug-, biologics- and vaccine-related platforms. These categories capture investments into technologies which were not yet directed towards a specific disease or product
- 3. 'Multi-disease vector control products', which captures funding for vector control product R&D that is not yet targeted at a specific disease, or that is targeted at multiple vector-borne diseases
- 'Multi-purpose prevention technologies' which target more than one sexual & reproductive health issue (two or more indications for HIV, STIs or contraception)
- 5. 'Unspecified R&D' for any grants that still cannot be allocated to any of the above categories

## Data validation and analysis

#### VALIDATION

All grants reported in the G-FINDER survey are verified against the inclusion criteria. Cross-checking of grants reported by funders and recipients is then conducted using automated reconciliation reports – which match investments reported as disbursed by funders with investments reported as received by intermediaries and product developers – followed by manual grant-level review. Any discrepancies are resolved by contacting both groups. For grants from the US NIH, funding data is 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 figures are reviewed against industry portfolio information held by Policy Cures Research and against full-time equivalent (FTE) and direct costs provided by other companies. Costs that fall outside the expected range, for example, above average FTE costs for clinical staff, are queried with the company and corrected.

#### DATA AGGREGATION

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

#### INFLATION ADJUSTMENTS

All funding data we collect is adjusted for inflation and converted to US dollars for the relevant financial year to eliminate artefactual effects caused by inflation and exchange rate fluctuations, allowing accurate comparison of year-on-year changes. Due to these adjustments, historical funding data in tables and figures in the G-FINDER data portal and our most recent reports will differ from data published in older reports.

All reported data is adjusted for inflation using consumer price index (CPI) estimates from the International Monetary Fund (IMF) and any data entered by survey participants in their local currency is converted to USD based on the average annual exchange rate of the relevant financial year as reported by the IMF, Bank of England, United Nations Treasury and OANDA. The G-FINDER data portal also allows all data to be converted to Euros (EUR) or British pound sterling (GBP).

#### ANNUAL CHANGES IN SURVEY PARTICIPATION

While survey participation from the major funders has stabilised over the history of the G-FINDER survey, there remains significant annual variation in survey participation, as a result of survey dropout, increased response from long-term funders and entry of new players in the global health sector. The net effect of these changes is typically relatively small, other than between 2007 and 2008 (the first and second survey years). However, care should be taken in interpreting apparent changes in funding, which may, in some cases, have been contributed to by the artefactual effects of changes in survey participation. Detailed analysis of these changes and their effects is provided by the G-FINDER reports for the relevant year.

#### VARIATION BETWEEN SURVEYS

Other groups also publish annual surveys of global R&D investment into selected global health areas, such as HIV/AIDS and TB. Although we work in close collaboration with some of these groups, both to ease survey fatigue on the part of participants and to clarify any major variance in our findings, each survey nevertheless has slightly different figures. This is chiefly due to differences in scope, in particular inclusion in other surveys of funding for advocacy, capacity building and operational studies – all excluded from G-FINDER. Methodological differences also lead to variations, particularly the adjustment of G-FINDER figures for inflation and exchange rates, which is not always the case for other surveys. As noted above, classification of some funding as 'unspecified' in G-FINDER (e.g. multi-disease/multi-issue programmes) may in some cases also lead to different figures than those published in disease/issue-specific surveys.

#### **Data limitations**

While the survey methodology has been refined over the past decade, there are limitations to the data presented, including survey non-completion, time lags in the funding process, an inability to disaggregate some investments, and non-comparable or missing data.

#### SURVEY NON-COMPLETION

Some global health R&D funding may not be captured because organisations are not identified as active in this field and are therefore not invited to participate, or because organisations are invited to participate, but do not respond. Despite this, we are confident that the majority of neglected disease, emerging infectious disease, and sexual & reproductive health R&D funding is captured by G-FINDER, because large funders active in this area and target groups identified by our Advisory Committee are typically responsive and, where they are not, are prioritised during survey follow-up.

#### TIME LAGS IN THE FUNDING PROCESS

Time lags exist between disbursement and receipt of funding, as well as between receipt of funds and the moment they are actually spent. Thus, grants by funders will not always be recorded as received by recipients in the same financial year, and there may be a delay between R&D investments as reported by G-FINDER and actual expenditure on R&D programmes by product developers and researchers. Nevertheless, as most of our reports analyse trends over an extended period, the impact of time lags is minimal.

#### INABILITY TO DISAGGREGATE INVESTMENTS

A small proportion of funding (now typically well less than 3%) is reported to the survey each year as 'unspecified', usually for multi-disease/multi-issue programmes where investment cannot easily be apportioned by disease or issue. A proportion of funding for some health issues is also 'unspecified', for instance, when funders report a grant for research into TB basic research and drugs without apportioning funding to each product category. This means that reported funding for some diseases or issues and products will be slightly lower than actual funding, with the difference being included as 'unspecified' funding.

Another small, though increasing, fraction (to date always less than 10%) of global funding is given as core funding to R&D organisations that work in multiple health areas, for example, the European and Developing Countries Clinical Trials Partnership (EDCTP) and the Coalition for Epidemic Preparedness Innovations (CEPI). As this funding cannot accurately be allocated by disease or health issue, it is reported as unallocated core funding. In cases where grants to a multi-disease or multi-issue organisation are earmarked for a specific health area or product, they are included under the specific disease/issue-product area.

#### NON-COMPARABLE DATA

Due to a significant increase in the size of survey participation in 2009 (when we collected FY2008 data), data from 2008 (when we collected FY2007 data) is the least comparable to other years. Furthermore, the current public official databases for the US NIH data, the RCDC and RePORTER, used for data collection from 2009 onwards, uses a different structure than the US NIH database used in 2008, making this data less comparable. As such, apparent shifts in funding between 2007 and 2008 should be interpreted with caution.

#### MISSING AND INACCURATE DATA

G-FINDER can only report the data as it is given to us. Although strenuous efforts are made to check the classification, accuracy and completeness of grants, in a survey of this size it is likely that some data will have been incorrectly entered or that funders may have accidentally omitted some grants. We periodically make amendments to historical G-FINDER data after the publication of a report if better data is provided or errors are identified, which take immediate effect on the G-FINDER data portal. We believe that the checks and balances built into the G-FINDER process mean that mistakes, if present, have only a minor overall impact.

## ANNEXURE C - SURVEY PARTICIPANTS

- AbbVie
- Academy of Finland (including the Strategic Research Council)
- Access to Advanced Health Institute (AAHI)
- Adjuvant Capital
- Aelix Therapeutics\*
- American Leprosy Missions (ALM)
- amfAR, The Foundation for AIDS Research\*
- Argentinian Ministry of Science, Technology and Productive Innovation (MINCYT)
- Argentinian National Council for Scientific and Technical Research (CONICET)
- Australian Department of Foreign Affairs and Trade (DFAT) (including the Indo-Pacific Centre for Health Security)
- Australian Medical Research Future Fund (MRFF)#
- Australian National Health and Medical Research Council (NHMRC)
- Australian Research Council (ARC)
- Barcelona Institute for Global Health (ISGlobal) (including FCRB, CRESIB and CREAL)
- BASF SE
- Baver Healthcare
- Baylor College of Medicine
- BC Women's Health Foundation
- Becton, Dickinson and Company (BD)
- Bernhard Nocht Institute for Tropical Medicine (BNITM)
- Bill & Melinda Gates Foundation
- Bio Manguinhos
- Biological E Limited
- Bolivian National Institute of Health Laboratories (INLASA)
- BPI France#
- Brazilian Araucária Support Foundation for Scientific and Technological Development in the State of Paraná (FA)
- Brazilian Development Bank (BNDES)
- Brazilian Ministry of Health: Department of Science and Technology (DECIT)
- Brazilian Ministry of Health: National STD and AIDS Programme
- Brazilian Support Foundation for Research and Innovation in the State of Santa Catarina (FAPESC)

- Brazilian Support Foundation for Research and Technological Innovation in the State of Sergipe (FAPITEC)
- Brazilian Support Foundation for Research in the Federal District (FAPDF)
- Brazilian Support Foundation for Research in the State of Alagoas (FAPEAL)
- Brazilian Support Foundation for Research in the State of Amapá (FAPEAP)
- Brazilian Support Foundation for Research in the State of Amazonas (FAPEAM)
- Brazilian Support Foundation for Research in the State of Bahia (FAPESB)
- Brazilian Support Foundation for Research in the State of Minas Gerais (FAPEMIG)
- Brazilian Support Foundation for Research in the State of Rio Grande do Sul (FAPERGS)
- Brazilian Support Foundation for Research in the State of São Paulo (FAPESP)
- Brazilian Support Foundation for Research of Acre (FAPAC)
- Brazilian Support Foundation for Science and Technology in the State of Pernambuco (FACEPE)
- Brazilian Support Foundation for the Development of Education, Science and Technology in the State of Mato Grosso do Sul (FUNDECT)
- Brazilian Support Foundation for the Development of Scientific and Technological Actions and Research in the State of Rondônia (FAPERO)
- Burnet Institute
- Butantan Institute, Fundação Butantan
- California Institute for Regenerative Medicine (CIRM)#
- Campbell Foundation\*
- Canadian Department of Foreign Affairs, Trade and Development (Global Affairs Canada, DFATD)
- Canadian Institutes of Health Research (CIHR)
- Canadian Natural Sciences and Engineering Research Council (NSERC Canada)<sup>#</sup>
- Cebu Leprosy and Tuberculosis Research Foundation (CLTRF)
- CEMAG Care
- Center for Production and Research of Immunobiology (CPPI)
- Children's Investment Fund Foundation (CIFF)
- Chilean National Fund for Scientific and Technological Development (FONDECYT)

<sup>#</sup> Denotes organisations where funding data was taken from publicly available sources

Denotes organisations where funding data was taken norm publicly available sources.

Denotes organisations where funding data was only received via the Resource Tracking for HIV Prevention Research and Development Working Group

- Coalition for Epidemic Preparedness Innovations (CEPI)
- Colombian Ministry for Science, Technology and Innovation (Minciencias)
- Confluence For Health Action And Transformation Foundation (India Health Fund, IHF)
- CONRAD
- Contrel Europe
- CSL Ltd (including Segirus)
- Cuban Center for Genetic Engineering and Biotechnology (CIGB)\*
- Czech Republic Ministry of Agriculture, Ministerstvo zemedelství (eAGRI / MZe)#
- Czech Republic Ministry of Education, Youth and Sport, Ministerstvo školství, mládeže a telovýchovy (MSMT)#
- Czech Republic Ministry of Health, Ministerstvo zdravotnictví (MZ, MZCR)#
- Czech Republic Ministry of Industry and Trade, Ministerstvo prumyslu a obchodu (MPO)#
- Czech Republic Ministry of the Interior, Ministerstvo vnitra (MV)<sup>#</sup>
- Czech Science Foundation, Grantová agentura Ceské republiky (GA CR)#
- Daiichi Sankyo Company, Ltd
- Damien Foundation (DFB)
- Danish Ministry of Foreign Affairs and/or Danish International Development Agency (DANIDA)#
- Danish Ministry of Higher Education and Science (UFM)#
- Drugs for Neglected Diseases initiative (DNDi)
- Dutch Ministry of Foreign Affairs Directorate General of Development Cooperation (DGIS)
- effect:hope (The Leprosy Mission Canada)
- Eisai Co. Ltd.
- Eli Lilly and Company
- Eppin Pharma Inc
- European & Developing Countries Clinical Trials Partnership (EDCTP)
- European Commission (EC)#
- European Vaccine Initiative (EVI)
- Evofem Inc.
- FAIRMED Health for the Poorest
- FHI 360
- Fontilles
- Formas, Swedish Research Council for Sustainable Development#

- Forte, Swedish Research Council for Health, Working Life and Welfare#
- Foundation for Innovative New Diagnostics (FIND)
- Foundation for Neglected Disease Research (FNDR)
- French National Agency for Research on AIDS and Viral Hepatitis (ANRS)
- French National Institute of Health and Medical Research (Inserm)
- French Research Institute for Development (IRD) (including CERMES)
- Fundació La Caixa
- Fungal Infection Trust (FIT)
- Gavi, the Vaccine Alliance
- GeneOne Life Science
- German Centre for Infection Research (Deutsches Zentrum für Infektionsforschung) (DZIF)
- 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)
- Gesea Biosciences
- GlaxoSmithKline (GSK)
- Global Access Diagnostics (GADx)
- Global Action Fund for Fungal Infections (GAFFI)
- Global Antibiotic Research and Development Partnership (GARDP)
- Global Health Innovative Technology Fund (GHIT Fund)
- Grand Challenges Canada (GCC)
- GSK Bio
- Gynuity Health Projects
- Health Research Council of New Zealand (HRC)
- Huesped Foundation, Fundacion Huesped\*
- ImmunityBio, Inc.
- 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 National Snakebite Initiative, including IndianSnakes.org
- Innovate UK (IUK)#
- Innovative Medicines Initiative (IMI)
- Innovative Vector Control Consortium (IVCC)

 $<sup>^{\#}</sup>$  Denotes organisations where funding data was taken from publicly available sources

<sup>\*</sup> Denotes organisations where funding data was only received via the Resource Tracking for HIV Prevention Research and Development Working Group

- INOSAN Biopharma SA
- Institut Pasteur
- Institute of Tropical Medicine Antwerp/Prince Leopold Institute of Tropical Medicine (ITM)
- Instituto Nacional de Producción de Biológicos (ANLIS)
- Integral Molecular
- International AIDS Vaccine Initiative (IAVI)
- International Development Research Centre (IDRC)#
- International Partnership for Microbicides (IPM)\*
- International Vaccine Institute (IVI)
- Irish Aid
- Italian Association Amici di Raoul Follereau (AIFO)
- Italian National Institute of Health, Istituto Superiore di Sanita (ISS)\*
- James Cook University (including the Australian Institute of Tropical Health and Medicine (AITHM))
- Japan Society for the Promotion of Science (JSPS)#
- Japanese Ministry of Health, Labour and Welfare (MHLW)#
- Jhpiego
- Johnson & Johnson
- KfW Group
- Laboratório Farmacêutico do Estado de Pernambuco (LAFEPE)
- Laboratorios Probiol
- Leibniz Institute of Virology (LIV)
- Lepra
- Leprosy Research Initiative (LRI)
- Liverpool School of Tropical Medicine (LSTM)
- London School of Hygiene and Tropical Medicine (LSHTM) (including MEIRU)
- Ludwig Maximilians University of Munich (LMU) (including Klinikum der Universitat Munchen)
- Luna Labs USA
- Lvndra Therapeutics
- Malaysian University Sarawak (UNIMAS) (including the Malaria Research Centre)
- Male Contraceptive Initiative (MCI)
- Mapp Biopharmaceutical
- Matinas BioPharma (including Aquarius Biotechnologies)
- Max Planck Society Max Planck Institute for Infection Biology (MPIIB)
- Max Planck Society Max Planck Institute for Multidisciplinary Sciences
- Médecins Sans Frontières (MSF)

- Medical Research Network of the Consortium of the Thai Medical schools (MedResNet)
- Medicines Development for Global Health (MDGH) Ltd
- Medicines for Malaria Venture (MMV)
- Medicor Foundation
- Melbourne Children's
- Meningitis Research Foundation (MRF)
- Mérieux Foundation, Fondation Mérieux
- Mexican National Institute of Public Health, Instituto Nacional de Salud Publica (INSP)
- Mexican National Polytechnic Institute, Instituto Politécnico Nacional (IPN)
- Michael & Susan Dell Foundation
- MicroPharm Ltd
- Monash University (including CDCO)
- MSD (Merck)
- Mundo Sano Foundation (Fundación Mundo Sano)
- Mymetics
- Netherlands Leprosv Relief (NLR)
- Novartis
- Novo Nordisk Foundation#
- Oak Foundation\*
- Open Philanthropy#
- Ophirex Inc
- Osel\*
- Otsuka Pharmaceutical Co. Ltd
- Parsemus Foundation
- Particles for Humanity
- PATH (including Meningitis Vaccine Project (MVP) and Malaria Vaccine Initiative (MVI))
- Philippine Council for Health Research and Development
- Population Council
- QIAGEN Sciences LLC
- Raoul-Follereau Foundation, Fondation Raoul Follereau (FRF)
- Reproductive Health Investors Alliance (RHIA Ventures)
- Research Centre Borstel
- Research Council of Norway (RCN)
- Research Investment for Global Health Technology Fund (RIGHT Fund)
- Royal Norwegian Ministry of Foreign Affairs (including NORAD)
- Royal Society of New Zealand (RSNZ)

<sup>#</sup> Denotes organisations where funding data was taken from publicly available sources

Denotes organisations where funding data was taken form publicly available sources
 Denotes organisations where funding data was only received via the Resource Tracking for HIV Prevention Research and Development Working Group

- Sabin Vaccine Institute
- · Saint Francis Leprosy Guild (SFLG)
- Sanofi
- Sasakawa Health Foundation (SHF)
- Serum Institute of India (SII)
- Shionogi & Co., Ltd.
- Sidaction\*
- Solidarity Fund
- South African Department of Science and Innovation (DSI)
- South African Medical Research Council (SAMRC)
- Spanish AIDS Research Institute (Institut de Recerca de la Sida) (IrsiCaixa)\*
- Spanish Ministry of Foreign Affairs, European Union and Cooperation (MAEUEC) (including AECID)
- St. George's, University of London
- Sumagen Co. Ltd.\*
- Swedish Heart-Lung Foundation, Hjärt-Lungfonden#
- Swedish International Development Agency (SIDA)#
- Swedish Postcode Lottery\*
- 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)
- Takeda Pharmaceutical Company
- TB Alliance
- Technology Agency of the Czech Republic (TA CR), Technologická agentura CR#
- Telethon Kids Institute
- Thai Government Pharmaceutical Organisation (GPO)
- Thai National Science and Technology Development Agency (NSTDA)
- The David and Lucile Packard Foundation
- The ELMA Foundation
- The Geneva Foundation
- The Leprosy Mission International (TLMI)
- The Paul G Allen Family Foundation
- The Task Force for Global Health
- TuBerculosis Vaccine Initiative (TBVI)
- Turing Foundation
- UK Department of Health and Social Care (DHSC)
- UK Foreign, Commonwealth & Development Office (FCDO)

- UK Medical Research Council (MRC)
- UK National Health Service (NHS) (including National Institute for Health Research NIHR)#
- Unitaio
- University Hospital Bonn, Universitaetsklinikum Bonn (UKB)
- University of Dundee
- University of Geneva
- University of Khartoum (including the Mycetoma Research Center)
- University of Melbourne (including the Australian Venom Research Unit (AVRU) and Bio21 Institute)
- University of Pittsburgh
- University of Sussex (including the Brighton and Sussex Medical School Centre for Global Health)
- University of Tubingen (including the Natural and Medical Sciences Institute, NMI)
- University of Wollongong
- US Agency for International Development (USAID)
- US Biomedical Advanced Research and Development Authority (BARDA)#
- US Centers for Disease Control and Prevention (CDC)
- US Department of Defense (DOD) including DARPA, DTRA, JPEO-CBD, MEDCOM, MRDC, NMRC, NRL, USAMMDA, USAMRAA, USAMRIID, and WRAIR#
- US National Institutes of Health (NIH) including NIAID, NCI, and NICHD#
- Vaccine Research Insitute (VRI)
- Vaccitech Limited
- ViiV Healthcare
- Vinnova#
- Vir Biotechnology
- Volkswagen Foundation, Volkswagen-Stiftung
- Wellcome
- WHO: Special Programme for Research and Training in Tropical Diseases (WHO / TDR)
- WHO: Special Programme of Research, Development and Research Training in Human Reproduction (WHO/HRP)
- Women's Global Health Innovations (WGHI)
- ZonMw (Netherlands Organisation for Health research and Development)

<sup>#</sup> Denotes organisations where funding data was taken from publicly available sources

<sup>\*</sup> Denotes organisations where funding data was only received via the Resource Tracking for HIV Prevention Research and Development Working Group

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