

NEGLECTED DISEASE RESEARCH AND DEVELOPMENT: THE HIGHER COST OF LOWER FUNDING



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NEGLECTED DISEASE RESEARCH AND DEVELOPMENT: THE HIGHER COST OF LOWER FUNDING

INTRODUCTION	5
The G-FINDER report	5
What types of funding does G-FINDER include?	5
FUNDING BY NEGLECTED DISEASE	12
HIV/AIDS	14
Tuberculosis	16
Malaria	18
Diarrhoeal diseases	20
Kinetoplastid diseases	22
Helminth infections (worms and flukes)	24
Dengue	26
Salmonella infections	28
Bacterial pneumonia & meningitis	30
Hepatitis B	32
Snakebite envenoming	34
Hepatitis C	36
Leprosy	38
Cryptococcal meningitis	40
Histoplasmosis	42
Rheumatic fever	44
Scabies	46
Leptospirosis	48
Buruli ulcer	50
Mycetoma	52
Trachoma	54
Yaws	56
R&D for more than one disease	57
NEGLECTED DISEASE FUNDERS	60
Public funding	61
Philanthropic funding	64
Private sector funding	66
Top funding organisations	68
FUNDING FLOWS	69
Funding flow trends	69
Funding by R&D stage	70
Funding for product development partnerships	71
Funding for other intermediaries	73
DISCUSSION	75

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 low- and middle-income countries, making it the gold standard in tracking and reporting global funding for neglected disease R&D.

This year's report, the sixteenth overall, focuses on investments made in participants' 2022 financial year ('FY2022') and, for the first time, adds comprehensive coverage of the product pipeline in each disease area. Additional graphs and tables based on the underlying investment data used in creating this report can be generated using our online data portal: https://gfinderdata. policycuresresearch.org/, while interactive pipeline data can be accessed in our pipeline database: https://www.policycuresresearch.org/pipeline-database/.

This year's report contains an overview of the changes in neglected disease funding in 2022, measured in 2022 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 ("PDPs"), 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. The disease areas for which headline funding totals are potentially misleading due to changes in survey participation 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 in funding.

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 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.





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

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

922			'es	alle	- eS	S.CS.	ostics	³ vicid	es cor
sease			Basic res	Drugs	Vaccines	Biologics	Diagnostics	Nicrobicid	produce
HIV/AIDS			Restricted			Restricted	~	~	-
Tuberculosis			~	~	~	~	~	-	-
Malaria	P. falciparur	n	~	~	~	~	~	-	~
	P. vivax		~	~	~	~	~	-	~
	Multiple / ot	her malaria strains	~	~	~	~	~	-	~
Diarrhoeal diseases			~	Restricted	~	Restricted	~	-	-
	Cholera		~	Restricted	~	Restricted	~	-	-
	Cryptospori	diosis	~	Restricted	~	Restricted	~	-	-
	Rotavirus		Restricted	_ k	Restricted	-	-	-	-
	Enterotoxige	enic <i>E. coli</i> (ETEC)	Restricted	- i	~	-	~	-	-
	Enteroaggre	egative <i>E. coli</i> (EAEC)	-	-	~	-	~	-	-
	Multiple diar	rhoeal diseases	~	Restricted	~	Restricted	~	-	-
Kinetoplastid disea	ses Chagas' dis	ease	~	~	~	~	~	-	~
	Leishmanias	sis	~	~	~	~	~	-	-
	Sleeping sic	kness (HAT)	~	~	~	~	~	-	~
	Multiple kine	etoplastid diseases	~	~	~	~	~	-	~
Helminth infections	Schistosom	iasis (bilharziasis)	~	~	~	~	~	-	~
(worms & flukes)		lariasis (elephantiasis)		~	-	-		-	
		asis (river blindness)			~	-		_	
		ancylostomiasis & necat					-		-
		taeniasis / cysticercosis)		~	-	_		_	
	Whipworm (`	-	_	-	-	
		asis & other intestinal	×	~	~	-	~	-	-
		n (ascariasis)	~	~	-	-	-	-	-
		minth infections		~	~	-	~	-	~
Dengue			~	~	-	~	~	-	
Salmonella infection		l paratyphoid fever Paratyphi A)	~	~	~	~	~	-	-
	Non-typhoid	dal S. enterica (NTS)	~	~	~	~	~	-	-
	Multiple Sali	monella infections	~	~	~	~	~	-	-
Bacterial pneumoni meningitis	a & S. pneumor	iae	Restricted	- 1	Restricted	-	~	-	-
	N. meningiti	dis	Restricted	- 1	Restricted	-	~	-	-
	Both S. pne	umoniae and N. mening	itidis Restricted	- t	-	-	~	-	-
Hepatitis B			Restricted	Restricted	-	Restricted	~	-	-
Snakebite envenom	ing		Restricted	Restricted	-	Restricted	Restricted	-	-
Hepatitis C			-	Restricted	~	-	~	-	-
Leprosy			~	~	~	~	~	-	-
Cryptococcal meningitis			-	~	-	~	-	-	-
Histoplasmosis			~	~	-	-	~	-	-
Rheumatic fever			-	-	~	-	-	-	-
Scabies			Restricted	4 🗸	-	-	~	-	-
Leptospirosis			-	-	-	-	Restricted	-	-
Buruli ulcer			~	~	~	-	~	-	-
Mycetoma			~	~	-	-	~	-	-
Trachoma			-	-	~	-	~	-	-
Yaws			Restricted	- k	-	-	Restricted	-	-
Inves	tment applicable	to more than one neg	lected disease	, or <u>to mo</u>	re t <u>han or</u>	ne global	health ar	ea*	
Vaccine-related		atform technologies	Adjuvants &	Biolog	gics-related technologie	Multi	-disease or control	Core fu multi-di	nding of a sease R&I nisation
	atform technologies disease diagnostics technologies immunor								

denotes a category where a disease or product is included in the survey
 Restricted denotes a category where only some investments are eligible, as defined in the G-FINDER neglected disease R&D scope document
 * The G-FINDER project covers three global health areas: neglected diseases, emerging infectious diseases, and sexual & reproductive health issues

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 development & post-registration studies':

- Basic & early-stage research, includes:
 - Basic research
 - Discovery and pre-clinical development
- Clinical development & post-registration studies, includes:
 - · 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 the neglected disease R&D scope on our <u>website</u>.

CHANGES TO THE LIST OF NEGLECTED DISEASES

The G-FINDER scope is reviewed annually. This year saw two changes to our survey scope: the additional inclusion of R&D funding for yaws – including funding for yaws basic research and diagnostic R&D – and the removal of funding for giardiasis thanks several years of inactivity and a lack of major unmet needs. Earlier funding for giardiasis has been retrospectively removed from previous years' totals presented in this report. While these, and all other 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.

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. The high rate of global inflation in 2022 (8.0% in the US, 8.4% in the Eurozone) led to a reduction in the real value of 2022 funding despite relatively consistent nominal spending. We discuss this effect and our treatment of it elsewhere in the report.

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 on 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 FY2022 figures) are available via the G-FINDER data portal.

SUPPLEMENTARY MATERIALS

Details on the survey methodology and data validation are available at www.policycuresresearch.org/g-finder

All data behind the G-FINDER report is available through our online data portal at https://gfinderdata.policycuresresearch.org/

Table 2. Disease and product R&D funding 2022 (US\$ millions)

acae or aD area	resear	on	ines_	dics_	ostics	picides	ctor conve	Inspecified	
80 a	Basic resear	Drugs ,	Vaccines	Biologics	Diagnostics	Microb Ve	actor control	INSPECT	iotal
HIV/AIDS	216.16	232.13	674.43	68.48	24.73	37.19		98.66	1,351.80
Tuberculosis	186.01	336.68	91.18	5.00	62.28			21.27	702.43
Malaria	154.83	235.46	106.29	26.59	11.51		57.86	10.99	603.53
P. falciparum	70.49	78.45	88.60	20.27	2.93		6.04	3.59	270.36
P. vivax	14.70	26.60	7.02	0.49	2.39		0.25	0.16	51.62
Multiple / other malaria strains	69.64	130.40	10.68	5.82	6.19		51.58	7.24	281.55
Diarrhoeal diseases	49.09	21.87	73.84	5.13	5.71			0.60	156.25
Shigella	10.91	1.29	29.74	3.22	4.55			-	49.71
Cholera	21.67	1.26	11.91	1.91	0.31			-	37.07
Cryptosporidiosis	7.78	15.45	0.44	-	0.06			-	23.74
Rotavirus	2.12		18.84					-	20.97
Enterotoxigenic E. coli (ETEC)	0.67		9.62		0.06			-	10.35
Enteroaggregative E. coli (EAEC)			-		0.02			-	0.02
Multiple diarrhoeal diseases	5.93	3.87	3.29	-	0.70			0.60	14.39
Kinetoplastid diseases	45.10	71.44	4.20	0.06	4.12		0.93	0.03	125.87
Chagas' disease	7.39	29.71	2.87	0.03	2.70		0.02	0.01	42.71
Leishmaniasis	20.66	15.58	1.02	0.04	0.49			0.02	37.81
Sleeping sickness (HAT)	14.76	9.51	0.31	-	0.94		0.91	-	26.44
Multiple kinetoplastid diseases	2.28	16.64	-	-	-		-	-	18.92
Helminth infections (worms & flukes)	37.77	38.33	10.82	0.20	7.95		0.03	8.74	103.85
Schistosomiasis (bilharziasis)	11.58	14.24	9.10	0.20	3.25		-	0.50	38.88
Lymphatic filariasis (elephantiasis)	6.86	3.96			1.89		0.02	7.81	20.53
Onchocerciasis (river blindness)	2.46	10.67	0.04		1.05		0.02	-	14.23
Hookworm (ancylostomiasis & necatoriasis)	2.18	1.12	1.31		1.00		0.02	_	4.61
Tapeworm (taeniasis / cysticercosis)	3.03	0.13	1.01		0.70		-	0.30	4.16
Whipworm (trichuriasis)	2.17	0.13			0.70		_	0.00	2.40
Strongyloidiasis & other intestinal	1.92	0.23	0.06		0.16			-	2.34
roundworms									
Roundworm (ascariasis)	1.31	0.09						-	1.40
Multiple helminth infections	6.27	7.67	0.32		0.90		-	0.13	15.29
Dengue	21.43	47.64		6.86	3.87		1.53	0.49	81.83
Salmonella infections	35.05	1.59	41.82	0.20	1.46			0.20	80.32
Typhoid and paratyphoid fever (S. Typhi, S. Paratyphi A)	25.80	1.59	24.76	0.20	1.30			0.20	53.85
Non-typhoidal S. enterica (NTS)	2.10	-	11.99	-	-			-	14.09
Multiple Salmonella infections	7.16	<0.01	5.07	-	0.16			-	12.39
Bacterial pneumonia & meningitis	5.73		40.36		0.94			0.58	47.62
S. pneumoniae	4.57		34.61		0.61			0.58	40.38
N. meningitidis	1.16		5.74		0.33			-	7.24
Both S. pneumoniae and N. meningitidis	-				-			-	
Hepatitis B	3.28	2.57		22.86	1.72			-	30.43
Snakebite envenoming	0.57	11.92		7.87	0.48			0.15	20.99

sease or ABD area	Basic resear	prugs ,	Vaccines	Biologics	Diagnostics	Nicrobicides	ector contro products	Unspecified	Total
40	Bac		Vae	310 1	Jide N	VIIC	pro		,01
Hepatitis C		1.43	9.38		4.93			-	15.74
Leprosy	6.28	6.56	0.30	0.03	0.42			-	13.58
Cryptococcal meningitis		5.89		0.76				-	6.65
Histoplasmosis	3.35	0.09			<0.01			-	3.44
Rheumatic fever			3.43						3.43
Scabies	0.62	1.15			-			0.12	1.89
Leptospirosis					1.17				1.17
Buruli ulcer	0.45	-	0.03		0.09			-	0.57
Mycetoma	0.25	0.23			-			-	0.49
Trachoma			-		0.17			-	0.17
Yaws	-				-			-	-
Platform technologies									194.12
Vaccine-related platform technologies									83.60
General diagnostic platforms & multi-disease diagnostics									52.31
Drug-related platform technologies									26.65
Adjuvants and immunomodulators									20.96
Biologics-related platform technologies									10.61
Multi-disease vector control									63.24
Core funding of a multi-disease R&D organisation									248.74
Other R&D									73.10
Total R&D funding									3,931.24

INTRODUCTION

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 2022 was \$3,931m, a drop of \$446m (-10%) from 2021.

A slight net decrease in survey participation made almost no difference to the headline change, with funding from continuing survey participants falling by the same percentage as overall funding. Similarly, the addition of yaws to the 2022 survey scope (with a depressing zero dollars in 2022 R&D funding) and the retrospective removal of giardiasis diagnostics (with no reported funding in 2021) contributed nothing to the overall change.

Instead, this year's fall in funding - after several years of relative stability - was mostly the result of increased global inflation in 2022, which eroded the real value of R&D funding even as nominal dollar amounts once again remained relatively stable. In fact, in the absence of any inflation, global funding would have fallen by only 3.0%, far below our 10% estimate of the inflation-adjusted change.



Figure 2. Total R&D funding for neglected diseases 2007-2022

2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2022

We remain convinced that buying power, not number of dollars spent, is the best measure of investment in research and development; but the measures of overall national inflation we use are not perfectly adapted for measuring the immediate impact of overall price rises on the costs specific to R&D. The US NIH, for example, estimates the increase in its 2022 costs at 4.9%, as opposed to our 8.0% figure for overall US inflation. As part of our discussion of this year's findings later in the report, we consider the potential impact of adopting different measures of inflation.

Funding for the WHO neglected tropical diseases (NTDs) covered by the G-FINDER survey totalled \$349m, remaining almost unchanged – in real, inflation-adjusted terms – from 2021 (down just \$0.2m, -0.1%). On the other hand, the three diseases with the highest funding - HIV/AIDS, tuberculosis, and malaria - all saw sharp falls, headlined by a record \$241m (-15%) drop for HIV/AIDS, alongside smaller, but still substantial, falls for malaria (down \$73m, -11%) and tuberculosis (down \$70m, -9.1%).

In fact, most individual disease areas saw reductions in funding in 2022, with several - including Buruli ulcer, trachoma and kinetoplastid diseases - experiencing record lows. Even non-diseasespecific funding, which had grown every year since 2014, stumbled, falling by \$52m, or 8.2%, mostly as a result of reduced core funding to multi-disease R&D organisations.

Only six areas experienced any growth at all: funding for hepatitis B jumped by \$14m (87%) to a record high; helminth R&D increased by \$11m (12%); diarrhoeal diseases by \$7.9m (5.3%); Salmonella by \$5.8m (7.8%); leprosy by \$3.7m (37%); and snakebite by \$2.6m (14%).

Table 3. R&D funding by disease 2013-2022^

ease or 20 area	5\$ Imillic	INSI								2	022 % of
30 a	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
HIV/AIDS	1,335	1,354	1,288	1,389	1,487	1,668	1,685	1,535	1,593	1,352	34
Tuberculosis	648	675	673	688	713	768	794	758	772	702	18
Malaria	631	679	666	693	740	756	707	696	676	604	15
Diarrhoeal diseases	237	206	188	180	189	202	189	167	148	156	4.0
Kinetoplastid diseases	146	173	145	166	170	177	178	170	141	126	3.2
Helminth infections (worms & flukes)	109	107	92	89	101	109	107	90	93	104	2.6
Dengue	82	97	106	129	93	89	90	84	84	82	2.1
Salmonella infections	77	77	81	108	95	103	90	86	75	80	2.0
Bacterial pneumonia & meningitis	118	85	109	108	86	100	77	72	66	48	1.2
Hepatitis B						11	11	18	16	30	0.8
Snakebite envenoming						8.7	13	17	18	21	0.5
Hepatitis C	56	54	40	34	17	54	12	18	17	16	0.4
Leprosy	14	12	12	13	13	10	11	9.0	9.9	14	0.3
Cryptococcal meningitis	3.5	6.6	6.0	6.7	13	9.2	9.1	7.9	15	6.6	0.2
Histoplasmosis								4.6	3.9	3.4	<0.1
Rheumatic fever	1.2	1.9	3.2	2.1	2.0	2.2	18	24	13	3.4	<0.1
Scabies								1.3	1.9	1.9	<0.1
Leptospirosis	0.4	1.4	1.4	2.6	3.4	1.8	2.3	1.6	1.5	1.2	<0.1
Buruli ulcer	7.2	4.1	2.0	3.1	4.7	2.8	3.0	2.7	0.6	0.6	<0.1
Mycetoma						0.7	1.0	0.8	0.8	0.5	<0.1
Trachoma	2.6	1.6	1.4	2.6	2.9	2.1	2.0	2.0	0.7	0.2	<0.1
Yaws										-	-
Platform technologies Vaccine-related	53 5.5	28 2.9	43 5.6	89 18	61 4.1	78 17	108 37	140 53	163 57	194 84	4.9 2.1
platform technologies General diagnostic platforms & multi- disease diagnostics	20	12	18	46	34	36	39	52	50	52	1.3
Drug-related platform technologies	2.1	2.9	4.2	3.9	7.6	2.5	6.3	8.3	25	27	0.7
Adjuvants and immunomodulators	26	10	15	22	16	22	26	26	17	21	0.5
Biologics-related platform technologies									13	11	0.3
Multi-disease vector control				22	33	45	71	71	82	63	1.6
Core funding of a multi-disease R&D organisation	125	114	154	173	295	339	331	341	323	249	6.3
Other R&D	87	45	54	42	49	73	43	59	62	73	1.9
Total R&D funding	3,734	3,723	3,664	3,940	4,169	4,609	4,553	4,375	4,377	3,931	100

FINDINGS - DISEASES

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. Yaws was added in 2022.

Biologics-related platform technologies were moved to a separate category in 2021. Yaws was added in 2022. 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.

- No reported funding



Global investment for HIV/AIDS R&D fell by \$241m (-15%), to its lowest level since 2015. The overall decrease was mostly the result of reduced funding from all five of the 2021 top funders: US NIH, industry and record low funding from the DOD and the Gates Foundation.

Funding from the NIH was down \$98m (-9.4%), falling across most product areas but most heavily on biologics (down \$29m, -45%) and basic research (down \$28m, -13%). A sizable reduction in their microbicide investment also drove down total microbicide funding to a historic low. More than half of the NIH cuts were in its HIV Prevention Trials Network (down \$46m, -50%) and Microbicide Trials Network (down \$9.4m, -100%).

Industry investment fell by \$29m (-13%), essentially all for vaccine R&D (down \$35m, -43%) as a major Phase III clinical trial was discontinued in late 2022 – contributing to 2022's record-low vaccine R&D investment.

Gates Foundation funding fell by 27% (down \$43m), mostly in drug R&D (down \$43m, -80%), the drop-off following the 2021 initial disbursements for the sub-Saharan Phase III islatravir IMPOWER drug trials.

Investment by the US DOD was reduced by almost two-thirds (down \$22m, -64%) – all in vaccine R&D – as part of a broader restructuring of its internal R&D funding.

USAID's total funding for MATRIX, a five-year, \$125m project to advance HIV microbicide and prevention technology, remained steady. Within the project, the proportions of R&D funding for HIV-only microbicides versus multi-purpose prevention technologies (MPTs) shifted, with the share for MPTs increasing in 2022. Because MPT R&D investment is captured within our sexual & reproductive health report, the apparent decrease is entirely artificial, with USAID in fact continuing a strong trend of consistent support.



Figure 3. HIV/AIDS R&D funding by product type 2013-2022

Table 4. Top HIV/AIDS R&D funders 2022

, , , , , , , , , , , , , , , , , , ,	JS\$ (millic	nsl								9	022 % of to
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
US NIH	848	880	867	912	881	1,033	1,106	1,046	1,039	941	70
Aggregate industry	19	55	67	102	173	232	210	155	230	201	15
Gates Foundation	150	137	134	160	163	155	173	143	157	114	8.5
USAID	81	72	72	58	75	56	47	56	67	44*	3.3
US DOD	69	77	35	46	43	27	23	33	35	13	0.9
Unitaid	0.8	8.4	6.2	5.2	40	61	30	23	12	4.9	0.4
UK MRC	5.9	6.9	5.2	6.4	5.1	2.6	3.5	3.1	1.0	3.4	0.2
Indian ICMR	2.6	2.1	0.3	-	1.8	0.4	1.5	1.8	3.5	3.3	0.2
South African DSI	4.6	2.0	2.0	3.0	3.0	3.5	4.0	3.7	2.4	3.1	0.2
Netherlands Ministry of Foreign Affairs	8.0	6.6	1.4	9.9	12	6.2	6.1	2.2	8.2	2.2	0.2
Subtotal of top 10^	1,241	1,289	1,232	1,337	1,424	1,612	1,633	1,491	1,562	1,330	98
Disease total	1,335	1,354	1,288	1,389	1,487	1,668	1,685	1,535	1,593	1,352	100

^ Subtotals for 2013-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022.

- No reported funding

* While USAID's HIV-specific funding fell in 2022, this is an artefact of its increased focus on HIV-targeted multi-purpose prevention technologies, which is captured separately in our report on sexual & reproductive health. USAID's overall contributions remained unchanged.

The most advanced HIV vaccine candidate, Ad26.Mos4.HIV, was discontinued in early 2023 after failing to meet interim endpoints, marking the end of purely non-neutralising approaches to <u>vaccination</u>. Focus shifted towards immunogen design directed at antigens eliciting bNAbs response in combination with approaches that elicit cellular/innate response, such as T-cell-based vaccines. Using the human cytomegalovirus vector platform, <u>Vir Biotechnology</u> dosed the first participants in a Phase I trial in South Africa and the US, investigating their novel T-cell VIR-1388 <u>vaccine</u>.

Another leading vaccine strategy, germline targeting, uses engineered proteins to raise B-cells with the genetic properties necessary for producing bNAbs. The nanoparticle-based engineered construct eOD-GT8 60-mer, from Fred Hutchinson Cancer Research Center, Scripps Research and <u>IAVI</u>, successfully induced robust CD4 T-cell responses in nearly all participants in a Phase I <u>trial</u>.

For the PEPFAR program, the US FDA approved taste-masked dispersible and immediate-release single tablet fixed-dose formulations of abacavir/dolutegravir/lamivudine for children, the second <u>child-friendly</u> drug specifically approved for LMICs behind DNDi's <u>'4-in-1'</u>. United Biopharma's UB-421, a CD4 attachment inhibitor-based monoclonal antibody, began Phase III <u>trials</u>.



Figure 4. HIV/AIDS R&D pipeline by product type



Funding for tuberculosis R&D totalled \$702m in 2022, a decline of -9.1% (or \$70m) bringing it back to levels last seen in 2017.

A key contributor to this fall was declining funding from Unitaid (down \$22m, -70%). It had more than doubled its contributions in 2021, focusing heavily on drug clinical development. This growth was reversed in 2021, with Unitaid's drug development falling by \$13m (-80%). The overall slump was worsened by a third consecutive fall in funding from the US NIH (down \$27m, -8.5%), though it remained the top funder in 2022.

These reductions were partly offset by an increase from the Gates Foundation (up \$28m, 22%), almost all of which went to vaccine development (up \$17m, 49%) and largely to the Gates MRI, where TB investment has more than doubled since its inception in 2019.

While drug R&D fell by \$45m (-12%), the largest proportional fall was for basic research, which fell \$34m to \$186m, mostly due to declining NIH investment (down \$19m, -12%). Vaccine R&D was the only area of growth (up \$15m, 19%), most thanks to the increase in funding from the Gates Foundation.

Both funding for early-stage research and clinical development fell. But while early-stage research remained well above its long-term average, clinical development fell to a 13-year low, with late-stage research buoyed only by industry funding for post-registration drug studies.

While TB R&D funding from the Gates Foundation rose slightly in 2022, forward-looking data suggest rapid growth over the next few years. The Gates Foundation has committed \$844m over three and a half years – up from \$475m over the previous six years – to the Gates MRI, focusing on the development of the M72/AS01E TB vaccine through Phase III.



Figure 5. TB funding by product type 2013-2022

Table 5. Top TB R&D funders 2022

	JS\$ (millic	nsl									022 % of to
Funder	154									2	024
FU	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
US NIH	209	241	245	262	288	318	360	337	323	296	42
Gates Foundation	158	166	159	122	107	120	134	134	127	155	22
Aggregate industry	118	108	110	102	110	108	94	89	107	102	14
EC	20	16	27	22	18	12	10	34	41	42	6.0
Indian ICMR	9.2	9.3	9.1	14	20	21	18	15	12	13	1.9
German BMBF	5.3	6.3	7.2	10	17	16	24	15	16	11	1.5
UK FCDO	14	15	13	8.4	15	25	18	14	8.8	9.9	1.4
Unitaid	2.4	0.6	7.4	40	14	15	17	13	31	9.2	1.3
US CDC	-	18	11	10	18	17	15	16	14	8.8	1.3
Wellcome	14	12	11	9.7	9.8	11	13	10	9.8	7.0	1.0
Subtotal of top 10^	572	612	608	612	620	671	707	679	690	654	93
Disease total	648	675	673	688	713	768	794	758	772	702	100

^ Subtotals for 2013-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022.

- No reported funding

After more than five years without any new vaccine candidates entering clinical development, in 2023 *two* new TB vaccines were slated to enter clinical trials: BioNTech's mRNA TB vaccine, a first of its kind, began its Phase I trial in July 2023; and Statens Serum Institut's H107e/CAF 10b, an adjuvanted subunit vaccine, is expected to start recruiting participants by late 2023.

Similarly, after more than five years since we last saw a positive result from a Phase II vaccine trial, the Gates MRI are set to begin Phase III trials of the M72/AS01E vaccine candidate in early 2024.

Results from the SUDOCU Phase IIb drug <u>trial</u> demonstrated that in different doses, sutezolid is a safe addition to bedaquiline, delamanid, and moxifloxacin regimen for treating <u>DS-TB</u>. In 2023, the WHO recommended a new class of tests: targeted next-generation sequencing (NGS) for detecting drug-resistant TB. At least one NGS technology, DeepChek DST, is undergoing WHO review.



Figure 6. Tuberculosis R&D pipeline by product type



Global funding for malaria R&D dropped to 603m in 2022. This represented its steepest fall ever – a drop of more than 10% (73m) – leaving funding at its lowest level in the past 15 years.

Funding for vaccines fell for a fifth consecutive year, to a record low of \$106m (down a further \$16m, -13%). The Gates Foundation accounted for over 30% of this fall, with its funding to PATH's Malaria Vaccine Initiative dropping over the course of the five year decline from \$36m to \$4.5m as it reduced its investment in the clinical development of fractional dose RTS,S for *P. falciparum* elimination.

Drugs continued to receive the largest share of funding, at \$235m (39% of the total), despite falling by \$33m (-12%). The decline was primarily driven by drops in funding from the US DOD (down \$21m, -74%), whose overall investment in malaria fell to a record low of \$11m – just one fifth of its 2018 peak.

Funding for basic research also declined, falling by one-fifth to \$155m (down \$38m), with the largest cuts coming from the US NIH (down \$12m, -11%), though it remained the overall top funder of malaria R&D. In contrast, funding for biologics again continued its rise, jumping more than 250% (up \$19m) to \$27m in 2022, nearly 14 times its 2018 level. This was almost entirely driven by the Gates Foundation, which was responsible for more than 80% of malaria biologics funding in 2022.

Most vaccine candidates target *P. falciparum* (51, 76%), followed by *P. vivax* (12, 18%), while most drugs target *P. falciparum* (26, 44%) and just three specifically target *P. vivax* (5%). All biologic candidates target *P. falciparum*, and all VCPs target the mosquito, not the malarial parasite.



Figure 7. Malaria R&D funding by product type 2013-2022

Table 6. Top malaria R&D funders 2022

, ct	JS\$ (millio	nsl								2	022 % of tots
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
US NIH	175	186	193	201	205	199	193	204	203	186	31
Gates Foundation	159	180	146	153	124	147	141	146	136	152	25
Aggregate industry	86	132	158	154	147	172	131	121	109	119	20
UK FCDO	27	20	18	13	40	35	37	34	17	18	2.9
Unitaid	7.0	10	9.5	4.6	4.6	3.1	8.3	9.4	27	17	2.8
Wellcome	27	24	18	15	16	18	20	21	19	15	2.4
Indian ICMR	8.4	8.0	8.8	10	17	16	17	16	19	14	2.3
US DOD	30	23	41	44	45	53	49	42	36	11	1.8
Australian NHMRC	13	12	3.6	3.8	4.8	11	12	15	13	10	1.7
UK MRC	17	15	9.0	12	14	9.7	11	9.9	9.8	8.2	1.4
Subtotal of top 10^	565	624	617	628	638	673	623	622	594	550	91
Disease total	631	679	666	693	740	756	707	696	676	604	100

[^] Subtotals for 2013-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022.

R21/Matrix-M – developed by the University of Oxford and Serum Institute of India – became the second malaria vaccine to be prequalified by the WHO in December <u>2023</u>. Ghana, Nigeria and <u>Burkina Faso</u> were the first countries to approve the <u>vaccine</u>.

Mitsui Chemicals Agro's VECTRON T500, an indoor residual spray with a novel mode of action effective against resistant mosquitoes, received WHO prequalification in March <u>2023</u>.

BioNTech initiated a Phase I trial in late 2022 for BNT165b1, a circumsporozoite protein targeting mRNA vaccine, the first candidate emerging from their multi-antigen vaccine <u>program</u>.

In 2023, Brazil became the first malaria-endemic country to approve single-dose tafenoquine for children with relapsing *P. vivax* infections.



Figure 8. Malaria R&D pipeline by product type



Funding for diarrhoeal disease^{*} R&D rebounded slightly from last year's record low, recovering to \$156m in 2022 (up \$7.9m, 5.3%), though this was still more than \$30m below its ten-year average.

While funding for cholera increased (up \$4.0m, 12%), alongside cryptosporidiosis (up \$2.5m, 12%) and enterotoxigenic *E. coli* (ETEC) (up \$0.3m, 3.4%), much of the overall rebound was due to increased funding for **multiple diarrhoeal diseases**, which reversed their five-year downward trend, with their funding almost doubling to \$14m (up \$7.0m, 94%). More than half of this jump was due to the US DOD, with new drug R&D funding making it the top funder in this area for the first time.

The 12% jump in **cholera** funding was driven by a doubling in its vaccine R&D, which reached \$12m (up \$6.5m, 121%). More than half of this went to Korea's International Vaccine Institute (IVI) including \$2.5m from Open Philanthropy to support a Phase I trial of a conjugate vaccine. Funding for **cryptosporidiosis** was buoyed by record funding from Wellcome and near-record funding from industry, both mostly for drug R&D.

In contrast, funding for **Shigella** fell by 10% (down \$5.4m), with a steep fall in vaccine funding from last year's record high (down \$10m, -26%). This was partially offset by the highest ever *Shigella* diagnostics funding at \$4.6m, accounting for 80% of diarrhoeal diagnostics.

The US NIH remained the top overall funder, though its contributions dropped by \$11m (-17%). In contrast, DOD funding more than doubled to \$12m – its highest level in the past decade.

Disease	Basic resear	onugs ,	Vaccines F	Biologics	Diagnostics	Unspecified	iotal c	20
Shigella	11	1.3	30	3.2	4.6	-	50	32
Cholera	22	1.3	12	1.9	0.3	-	37	24
Cryptosporidiosis	7.8	15	0.4	-	<0.1	-	24	15
Rotavirus	2.1		19			-	21	13
Enterotoxigenic E. coli (ETEC)	0.7		9.6		<0.1	-	10	6.6
Enteroaggregative E. coli (EAEC)			-		<0.1	-	<0.1	<0.1
Multiple diarrhoeal diseases	5.9	3.9	3.3	-	0.7	0.6	14	9.2
Total	49	22	74	5.1	5.7	0.6	156	100

Table 7. Diarrhoeal disease R&D funding 2022 (US\$ millions)^

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

- No reported funding

Category not included in G-FINDER

Table 8. Top diarrhoeal disease R&D funders 2022

,	JS\$ (millio	nsi								2	022 % oft
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
US NIH	58	54	46	46	48	52	51	63	65	54	34
Gates Foundation	63	51	49	60	56	51	50	29	33	42	27
Aggregate industry	53	46	38	34	38	51	51	41	23	22	14
US DOD	13	12	8.7	7.1	10	8.4	9.6	5.4	4.8	12	7.4
Wellcome	2.9	4.9	4.0	2.9	3.7	8.1	8.0	9.4	7.3	11	7.1
Indian ICMR	5.3	5.2	5.8	5.6	7.7	6.0	5.3	6.4	4.2	4.8	3.1
EC	3.4	3.4	3.3	0.6	2.1	3.1	3.5	3.5	3.6	2.8	1.8
Open Philanthropy					-	-	-	1.1	1.1	2.5	1.6
UK MRC	1.8	1.6	1.0	1.0	0.9	0.3	1.7	2.0	1.1	1.7	1.1
Swiss SNSF	1.3	0.2	-	0.4	0.3	0.3	0.3	0.4	1.2	1.4	0.9
Subtotal of top 10^	226	200	177	171	177	194	186	164	144	153	98
Disease total	237	206	188	180	189	202	189	167	148	156	100

^ Subtotals for 2013-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022.

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

Diarrhoeal diseases have 62 products in the pipeline, dominated by vaccines for *Shigella* (13) and rotavirus (16), of which four rotavirus candidates are in Phase III.

Bharat Biotech International's inactivated cholera vaccine, Hillchol entered a Phase III <u>trial</u> in February 2023. ETVAX, a multivalent oral whole-cell vaccine containing four inactivated ETEC strains and the heat-labile enterotoxin B subunit, has shown promising results in Phase I and II <u>studies</u>, suggesting that a safe and effective ETEC vaccine will soon be available, with Zambian Phase III trials to begin in 2024.

After generating positive human results with its monovalent *Shigella* vaccine, LimmaTech began developing a multivalent vaccine in 2018. Results of its Phase I and Phase II studies are expected in December 2023. A positive outcome for safety and immunogenicity will support the further development with pivotal efficacy trials in the target paediatric population.



Figure 9. Diarrhoeal diseases R&D pipeline by product type



Funding for kinetoplastid diseases fell for the third consecutive year, to a record low of \$126m. The fall was felt across almost every individual disease, with leishmaniasis most heavily affected (down \$8.1m, -18%), followed by sleeping sickness (down \$4.9m, -16%), and funding for multiple kinetoplastid diseases (down \$3.0m, -14%) – each of which was a record low.

The lone bright spot was **Chagas' disease**, which saw a modest increase of \$1.3m. This was primarily thanks to first-time funding from Unitaid (\$3.0m) for the development of drugs and diagnostics for blocking congenital transmission of Chagas'. Despite this new funding stream, overall funding for Chagas' drugs and diagnostics remained stable; only vaccine funding saw an overall increase, following \$1.0m of new investment from the US NIH towards early-stage development of a Chagas' DNA vaccine.

Sleeping sickness (HAT) drug funding dropped for the fourth year running (down \$3.4m, -26%), following the completion of a Phase II/III trial of acoziborole, which had been funded by the Gates Foundation. In 2022 we also saw the first funding for HAT VCPs since 2013: \$0.9m towards developing tools to control Kenyan tsetse fly populations.

The drop in **leishmaniasis** funding was primarily due to decreases in support from both Wellcome – whose funding fell by 47%, mostly in drug R&D – and the US NIH (down \$2.0m for leishmaniasis alone), which reduced its overall kinetoplastid funding by a total of \$4.5m (-10%) to reach a record low.

Disease	Basic resea	orugs	laccines F	Biologics	Diagnostics	actor contro products	Unspecified	rotal o	10
Chagas' disease	7.4	30	2.9	<0.1	2.7	<0.1	<0.1	43	34
Leishmaniasis	21	16	1.0	<0.1	0.5		<0.1	38	30
Sleeping sickness (HAT)	15	9.5	0.3	-	0.9	0.9	-	26	21
Multiple kinetoplastid diseases	2.3	17	-	-	-	-	-	19	15
Total	45	71	4.2	<0.1	4.1	0.9	<0.1	126	100

Table 9. Kinetoplastid disease R&D funding 2022

No reported funding

Category not included in G-FINDER

Table 10. Top kinetoplastid disease R&D funders 2022

ر مەر	JS\$ (millio	nsl								2	022 % of to
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
US NIH	56	51	44	49	51	48	50	47	44	39	31
Aggregate industry	19	21	23	16	18	38	45	36	31	29	23
Wellcome	11	14	13	13	10	11	11	14	13	10	8.1
UK FCDO	9.2	14	14	15	25	24	21	21	7.1	9.2	7.3
Gates Foundation	11	23	3.3	16	12	9.3	5.8	7.0	5.6	4.8	3.8
Indian ICMR	5.4	4.7	3.3	3.8	6.4	3.6	4.2	4.2	4.4	4.4	3.5
German BMBF	4.4	5.9	3.4	1.8	3.2	2.8	3.2	6.9	4.2	4.2	3.4
EC	4.1	12	15	13	6.0	3.5	3.3	4.7	4.4	4.0	3.2
Unitaid	-	-	-	-	-	-	-	-	-	3.0	2.4
Brazilian FAPESP			1.8	3.1	2.8	3.1	4.3	2.8	2.6	2.9	2.3
Subtotal of top 10^	127	153	127	139	143	149	152	147	121	111	88
Disease total	146	173	145	166	170	177	178	170	141	126	100

^ Subtotals for 2013-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022.

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

- No reported funding

The twelve Leishmania drugs accounted for just over two-thirds (67%) of the total drug pipeline, including all the preclinical candidates, all but one Phase I candidate, and a candidate each in Phases I and III. Chagas' disease has two candidates in Phase II and one each in Phase I and discovery. Both HAT drugs are currently in Phase III. The biologics pipeline is similarly dominated by Leishmania, including both clinical candidates; the remaining preclinical candidates target Chagas'. The vaccine pipeline remains in the preclinical stage; six candidates are in development for Chagas' disease and the remainder target Leishmania. ChAd63-KH, a vectored Leishmania therapeutic vaccine with demonstrated safety and immunogenicity, completed a Phase IIb efficacy trial for treating PKDL in 2023. Trial results published in 2023 showed acoziborole, a novel compound with the potential to be used as a one-day, single-dose treatment for sleeping sickness caused by *T.b. gambiense*, to be efficacious, with a cure rate of over 95%. A clinical trial is also underway investigating acoziborole for a paediatric indication.



Figure 10. Kinetoplastid diseases R&D pipeline by product type



Overall funding for helminth R&D increased by \$11m in 2022. The majority of this increase was invested in schistosomiasis (up \$12m to \$39m), followed by lymphatic filariasis (up \$7.2m to \$21m) and funding for multiple helminth infections (up \$2.0m to \$15m). These increases trumped decreased funding in other areas, including substantial drops in funding for onchocerciasis (down \$4.6m to \$14m) and tapeworm (down \$3.5m to \$4.2m).

The \$12m increase for **schistosomiasis** was largely due to new industry participation, representing the largest industry investment in R&D for schistosomiasis ever reported. Though this apparent growth reflects ongoing activity not captured in previous years' data, rather than genuinely new funding. Record support from Wellcome and increased contributions from the Gates Foundation also drove an increase in schistosomiasis vaccine funding, which rose by \$3.7m (up 69%), with investment in multiple Phase I/II trials.

The increase in **lymphatic filariasis** funding interrupted a five-year downward trend, and came primarily from the German BMBF, which ramped up funding to the TAKeOFF consortium – a mix of drug and basic research projects – with a near sixfold increase in their funding, displacing the US NIH as the top lymphatic filariasis funder for the first time ever.

The fourth consecutive decline in **onchocerciasis** funding was primarily driven by decreasing drug development support from the Gates Foundation and industry.

Overall funding for helminths basic research fell across every disease area as NIH funding dropped to near-record lows, reflecting both an overall reduction and its pivot towards product-focused funding.

Disease	Basic resea	orugs ,	Vaccines F	Biologics	Diagnostics	actor contro	Unspecified	jotal o	0_
Schistosomiasis									
(bilharziasis)	12	14	9.1	0.2	3.3	-	0.5	39	37
Lymphatic filariasis (elephantiasis)	6.9	4.0			1.9	<0.1	7.8	21	20
Onchocerciasis (river blindness)	2.5	11	<0.1		1.0	<0.1	-	14	14
Hookworm (ancylostomiasis & necatoriasis)	2.2	1.1	1.3				-	4.6	4.4
Tapeworm (taeniasis / cysticercosis)	3.0	0.1			0.7	-	0.3	4.2	4.0
Whipworm (trichuriasis)	2.2	0.2					-	2.4	2.3
Strongyloidiasis & other intestinal roundworms	1.9	0.2	0.1		0.2		-	2.3	2.3
Roundworm (ascariasis)	1.3	0.1					-	1.4	1.4
Multiple helminth infections	6.3	7.7	0.3		0.9	-	0.1	15	15
Total	38	38	11	0.2	7.9	<0.1	8.7	104	100

Table 11. Helminth R&D funding 2022 (US\$ millions)

No reported funding
 Category not included in G-FINDER

Table 12. Top helminth R&D funders 2022

	JS\$ (millio	nsi								2	022 % of tota
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
US NIH	36	36	35	38	46	42	48	45	47	41	40
Aggregate industry	10	16	14	9.5	11	23	17	8.7	6.8	17	16
Gates Foundation	27	29	22	22	17	19	11	9.7	13	12	12
German BMBF	0.7	0.3	0.3	<0.1	3.9	3.6	5.3	2.8	3.4	9.4	9.0
EC	7.6	7.2	5.2	3.8	3.3	1.1	2.1	3.9	4.1	4.4	4.3
German DFG	3.1	-	2.2	1.5	1.6	2.4	4.8	3.1	4.4	3.6	3.5
Wellcome	7.3	4.8	3.9	3.9	3.6	2.8	2.3	1.6	1.5	3.2	3.1
Indian ICMR	1.7	1.6	1.5	1.3	2.2	1.5	2.6	3.0	2.7	2.6	2.5
Medicines Development for Global Health					3.2	1.2	2.3	2.5	2.3	2.4	2.3
Open Philanthropy					-	-	-	-	0.2	1.9	1.8
Subtotal of top 10^	101	102	88	84	94	100	98	82	87	97	94
Disease total	109	107	92	89	101	109	107	90	93	104	100

^ Subtotals for 2013-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022.

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

Onchocerciasis has 11 active candidates and schistosomiasis 13. Of these, five are onchocerciasis diagnostics and five schistosomiasis vaccines.

The Pediatric Praziquantel Consortium program completed clinical development of arpraziquantel – a new pediatric treatment for schistosomiasis – with the positive results from the pivotal clinical Phase III trial leading to a positive scientific <u>opinion</u> from the EMA in December 2023. Emodepside is an anti-filarial agent long approved for treating veterinary helminthic infections now being developed by a consortium including DNDi as a potential treatment for onchocerciasis. It succeeded in a Phase I human clinical trial and is now in Phase II; as of December 2022, the trial has reached 50% recruitment, with no safety signal <u>observed</u>. Sm-TSP-2 has been successfully investigated as a schistosomiasis vaccine in Phase I clinical trials in Brazil and Texas, and has been shown to be safe, well-tolerated and to induce a strong immune response in healthy adults. A Phase II trial of its efficacy is ongoing in Uganda, with estimated completion in November 2025.

Figure 11. Helminth infections (worms & flukes) R&D pipeline by product type





Funding for dengue R&D remained relatively stable in 2022, dropping slightly (down 2.2%) to \$82m, substantially below its ten-year average of \$94m.

A sharp rise in industry investment saw it provide a record high \$45m (up 52%, \$16m), while funding from the US NIH fell to a record low of \$28m (down \$6.2m, -18%).

Funding from both the Gates Foundation and Wellcome fell further in 2022. Gates funding dropped to just \$0.6m – down from \$19m in 2014 – and Wellcome's to just \$0.5m, leaving philanthropic contributions at a new low, accounting for just 1% of dengue R&D.

While funding for early-stage drug R&D increased by \$10m thanks to the rise in industry funding, Phase I drug development fell sharply alongside a huge increase in Phase II, as an antiviral drug advanced through the pipeline. Biologics R&D also increased, more than doubling after rises in clinical development, mostly from India-based industry. This growth helped sustain last year's record level of clinical development for dengue products.

The wind-up of a US DOD diagnostics programme saw diagnostics funding drop by more than half, to \$3.9m. Basic research funding fell for the sixth consecutive year, almost entirely due to decreasing support from NIH. The cuts in philanthropic funding fell heavily on VCPs, which dropped in tandem with reductions in multi-disease vector control targeting the mosquitos that transmit dengue – which is covered in the non-disease-specific section of this report.

The majority of the dengue product development pipeline consists of therapeutics, of which 16 are still in the early stages. There has been a significant focus on diagnostics, with over half of the candidates in late-stage development, alongside three biological VCPs.



Figure 12. Dengue R&D funding by product type 2013-2022

Table 13. Top dengue R&D funders 2022

Ň	JS\$ (millio	nsl								0	022 % of total
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	~
Aggregate industry	9.0	9.3	17	21	14	21	24	22	30	45	56
US NIH	43	49	56	69	53	44	40	34	34	28	34
Indian BIRAC				<0.1	<0.1	<0.1	1.2	1.1		1.6	2.0
Indian ICMR	2.0	1.9	2.1	3.8	5.2	4.6	2.7	1.6	1.1	1.2	1.5
US DOD	1.5	0.2	1.2	2.0	4.2	3.5	4.0	6.1	4.5	1.1	1.3
Colombian Minciencias		0.2	0.3	-	-	0.4	2.2	0.2	0.2	0.6	0.8
French Development Agency						-		-		0.6	0.7
Gates Foundation	12	19	8.7	15	5.6	5.1	7.6	9.5	4.0	0.6	0.7
Wellcome	3.7	6.5	6.1	6.0	3.7	2.9	2.6	2.7	2.5	0.5	0.6
Australian NHMRC	1.7	3.2	0.7	0.8	0.4	1.1	1.0	0.9	0.9	0.5	0.6
Subtotal of top 10^	78	95	101	124	88	85	86	80	80	80	98
Disease total	82	97	106	129	93	89	90	84	84	82	100

^ Subtotals for 2013-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022.

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

Early results from a Phase IIa human challenge study on Janssen's novel oral antiviral, JNJ-1802, demonstrated its preventive antiviral action against <u>dengue</u>. The compound is now advancing to a community-based field study, evaluating its effectiveness against multiple circulating dengue serotypes in over 30 countries. Results from the World Mosquito Program's deployment of *Wolbachia*-infected mosquitoes in Colombia demonstrated a resulting 94-97% reduction in dengue incidence. Oxitec's large-scale field trials in Brazil using male-only, female-lethal Friendly *Aedes aegypti* intervention also achieved up to a 96% suppression of the local *Aedes aegypti* mosquito population. Note that much of the funding for mosquito control R&D is captured under our multi-disease vector control categories, since it intended to target other mosquito-borne diseases alongside dengue.



Figure 13. Dengue R&D pipeline by product type



Global funding for *Salmonella* R&D rebounded to \$80m in 2022 (up \$5.8m, 7.8%) following three years of decline; but it remained below its ten-year average of \$87m. The rise was slightly larger – an increase of \$8.0m (11%) – when adjusted for a small drop in survey participation.

Typhoid & paratyphoid fever remained the focus of funding, with 67% of the total, but dropped by \$1.8m (-3.0%). Funding for non-typhoidal *S. enterica* (NTS) surged by two-thirds to reach \$14m, its highest level in more than a decade. This rise was even more substantial – a \$7.4m (111%) increase – after adjusting for decreased survey participation.

Vaccine funding rebounded by \$9.5m (29%), mainly driven by new industry funding for Phase I evaluation of an iNTS bivalent GMMA vaccine. Drug funding fell to a decade-low (down \$1.3m, -45%), while biologics recorded its first funding in three years, totalling \$0.2m. Both were almost entirely funded by the US NIH, and focused on early-stage research for typhoid & paratyphoid fevers.

While industry did not continue last year's small amount of diagnostic funding, its overall contributions rose sharply (up \$8.0m, 61%) leaving it responsible for 26% of funding, behind only the US NIH (up 4.5%, \$1.4m) with 41%. The Gates Foundation reduced its investment by \$2.9m (-25%), with more than three-quarters (\$6.8m) going to impact studies on typhoid conjugate vaccine introduction in high-burden populations.

Disease	Basic resea	prugs	laccines F	Biologics	Diagnostics	Inspecified	iotal o	10
Typhoid and paratyphoid fever (S. Typhi, S. Paratyphi A)	26	1.6	25	0.2	1.3	0.2	54	67
Non-typhoidal S. enterica (NTS)	2.1	-	12	-	-	-	14	18
Multiple Salmonella infections	7.2	<0.1	5.1	-	0.2	-	12	15
Total	35	1.6	42	0.2	1.5	0.2	80	100

Table 14. Salmonella R&D funding 2022 (US\$ millions)

⁻ No reported funding

Table 15. Top Salmonella R&D funders 2022

10 ¹ .	JS\$ (millio	nsl								2	022 % of to
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
US NIH	39	37	35	47	37	41	41	32	32	33	41
Aggregate industry	12	18	16	27	26	28	10	13	13	21	26
Gates Foundation	12	8.4	15	15	18	19	22	21	12	8.9	11
CARB-X						-	-	2.5	1.4	4.6	5.8
Wellcome	5.1	4.1	3.6	3.2	2.6	2.6	3.9	5.6	5.7	4.4	5.5
EC	-	<0.1	<0.1	0.2	0.6	0.9	1.2	2.5	2.5	2.0	2.5
Indian ICMR	0.5	0.5	<0.1	<0.1	<0.1	1.6	1.4	1.6	1.3	1.7	2.1
Swiss SNSF	-	0.9	0.5	0.7	0.8	0.4	0.6	1.1	0.8	1.2	1.5
UK MRC	1.4	2.0	2.4	2.2	1.9	2.6	2.4	1.2	1.2	1.0	1.2
Gavi	0.2		0.4	-	-	-	0.4	0.6	1.3	0.9	1.1
Subtotal of top 10^	75	76	79	104	92	100	86	82	72	79	98
Disease total	77	77	81	108	95	103	90	86	75	80	100

^ Subtotals for 2013-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022.

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

- No reported funding

The *Salmonella* infections pipeline predominantly targets typhoid & paratyphoid fever – accounting for 12 (out of 17) vaccines and all nine diagnostics in development, including all Phase III candidates, all but one Phase II candidate and two candidates in Phase I. Although NTS accounts for a smaller portion of the pipeline, all currently active vaccine clinical trials target NTS, including the bivalent vaccine iNTS GMMA, and trivalent vaccines iNTS-TCV and Trivalent *Salmonella* Conjugate Vaccine (TSCV). The latter entered Phase II trials in early 2023. iNTS GMMA and iNTS-TCV are the first NTS vaccines tested in humans; and are currently undergoing a joint Phase I/Ila trial. These vaccines will be evaluated in two stages: initially among European adults in stage 1, followed by African adults in stage 2.

Prokarium has submitted results to the National Library of Medicine for their Phase I trial investigating a bivalent oral vaccine targeting both typhoid and paratyphoid <u>fevers</u>.



Figure 14. Salmonella infections R&D pipeline by product type



Global investment in bacterial pneumonia & meningitis R&D totalled \$48m in 2022, dropping by more than a quarter (down \$18m, -27%). This was the fourth consecutive decrease, and took investment to its lowest level since 2007, around half of its ten-year average.

Funding fell across all disease areas: pneumonia was down \$14m (-26%), meningitis by \$3.6m (-33%) and, for the first time, there was no reported funding for R&D targeting both diseases.

Pneumonia vaccine funding fell by a third (down \$16m, -32%) after several projects ended in 2021. This included several projects supported by the Gates Foundation, whose funding dropped by \$9.6m (-61%), as well as the wind-up of industry-led LMIC-based post-registration studies of a 13-valent vaccine, which fell by \$8.5m (-29%). These decreases outweighed the near tripling of US NIH investment (up \$6.4m, 188%), with \$3.3m in new funding for basic research and their highest investment in diagnostic R&D since 2013 (\$0.6m, up from zero in 2021).

The historic low for **meningitis** R&D funding resulted from record-low support for vaccine R&D (down \$2.6m, -31%) and a halving of basic research investment (down \$1.2m, -51%). The end of UK FCDO funding to PATH for NmCV-5 vaccine development, and a 70% drop in Bio Manguinhos' intramural investment more than offset \$1.5m in new funding from the Gates Foundation for multivalent meningitis vaccines. The small amount of meningitis diagnostics investment tripled (up \$0.2m) as MSF increased their funding to Institut de Dakar for the DiaTropix rapid diagnostic test.



Figure 15. Bacterial pneumonia & meningitis R&D funding by product type 2013-2022

Table 16. Top bacterial pneumonia & meningitis R&D funders 2022

, of	JS\$ (millio	nsl								2	022 % of to
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
Aggregate industry	56	56	41	63	40	45	24	35	32	23	48
US NIH	7.8	2.7	1.5	4.1	2.7	2.7	1.4	3.6	3.5	11	22
Gates Foundation	18	6.6	41	24	29	36	34	24	18	8.7	18
Wellcome	2.0	2.0	1.2	1.0	0.4	<0.1	0.4	1.9	1.5	1.2	2.6
Indian BIRAC				-	-	1.3	0.7	1.6		0.8	1.7
Bio Manguinhos		0.3							2.6	0.8	1.6
Australian NHMRC	0.4	-	0.3	0.3	0.5	0.4	0.6	1.2	0.9	0.6	1.3
Gavi	13		7.7	5.7	5.8	3.1	3.5	2.6	2.1	0.6	1.3
UK MRC	0.6	0.5	0.9	1.9	1.2	0.9	1.8	1.8	0.4	0.4	0.7
MSF	-	-	-	0.2	<0.1	-	-	<0.1	<0.1	0.3	0.7
Subtotal of top 10^	116	85	107	106	85	100	76	72	64	47	99
Disease total	118	85	109	108	86	100	77	72	66	48	100

^ Subtotals for 2013-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022.

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

- No reported funding

The bacterial pneumonia & meningitis vaccine pipeline is concentrated on *S. pneumoniae*, with just four candidates (15%) targeting *N. meningitidis*. Almost three-quarters of the diagnostics pipeline target pneumonia (five candidates, 71%), with the remainder for meningitis infections.

MenFive, a pentavalent meningococcal vaccine co-developed by PATH and the Serum Institute of India was prequalified by the WHO following strong safety and immunogenicity in a Phase III trial conducted among participants aged 2-29 years in Mali and the <u>Gambia</u>. Almost all participants displayed an immune response to serogroup X, making this the first meningococcal vaccine to protect against this specific strain, which is becoming increasingly important as its prevalence increases across the African meningitis <u>belt</u>.

In April 2023, the US FDA approved Pfizer's PREVNAR 20 vaccine, a 20-valent pneumococcal conjugate vaccine for infants and <u>children</u>. The vaccine is yet to be prequalified by the WHO and is not a part of Gavi's portfolio, meaning LMIC access remains limited.



Figure 16. Bacterial pneumonia & meningitis R&D pipeline by product type



The hepatitis B funding landscape underwent a major shift in 2022 with funding nearly doubling (up \$14m, 87%) to a record \$30m. This was thanks to an unprecedented \$17m investment from industry, mostly in biologics R&D. It represents industry's first meaningful investment in LMIC-focused hepatitis B R&D – its previous funding totalling just over \$0.1m

Industry's additional funding compensated for the sharp decrease in public funding between 2021 and 2022 (-18%, from \$16m to \$13m), mostly caused by the cessation of funding from France's Inserm, which had provided more than \$2m in each of the previous three years. Funding from the US DOD continued to grow, rising by 27% (\$0.4m), the increase focusing on early-stage drug R&D.

The massive private investment in LMIC-focused biologics shifted the distribution of funding even further towards biologics R&D, which now accounts for 75% of the 2022 total. The remaining funding was split relatively evenly between basic research (\$3.3m), diagnostics (\$1.7m, down 5.1%) and drugs (\$2.6m) – the latter up 14% thanks to increased DOD and NIH funding.

Overall funding in 2022 continued the trend of the last five years: a gradual decrease in the share of basic & early-stage research (down 11% since 2018) coupled with a steady increase in clinical development funding (up nearly eightfold over the same period).



Figure 17. Hepatitis B R&D funding by product type 2018-2022

US\$ (millions)

Table 17. Top hepatitis B R&D funders 2022

Ň	US\$ (millio	nsi			2	022 % of tote
Funder	2018	2019	2020	2021	2022	
Aggregate industry	<0.1	-	0.1	-	17	56
US NIH	4.0	4.0	5.8	6.4	6.3	21
EC	-	-	4.8	4.7	4.3	14
US DOD	-	-	0.4	1.5	2.0	6.4
Wellcome	-	0.5	0.5	0.5	0.5	1.6
Dutch ZonMw	-	0.1	0.1	0.1	0.1	0.3
French ANRS	0.1	0.3	-	-	<0.1	0.3
South African MRC	-	<0.1	<0.1	<0.1	<0.1	0.3
Thai GPO	<0.1		0.3	0.5	<0.1	0.1
Japan Society for the Promotion of Science (JSPS)	-	-	<0.1	<0.1	<0.1	<0.1
Subtotal of top 10^	11	10	17	16	30	100
Disease total	11	11	18	16	30	100

^ Subtotals for 2018-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022. 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

Bepirovirsen, an antisense oligonucleotide that targets HBV mRNA, resulting in cessation of HBsAg production, has entered a Phase III <u>trial</u> after demonstrating potential efficacy in two Phase II <u>studies</u>. If found effective, it would be the first compound to provide a functional cure, offering substantial improvement on the current standard of care. Bepirovirsen is also being investigated as part of combination therapy with GSK3528869A, a viral-vectored <u>immunotherapeutic</u>.

A Phase II safety and efficacy study of combination treatment of BRII-835 (VIR-2218), an RNA interference compound, and BRII-179 (VBI-2601), a protein-based HBV immunotherapeutic candidate, in adult participants with chronic HBV infection was completed in July 2023. Interim data suggested the combination induced meaningfully stronger anti-hepatitis B surface antigen (HBsAg)-specific T-cell and antibody responses than BRII-835 alone.

Figure 18. Hepatitis B R&D pipeline by product type





Funding for snakebite envenoming reached a new high of \$21m in 2022 (up \$2.6m, 14%), marking a fourth consecutive year of growth.

Essentially all of the increase came from two funders, Wellcome and the US DOD. Both reported record-high contributions as part of their ongoing support for Ophirex's Phase II trial of the small molecule therapy, varespladib. While the US DOD's investment remained focused on drug development (up \$1.1m, 21%), Wellcome doubled its funding for both drugs (up \$2.7m, 107%) and biologics (up \$1.6m, 104%). Since 2018, the collective share of total funding from Wellcome and the DOD has risen from a low of 7% in 2019 to 71% in 2022. This narrow funder base raises concerns as to sustainability, particularly given that Wellcome's funding programme will end in 2026 and the DOD's is linked to a single developer and drug.

Funding for diagnostics and basic research both fell to their lowest level ever, the latter mostly due to the conclusion of funding from the Swiss SNSF. Several funders active in 2018 are no longer contributing, including the French ANR and UK FCDO.

The apparent decline in diagnostic funding excludes \$1m in non-grant financing – including \$0.5m from Open Philanthropy – to VenomAid Diagnostics, who are working to develop cheap, rapid diagnostics to support both diagnosis and the trialling of new therapeutics.



Figure 19. Snakebite envenoming R&D funding by product type 2018-2022

US\$ (millions)

Table 18. Top snakebite envenoming R&D funders 2022

مەنى ر م	JS\$ (millic	nsl			2	022 % of tot
Funder	2018	2019	2020	2021	2022	
Wellcome	0.3	0.4	2.6	4.3	8.3	40
US DOD	1.5	0.5	5.4	5.5	6.6	31
Aggregate industry	0.7	1.5	<0.1	1.5	1.4	6.9
EC	-	-	0.6	1.4	1.3	6.1
US NIH	0.1	0.2	0.2	1.4	1.1	5.2
Center for Production and Research of Immunobiology		-	0.1	0.8	0.6	2.8
UKRI			<0.1	0.3	0.4	1.8
Brazilian FAPESP	0.4	0.3	0.2	0.4	0.3	1.7
UK DHSC	0.3	0.9	0.9	0.8	0.3	1.2
Danish Innovation Fund					0.2	0.7
Subtotal of top 10^	7.0	12	16	17	20	98
Disease total	8.7	13	17	18	21	100

^ Subtotals for 2018-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022. Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete.

- No reported funding

The BRAVO Phase II clinical trial of the drug Varespladib-methyl, a repurposed PLA2 inhibitor, was completed in June 2023, after demonstrating activity against anti-coagulant PLA2 toxins and procoagulant venom toxins in preclinical <u>studies</u>.

The Novel ICP-AVRIUOP Sri Lankan polyspecific antivenom, with neutralizing abilities against the venom of four snake species highly prevalent in <u>Sri Lanka</u>, is currently registered for two Phase II/III studies testing several different dosages and efficacy relative to the Indian <u>AVS</u>. Preclinical research is being conducted on monoclonal antibody-based candidates, a potentially more efficient, tailored, and less immunogenic alternative to traditional plasma-derived antivenoms. These include the broad spectrum human monoclonal antibodies (IgG), developed by <u>Centivax</u>, which has a clinical trial scheduled to launch by the end of <u>2023</u>.



Figure 20. Snakebite envenoming R&D pipeline by product type



Global funding for hepatitis C R&D totalled \$16m in 2022, a decrease of 8.6% (\$1.5m). Despite record funding from the US NIH, the drop still carried funding further below its industry-driven peak in 2018.

The overall decrease was driven by the near absence of funding from Unitaid and MSF, which comes after they jointly provided \$3.2m in 2021 – and more than \$11m in 2020. Unitaid's funding is expected to return, as its LONGEVITY early-stage drug project remains ongoing, while MSF's 2022 total of just \$17k (a drop of 97%) reflects the 2021 wind-up of its STORM-C drug trial. These two falls also resulted in record-low drug R&D funding (down 74%).

The new peak in funding from the US NIH went some way to offsetting the absence of these previously reliable funders, but left it with a 90% share of global funding. Much of the NIH's increase went to diagnostics (up \$1.6m, 52%), with a smaller rise in its vaccine funding (up \$1.0m, 12%), which – after several years of growth – was enough to lift vaccine R&D to a record high. Vaccine R&D remained almost exclusively focused on early-stage research, and investment in clinical development fell across drug and vaccine product areas, with clinical development falling to new lows both in terms of amount and share of global funding (\$1.0m, 6.1% of the total).



Figure 21. Hepatitis C R&D funding by product type 2013-2022
Table 19. Top hepatitis C R&D funders 2022

101	JS\$ (millio	nel								2	022% of total
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
US NIH	13	8.0	5.6	5.1	4.1	3.2	4.4	4.1	12	14	90
Wellcome	<0.1	<0.1	<0.1	<0.1	-	0.8	0.9	0.9	0.8	0.7	4.6
Canadian CIHR	-	-	-	0.6	0.1	<0.1	<0.1	0.1	0.1	0.2	1.3
Australian NHMRC	0.3	0.2	-	-	0.1	0.3	0.2	0.3	0.3	0.2	1.3
French ANRS	2.0	9.6	4.5	5.0	2.4	1.5	0.8	-	0.3	0.2	1.0
Australian Centre for HIV and Hepatitis Virology	<0.1	0.2		0.1	0.1		0.1	0.1		0.1	0.9
Thai GPO	<0.1	<0.1	0.3	0.1	0.3	0.5		1.0	0.4	<0.1	0.2
MSF	-	-	-	-	0.5	4.4	1.7	2.9	0.7	<0.1	0.1
Brazilian FAPESP				<0.1	-	-	0.1	-	<0.1	<0.1	0.1
Brazilian FAPERO						-		-	-	<0.1	<0.1
Subtotal of top 10^	56	53	40	34	17	54	12	18	17	16	100
Disease total	56	54	40	34	17	54	12	18	17	16	100

^ Subtotals for 2013-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022.

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

Hepatitis C has 23 products in the pipeline, dominated by vaccines (11) and diagnostics (7). However, out of just five drug candidates, at least two are known to have reached Phase III. A hepatitis C drug regimen partly developed in Malaysia has been added to the World Health Organization's essential medicines list (EML): the WHO endorsed the use of ravidasvir in combination with sofosbuvir as a direct-acting antiviral for the treatment of chronic hepatitis C virus infection in adults. The development of ravidasvir was initiated by Malaysia's health ministry and DNDi, in partnership with Thailand's health ministry, Médecins Sans Frontières, Presidio Pharmaceuticals, Pharco Pharmaceuticals and Pharmaniaga Berhad.

Figure 22. Hepatitis C R&D pipeline by product type





Global funding for leprosy R&D saw a second successive year of funding growth in 2022, rising by \$3.7m (37%) to reach \$14m, just below its peak from 2012 to 2013.

The rise was mainly due to a third consecutive increase in MNC's drug funding, which rose by \$3.5m (186%) to reach \$5.4m – nearly triple last year's record high – mostly driven by funding of late-stage clinical trials for Bedaquiline. Drug R&D climbed to a new high, at 48% of total funding, surpassing the share going to basic research funding for the first time. Drug R&D was also buoyed by Medicines Development for Global Health, which more than doubled its drug funding for Phase IIa clinical trials of Dovramilast in Nepal, investing \$0.8m in its second year of support for leprosy drug R&D. Vaccine R&D – in scope since 2018 – fell by 53% to an all-time low of \$0.3m following the completion of US NIH-funded immunogenicity assessments which formed part of the final stages of Phase I LepVax trials.

The number of individual leprosy R&D funders remained stable, but funding grew more concentrated, as the top five contributors provided 91% of overall funding – up from 86% in 2021. The growth in drug R&D also caused a surge in funding for clinical development, to a record high of \$6.5m (48% of total funding). More than 80% of recorded investment in clinical development for leprosy has occurred over the past five years, and more than a third in 2022 alone.



Figure 23. Leprosy R&D funding by product type 2013-2022

Table 20. Top leprosy R&D funders 2022

	JS\$ (millio	nsl								9	022 % of to
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
Aggregate industry	<0.1	<0.1	0.8	0.4	0.5	1.5	0.5	1.0	1.9	5.4	40
US NIH	7.3	6.9	5.2	5.9	2.8	2.8	3.0	3.2	3.2	3.1	23
Indian ICMR	3.8	3.9	5.2	4.4	6.5	2.3	3.3	3.1	2.6	2.6	19
Medicines Development for Global Health					-	-	-	-	0.1	0.8	6.1
ALM	0.3	<0.1	-	-	0.1	0.7	0.6	0.3	0.5	0.5	3.7
UK MRC	-	<0.1	<0.1	0.2	0.6	0.6	1.0	0.2	<0.1	0.2	1.4
Inserm	-	-	-	<0.1	<0.1	<0.1	0.2	<0.1	0.1	0.2	1.4
Leprosy Research Initiative			0.6	0.6	0.5	0.3	0.4	0.1	0.1	0.2	1.3
Flemish EWI						<0.1			0.2	0.2	1.2
effect:hope				0.1	0.7	0.7	0.3	0.2	0.2	<0.1	0.7
Subtotal of top 10^	14	12	12	12	12	9.6	10	8.7	9.4	13	97
Disease total	14	12	12	13	13	10	11	9.0	9.9	14	100

^ Subtotals for 2013-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022.

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

Excluding LepVax, the lone vaccine candidate approaching Phase II development, drugs are the most advanced product category, with three candidates currently undergoing Phase II clinical trials.

Dovramilast (previously AMG 634) has received the United States Food and Drug Administration's Orphan Drug Designation for the treatment of erythema nodosum <u>leprosum</u>. Janssen is currently funding Phase III clinical trials by the Institute of Tropical Medicine, Antwerp, evaluating a combination of Bedaquiline and Rifampicin as post-exposure prophylaxis (PEP) for leprosy in <u>Comoros</u>. Early development of an Al-powered image-based diagnostic tool for leprosy, known as Al4Leprosy, is underway with support from Novartis Foundation and <u>Microsoft</u>.

Figure 24. Leprosy R&D pipeline by product type





Funding for cryptococcal meningitis drug and biologics R&D was \$6.6m in 2022. While this appears to represent a significant drop (down \$8.6m, -56%), the 2021 spike in funding was due to roughly \$8m in drug R&D funding from industry funders that did not participate in the G-FINDER survey in 2022. A key industry player initiated a Phase III trial in late 2022, making it likely that industry investment continued at similar levels – or even increased – in 2022. Adjusting for absent industry funders, funding would have shifted only slightly, dropping by \$0.9m (-11%).

In line with previous years, drugs received the vast majority of funding, at \$5.9m (89% of the total), with biologics accounting for the remaining \$0.8m (11%). With reduced survey participation from industry, the US NIH was again the top participating funder of cryptococcal meningitis R&D – as it had been every year except 2021 – accounting for 70% of drug R&D funding and more than 99% of biologics. Its support, though, slumped to a near-record low (down \$0.6m, -11%), as did funding from Wellcome.

A little over half of all recorded funding, including all biologics funding, went to early-stage research (\$3.8m, 57%). Most of the remainder was for either clinical development (40%) or post-registration studies (2.3%). Even adjusting for the absence of (ongoing) industry funding, clinical development funding declined throughout the product pipeline, most notably an 85% reduction in funding for Wellcome's Phase III High Dose AMBISOME trial.



Figure 25. Cryptococcal meningitis R&D funding by product type 2013-2022

JS\$ (millions)

Table 21. Cryptococcal meningitis R&D funders 2022

, Ala	JS\$ (millic	nsi								r	022 % of total
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
US NIH	1.7	5.1	3.7	5.2	8.6	6.0	8.3	7.3	5.5	4.9	73
UK MRC	1.4	1.3	2.2	1.2	1.1	0.6	0.3	-	1.6	1.4	22
UK NHS						-	-	-	-	0.2	2.3
EC	-	-	-	-	-	-	-	-	0.1	0.1	1.6
Wellcome	0.3	<0.1	<0.1	<0.1	0.4	0.5	0.3	0.3	0.4	<0.1	0.8
Brazilian FAPESP				<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	0.6
Brazilian FAPERO						-		-	-	<0.1	0.1
Aggregate industry	-	-	-	-	-	-	-	-	7.7	-	-
UK DHSC					1.8	1.2	-	-	-	-	-
UK FCDO	-	-	-	-	0.9	0.8	-	-	-	-	-
Disease total	3.5	6.6	6.0	6.7	13	9.2	9.1	7.9	15	6.6	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

There are seven cryptococcal meningitis drugs in the pipeline, the most advanced of which is Matinas BioPharma's MAT2203, which began its pivotal non-inferiority Phase III <u>trial</u> of in January <u>2023</u>. The drug is a lipid nanocrystal formulation of amphotericin B. This non-toxic oral formulation of MAT2203 is more suitable to low-resource settings than the standard amphotericin B, which is expensive, requires careful toxicity monitoring and is administered intravenously. The current trial builds on positive Phase II <u>results</u>, which demonstrated similar survival rates in people living with HIV infected with cryptococcal meningitis as when treated with intravenous <u>amphotericin B</u>.

Figure 26. Cryptococcal meningitis R&D pipeline by product type





In 2022, the third year of its inclusion in the G-FINDER report, histoplasmosis R&D received \$3.4m. This was a drop of \$0.4m (-11%) from the previous year, and a potentially worrying fall of 25% (\$1.1m) from 2020.

The US NIH continued to dominate the funding landscape, again providing more than 99% of global funding, with the vast majority (97%) of its contributions going to basic research and the remaining \$0.1m to early-stage drug R&D. This year's 11% (\$0.4m) fall in NIH disbursements was mostly due to the conclusion of its funding to the University of California for the study of opportunistic histoplasmosis infections in HIV patients.

Overall funding remained almost exclusively concentrated on basic research (\$3.4m, 97%) even after a slight drop in its funding (down \$0.4m, -11%). A further decline in drug R&D (down \$15k, -14%, to just \$90k) left it with just 2.6% of the total, while the already small amount of 2021 diagnostics funding fell by 75% to \$11k.

There were just two other funders besides the US NIH in 2022: the Brazilian FAPESP invested \$21k in basic research (up from \$5k in 2021), and the Argentinian MINCYT provided \$4k in diagnostic R&D funding for production of recombinant antigens for the development of low-cost immunoassays, which represented the only remaining diagnostic funding in 2022. There were no reported funds from the Fungal Infection Trust, previously the only provider of funding for histoplasmosis clinical development.



Figure 27. Histoplasmosis R&D funding by product type 2020-2022

Table 22. Histoplasmosis R&D funders 2022

Funder	US\$ (millio	nsi	2	022 % 01	rotal
Fulle	2020	2021	2022		
US NIH	4.6	3.8	3.4	99	
Brazilian FAPESP	<0.1	<0.1	<0.1	0.6	
Argentinian MINCYT	<0.1	-	<0.1	0.1	
Fungal Infection Trust	<0.1	<0.1	-	-	
Disease total	4.6	3.9	3.4	100	

- No reported funding

An in-vitro study showed that mebendazole could potentially be repurposed for the treatment of <u>histoplasmosis</u>. Ibrexafungerp, developed by Scynexis Inc, reported interim analysis from its ongoing Phase III trial showing positive responses for invasive candidiasis, vulvovaginal candidiasis, and invasive aspergillosis. Although histoplasmosis was one of the fungal conditions included in the trial, investigators have not yet reported any data showing effectiveness against histoplasmosis, potentially suggesting there are no significant effects.

An enzyme-linked immunospot (ELISpot) assay was developed using yeast cell lysate antigen prepared from a representative North American *Histoplasma capsulatum* strain. The histoSPOT assay was found to be 78% sensitive and 100% specific as an aid to diagnosing histoplasmosis in people with suspected active <u>disease</u>.



Figure 28. Histoplasmosis R&D pipeline by product type



Funding for rheumatic fever vaccines – the only rheumatic fever product included in G-FINDER – plummeted for a second year in a row, falling to \$3.4m in 2022 (down \$9.2m, -73%). With this drop, the higher funding seen between 2019 to 2021 – which averaged \$18m – stands out as an outlier, with the 2022 total representing a return to funding levels seen prior to this spike.

The cause of this drop in funding was two-fold. Firstly, the Australian Medical Research Future Fund (MRFF) wrapped-up its funding to the Australia-based Telethon Kids Institute, after providing \$27m over three years for the Australian Strep A Vaccine Initative. Secondly, there was no funding from CARB-X in 2022, after it provided a total of \$16m to GSK-Bio and Vaxcyte during the three-year spike in funding.

Without the Australian MRFF and CARB-X, just five organisations funded rheumatic fever vaccine R&D in 2022. Of these, the philanthropic Leducq Foundation – a new G-FINDER survey participant in 2022 – gave \$1.8m in clinical development funding. The Canadian CIHR also provided funding for the first time, via \$0.5m to the University of Alberta for the Phase I clinical trial of J8-K4S2 and p*17-K4S2. As a result, three-quarters of 2022 funding went towards clinical development – its highest share on record.

With the US NIH – the largest ongoing funder – sharply reducing its contribution to a near-record low (down \$0.9m, -63%), the Leducq Foundation's newly-reported contribution made it 2022's top funder.



Figure 29. Rheumatic fever R&D funding by product type 2013-2022

Table 23. Rheumatic fever R&D funders 2022

104	JS\$ (millic	Inst								2	022 % of tot
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
Leducq Foundation										1.8	54
US NIH	0.7	0.6	1.3	1.1	1.0	1.3	1.2	1.1	1.5	0.6	16
Canadian CIHR	-	-	-	-	-	-	-	-	-	0.5	15
Australian NHMRC	0.5	1.1	0.7	0.6	0.8	0.8	1.6	0.4	-	0.3	8.0
Colombian Minciencias		-	-	-	-	-	-	-	0.3	0.2	6.9
Australian MRFF							12	7.6	7.4	-	-
CARB-X						-	3.1	9.3	3.4	-	-
Open Philanthropy					-	-	-	6.0	-	-	-
Health Research Council of New Zealand (HRC)	-	-	0.6	0.4	-	0.1	0.1	-	-	-	-
Brazilian BNDES		-	0.6	-	-	-	-	-	-	-	-
Disease total	1.2	1.9	3.2	2.1	2.0	2.2	18	24	13	3.4	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

In the vaccine development pipeline, 8 out of 11 candidates are currently undergoing preclinical evaluation, including 4 subunit vaccines and a liposomal-based vaccine. Three of these candidates are designed for intranasal administration.

Two group A *Streptococcus* (GAS) vaccines are currently in active clinical development – J8-K4S2 and p*17-K4S2. Both are peptide vaccines constructed on highly conserved C-terminal of M protein and modified B-cell epitope from SpyCEP. The Phase I trial investigating these vaccines is expected to be completed by the end of 2023. Another M protein-based, 30-valent vaccine, StreptAnova, was found to be safe and <u>immunogenic</u>. Several non-M protein-based vaccines, including some utilising the Group A Carbohydrate (GAC) approach, are in preclinical development. GAC-based vaccines have the potential to provide protection against more than 99% of serotypes present <u>globally</u>.

Figure 30. Rheumatic fever R&D pipeline by product type





Funding for scabies R&D remained basically stable at \$1.9m in 2022 (down \$41k, -2.1%) after an increase of 50% in 2021.

Australian funders retained their key role, with 2021's top two funders both increasing their contributions in 2022: Australia's Medicines Development for Global Health (MDGH) upped its funding for moxidectin clinical trials to \$0.8m (up \$0.2m, 35%) while funding from the Australian NHMRC grew by \$0.1m (16%), to \$0.7m. Between them, these two organisations accounted for 81% of 2022's total funding.

The dominant share for the top two funders was partly due to UK public funding for the Global Health Research Unit on Neglected Tropical Diseases falling slightly (down \$0.1m) and the Australian philanthropic funder, the Macquarie Group Foundation, sharply reducing its contributions to Melbourne Children's (down \$0.3m, -63%).

These changes continued an ongoing shift away from basic research and towards drug R&D, which has seen its share of funding rise from 18% in 2020 to 61% by 2022, three-quarters of which was for clinical development, mostly MDGH's moxidectin dosing trials.

There were also two new funders in 2022: the Malaysian Ministry of Health – a new survey participant – and the Thrasher Research Fund, though they reported less than \$30k in funding between them. As in 2021, there was almost no funding for diagnostics, though one small NHMRC-funded project – categorised here as 'unspecified' – did include some elements of diagnostic research.



Figure 31. Scabies R&D funding by product type 2020-2022

Table 24. Scabies R&D funders 2022

Funder	JS\$ (millio	nsl	2	022 % of	total
Fulle	2020	2021	2022		
Medicines Development for Global Health	-	0.6	0.8	44	
Australian NHMRC	0.6	0.6	0.7	37	
UK NHS	-	<0.1	0.2	8.8	
Macquarie Group Foundation	0.4	0.4	0.2	8.5	
Thrasher Research Fund			<0.1	1.3	
Ministry of Health Malaysia			<0.1	0.2	
UK DHSC	0.3	0.2	-	-	
Disease total	1.3	1.9	1.9	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

There are just four candidates in the scabies pipeline, three diagnostics (two in late-stage development) and one drug, moxidectin, for which Medicines Development for Global Health initiated a Phase II efficacy study in late 2023 for treatment of scabies in an adult <u>population</u>. The current study follows a dose-ranging proof-of-concept trial that finished in early 2022.

Figure 32. Scabies R&D pipeline by product type





Funding for leptospirosis diagnostics R&D – the only product area included in the G-FINDER scope for leptospirosis – was \$1.2m in 2022, a 22% drop, continuing the downward trend in funding since its 2017 peak of \$3.4m.

The absence of funding data from France's Institut Pasteur – which provided just over \$30k in each of the previous two years but which did not participate in this year's survey – contributed slightly to the decline, as did a \$22k (-49%) drop in funding from the UK MRC. The major ongoing source of funding, and key driver of shifts in its distribution, continued to be the Indian ICMR – the top funder every year since 2018. The ICMR has provided nearly three-quarters of global funding over that period, and was responsible for 98% of the 2022 total.

The ICMR did reduce its funding by \$0.3m in 2022, a drop of 20%. This reflected a slight fall in its ongoing core funding (down \$0.2m, -12%) and the conclusion of two small standalone projects, including the first ever funding for clinical development of leptosporiosis diagnostics, in the form of \$65k toward development of a point-of-care apta-biosensor for early and rapid detection of leptospirosis.

The small amount of remaining funding was from the UK MRC, and went to the University of Cambridge for research into an affordable diagnostic nucleic acid testing platform.



Figure 33. Leptospirosis R&D funding by product type 2013-2022

Table 25. Leptospirosis R&D funders 2022

Funder	JS\$ Imillic	nsl								2	022 % of tot
Furle	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
Indian ICMR	-	-	-	1.3	1.5	1.0	1.2	1.4	1.4	1.1	98
UK MRC	-	-	-	-	-	<0.1	0.2	0.2	<0.1	<0.1	2.0
Argentinian MINCYT	-	-	-	-	-	-	<0.1	<0.1	-	<0.1	<0.1
Institut Pasteur	0.4	0.9	1.0	1.2	1.9	0.4	0.2	<0.1	<0.1		-
US NIH	-	0.4	0.4	-	-	0.3	0.7	-	-	-	-
Inserm	-	-	-	0.2	-	-	-	-	-	-	-
Aggregate industry	-	-	-	-	<0.1	<0.1	-	-	-	-	-
Colombian Minciencias		<0.1	-	-	-	-	-	-	-	-	-
plan:g	<0.1	-	-	-	-	-	-	-	-		-
Disease total	0.4	1.4	1.4	2.6	3.4	1.8	2.3	1.6	1.5	1.2	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

There are nine diagnostics in the pipeline for leptospirosis, of which three are undergoing latestage validation or launch readiness testing. Results from a recently published study show that a combination test using commercially available *Leptospira* IgM RDT and a CRISPR-based molecular diagnostic currently under development (RPA-CRISPR/Cas12a FBDA), achieved significantly higher sensitivity and specificity than the conventional, single test, approach. These findings should have a positive impact in aiding early detection of leptospirosis in resource-limited settings.

Figure 34. Leptospirosis R&D pipeline by product type





Global funding for Buruli ulcer R&D totalled just under \$0.6m in 2022, down 7.7% (\$44k) from last year's record low, after it had averaged more than \$4m a year over the preceeding decade.

Basic research accounted for almost four-fifths of the remaining 2022 funding, with diagnostic development receiving 17% (\$95k) and vaccine R&D just 5.5% (\$32k). Drug R&D again received no funding, after reporting \$6.1m in investment between 2016 and 2020.

Diagnostic R&D was the major victim of the 2022 funding cuts, dropping by 41% (\$65k). This was a result of the 2021 conclusion of three years of Medicor Foundation's funding to FIND for late-stage development and introduction of a rapid diagnostic test for Buruli ulcer. Medicor, a reliable funder of Buruli ulcer R&D since 2010, has indicated that it will no longer be providing funding for any neglected diseases, with its final disbursements having come in 2021.

The small amount of remaining diagnostic R&D also represents the only late-stage funding for Buruli ulcer: just \$0.1m from the Anesvad Foundation to FIND.

As in 2021, there were only six funders of Buruli ulcer R&D in 2022. Wellcome provided over a third of the global total (\$0.2m, 36%), with Inserm the only other organisation to contribute more than \$0.1m (21%). The return of the UK MRC after a two-year absence helped offset the loss resulting from Medicor's exit.



Figure 35. Buruli ulcer R&D funding by product type 2013-2022

Table 26. Top buruli ulcer R&D funders 2022

	JS\$ Imilio	nsi								2	022 % of total
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
Wellcome	0.3	0.2	<0.1	<0.1	0.3	0.3	0.3	0.3	0.2	0.2	36
Inserm	-	-	-	<0.1	<0.1	0.2	0.1	0.2	0.1	0.1	21
Anesvad Foundation					0.2			0.2	<0.1	0.1	17
UK MRC	0.2	0.2	0.1	0.1	0.2	0.2	<0.1	-	-	0.1	13
Raoul-Follereau Foundation	0.3	0.2					<0.1		<0.1	<0.1	8.5
Australian NHMRC	-	0.1	0.1	<0.1	1.4	0.3	0.6	0.3	<0.1	<0.1	5.5
Medicor Foundation	0.2	0.2	0.4	0.1	0.3	<0.1	0.1	0.1	0.1	-	-
Institut Pasteur	0.4	0.5	0.5	0.5	0.3	0.1	0.2	0.3	-		-
Fondation Mérieux	-	-	-	-	<0.1	-	-	-	-	-	-
EC	0.7	-	-	-	-	-	-	-	-	-	-
Subtotal of top 10^	7.1	4.1	2.0	3.1	4.6	2.8	3.0	2.7	0.6	0.6	100
Disease total	7.2	4.1	2.0	3.1	4.7	2.8	3.0	2.7	0.6	0.6	100

^ Subtotals for 2013-2021 top 10 reflect the top funders for those respective years, not the top 10 for 2022.

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

There are just three products each in the Buruli ulcer therapeutic and prophylactic pipelines, which remains mainly at an early stage of development. Only two (repurposed) drugs have reached the clinical stage of development – one in Phase I and the other in Phase II. The remaining candidates, including all potential vaccines, are in the preclinical or discovery stage. Repurposing of tuberculosis drugs is the most promising avenue for alternative Buruli ulcer treatments: several antitubercular agents, including investigational compounds, have been tested in animal models for treating Buruli ulcer. One such compound, telacebec (Q203), a cytochrome bc1 complex inhibitor, has shown promising results in a mouse model of Buruli ulcer.

Figure 36. Buruli ulcer R&D pipeline by product type 2022





Total funding for mycetoma R&D in 2022 was \$0.5m, down by more than a third after remaining steady at \$0.8m in both 2020 and 2021.

Funding continued to be divided relatively equally between basic research and drug R&D, and the drop in funding impacted both areas. The reduction in basic research was due to a fall in UK public funding to the NIHR Global Health Research Unit on Neglected Tropical Diseases (down \$0.2m, -41%), though it remained the largest single stream of funding. The fall in drug funding, on the other hand, was a result of cuts from the other two significant ongoing funders of mycetoma R&D: the Canton of Geneva, and the US NIH.

Firstly, the Canton of Geneva reduced its funding by \$48k (-23%) as its Phase II fosravuconazole trial with DNDi in Sudan came to a close – though it has announced a renewed three-year commitment starting in 2023, suggesting an imminent rebound.

Secondly, the US NIH dropped its funding by \$83k (-81%) to less than \$20k, capping a series of declines as two of its projects – early-stage research into broad spectrum antifungals, and T-cell therapy for invasive fungal infections – both tapered off.

These falls in public funding for drug R&D were marginally offset by a slight rise in industry's clinical development, which rose from \$41k to \$54k.



Figure 37. Mycetoma R&D funding by product type 2018-2022

Table 27. Mycetoma R&D funders 2022

Funder	US\$ Imillio	nal			2022 % of total			
Fulle	2018	2019	2020	2021	2022			
UK NHS	-	-	-	0.1	0.2	51		
Canton of Geneva		0.2	0.2	0.2	0.2	33		
Aggregate industry	<0.1	-	-	<0.1	0.1	11		
US NIH	0.2	0.1	0.1	0.1	<0.1	3.9		
Japan Society for the Promotion of Science (JSPS)	-	-	<0.1	<0.1	<0.1	0.8		
UK DHSC	0.5	0.6	0.4	0.3	-	-		
Disease total	0.7	1.0	0.8	0.8	0.5	100		

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

- No reported funding

The majority of in-scope mycetoma product development – which covers only diagnostics and drugs – remains in the early stages of development. Eisai, in partnership with DNDi and the University of Khartoum, has recently completed Phase II trials comparing fosravuconazole and itraconazole for eumycetoma treatment. Fosravuconazole demonstrated high cure rates, good tolerance, and a convenient weekly dosing regimen, setting it apart from current treatments. In light of this, the GHIT Fund provided DNDi with €2 million in 2023 to aid fosravuconazole registration and preparatory efforts for patient access in Sudan and is also supporting the current Phase IIb/III study. Two other promising compounds, a fenarimol analog and niclosamide, are being investigated for potential alternative mycetoma therapies based on encouraging preclinical results.







Global investment in trachoma R&D was down three-quarters from 2021, totalling only \$0.2m – or just 3% of its 2011 peak. This marks the second consecutive steep decrease in funding, leaving trachoma with the lowest level of funding that any neglected disease has received since we began tracking investment in 2007.

This record low is the combined result of the 2021 conclusion of the EC's TracVac project, and the failure of the Task Force for Global Health to continue its occasional diagnostics funding. This left the US NIH as the only remaining funder of trachoma R&D; and even the NIH's funding – for a University of Houston project to automate diagnosis using eyelid photos – fell by 36% (\$0.1m).

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 EC's TracVac in 2021, only funding for diagnostic R&D remains.



Figure 39. Trachoma R&D funding by product type 2013-2022

Table 28. Trachoma R&D funders 2022

Funder	JS\$ (millic	nsi								2	022 % of te
Fulle	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
US NIH	1.8	1.0	1.2	1.7	-	-	-	-	0.3	0.2	100
EC	-	-	-	-	1.7	2.0	2.0	2.0	0.3	-	-
German DFG	0.2	-	-	0.7	1.0	-			-		-
Wellcome	0.5	0.3	0.2	<0.1	-	-	-	-	-		-
Institut Pasteur	0.1	0.1	-	0.1	0.1	-	-	-	-	-	-
The Task Force for Global Health	-	-	-	-	-	<0.1	<0.1	-	0.1		-
US CDC		0.1				-	-	-	-	-	-
Disease total	2.6	1.6	1.4	2.6	2.9	2.1	2.0	2.0	0.7	0.2	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

The trachoma vaccine pipeline remains at a very early stages of development. The EU-funded TracVac project, completed in 2021, demonstrated that a vaccine (VD1-MOMP) can induce a neutralising ocular immune response – a positive step forward for further vaccine development. However, no further research has begun since TracVac's completion.

Figure 40. Trachoma R&D pipeline by product type



YAV	NS				-
Total R&D	% of global	% change from	Total R&D spend 2013-2022	Sector	R&D
spend in 2022	funding	2021	13 14 15 16 17 18 19 20 21 22	share	stage

In its first year in the G-FINDER survey, there was no funding for yaws basic research or diagnostic development which met our criteria for inclusion.

While there was no funding of any kind for yaws basic research, there was a small amount of diagnostics R&D funding provided in 2022 via the European & Developing Countries Clinical Trials Partnership (EDCTP). This funding totalled \$0.5m across eight different projects, the largest of which was a \$0.2m disbursement to the London School of Hygiene and Tropical Medicine for the clinical evaluation of a loop-mediated isothermal amplification test for *Treponema pallidum pertenue*.

Since our charts and tables already include the funding provided *to* the EDCTP – and other intermediary organisations, such as product development partnerships – we exclude the 'onward' funding they provide in order to avoid double counting these contributions in our overall measure of global funding.

As such, we recorded a zero total for global yaws R&D funding in 2022, although the onward funding from the EDCTP shows there is some slight level of activity in this space.

Note: yaws was added to the G-FINDER list of neglected diseases only after we had completed our analysis of the product pipeline, meaning that data on the pipeline for yaws is not available at this time.

The clinical evaluation of the LAMP4Yaws project's *Treponema pallidum, Haemophilus ducreyi* loopmediated isothermal test (TPHD-LAMP) was completed in September <u>2023</u>. Another LAMP assay, based on a lateral flow strip, is being developed as a point-of-care field test that can deliver results in 30 <u>minutes</u>.



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.

Other R&D captures any remaining grants that cannot be otherwise allocated across individual diseases or other multi-disease categories, including grants targeting multiple diseases for which disease-specific totals are unavailable.

Overall non-disease-specific (NDS) funding in 2022 was \$579m, down \$52m (-8.2%) from 2021. As in previous years, the largest portion of this total was core funding to multi-disease R&D organisations (\$249m, 43% of the NDS total), although this represented a fall of almost a quarter from 2021. This \$75m drop in core funding was partially offset by a further \$31m increase in funding for platform technologies (\$194m, 34%), the fifth consecutive year of increased investment in this area. Funding for multi-disease vector control products was down by \$19m, to \$63m, while funding for Other R&D increased by \$11m, though mostly as a result of increased survey participation.

The \$75m drop in **core funding** came from almost every major funder, most significantly the Gates Foundation (down \$20m, -39%), the EC (down \$17m, -15%), and the Japanese government (down \$16m, -74%), the latter reflecting the usual cyclical shifts in its funding to GHIT. These drops were slightly offset by new funding from the Czech Ministry of Education Youth & Sport (\$16m) to their National Institute of Virology and Bacteriology.

The core funding decreases were felt by every major recipient, headlined by: a big fall in contributions to the EDCTP; cyclical reductions in GHIT's funding; a 76% reduction in funding to FIND; and the shifting of Gates' core funding to the California Institute for Biomedical Research (Calibr) to – slightly reduced – disease-specific funding.

The \$21m (-18%) fall in EDCTP funding was despite the resumption of support from UK DHSC after a one year hiatus. Most of the decline came via reduced EC funding but was amplified by both cuts from the German BMBF and the absence of any funding from the Swedish SIDA – the third largest contributor to the EDCTP in 2021. Inflation contributed to, but does not completely explain, these declines, as amounts denominated in nominal euros also fell.



US\$ (millions)



Figure 41. Non-disease-specific funding by product type 2013-2022

Multi-disease vector control

- Vector control products
- Fundamental vector control research
- Core funding of a multi-disease R&D organisation

Almost all of the \$31m overall increase in **platform technology** funding was invested in vaccinerelated platforms, which rose by \$26m (45%) to reach \$84m. This was their fifth consecutive year of increase and took them to \$80m above their 2017 level. Almost all other platform product areas also experienced some growth – the sole exception being investment in biologic platforms, which fell by 20%. Half of the overall increase in platform funding (\$15m) was thanks to new industry investment in vaccine platforms – the first significant industry funding for platform technologies which has met our requirement that it focus on LMIC needs. The remainder of the rise in vaccine platform funding came from the Gates Foundation – still the largest overall funder of platforms – as well as Innovate UK and the EC. Most of the overall growth was in platforms potentially applicable to all three global health areas covered by the G-FINDER survey – neglected diseases, emerging infectious diseases and sexual & reproductive health – which saw their funding rise by \$24m (24%).

The drop in funding for **multi-disease VCPs** was spread across almost all major funders, and impacted most product areas. The US NIH remained the top funder – despite dropping by \$2.9m – and there were bigger falls in Wellcome's funding to Monash for the World Mosquito Programme (down \$5.9m, -76%) and from the Gates Foundation (down \$5.5m, -46%). Only funding from the UK MRC bucked the overall trend, rising by \$1.4m (up 471%). Fundamental vector control research was down by \$8.3m, biological VCPs by \$6.9m and chemical VCPs by \$4.0m, while funding for multi-disease reservoir targeted vaccines almost doubled – albeit from a very low base – to \$0.1m.

Funding included under the catchall category of **'Other R&D'** increased for the third consecutive year, by \$11m, returning it to 2018 funding levels.

Table 29. Top non-disease-specific R&D funders 2022 (US\$ millions)

under	Core funding	g ulti-disease ulti-contr vector contr t	ol atform echnologies	5 Other R&D	iotal o	10_
,						•
Gates Foundation	32	6.5	82	6.4	126	20
EC	92	2.7	13	1.6	110	17
US NIH	6.4	25	29	23	84	13
US DOD	-	6.3	35	7.3	48	7.6
Wellcome	40	1.9	-	0.6	42	6.7
Aggregate industry	12	<0.1	15	11	38	6.0
Czech Republic Ministry of Education, Youth and Sport	16	-	<0.1	<0.1	16	2.5
Korean Ministry of Health & Welfare	7.9	-	-	-	7.9	1.3
Unitaid	-	7.4	-	0.2	7.6	1.2
UKMRC	-	1.6	<0.1	5.8	7.5	1.2
Subtotal of top 10^	219	58	65	184	487	77
Total	323	82	163	62	631	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

Global funding for neglected disease basic research and product development totalled \$3,931m in 2022, a headline fall of \$446m, for a drop of just over 10%. Net survey participation was almost unchanged, as were the diseases included in the G-FINDER survey, meaning that this fall is almost entirely due to a genuine reduction in inflation-adjusted funding.

However, much of this decrease in real terms funding – about 71% of the overall reduction – was the result of high levels of global inflation in 2022. If we measured funding in purely nominal terms, the fall from 2021 would be just 3.0%.

Rising prices *do*, however, reduce the buying power of money disbursed for research and development; and it is changes in buying power – not simply the number of dollars and euros spent – that we aim to measure each year. But when there are big shifts in buying power, it does put more stress on how we choose to measure it: the consumer price indices maintained by the International Monetary Fund are not designed to measure specific changes in the cost of R&D. There is some evidence that we may be overestimating the immediate impact of inflation on R&D costs and therefore the true drop in global funding – see the Discussion for more details.

Looking only at the inflation-adjusted fall in overall funding, this was mostly the result of substantial cuts in public funding, which fell by a total of \$397m (-14%), leaving it \$187m below its ten-year average. Funding fell across all three groups of public funders, with high-income country public funding falling by \$344m (-13%) alongside a similarly sized proportional drop in public funding from low- and middle-income countries (down \$13m, -13%). Funding from public multilaterals, after peaking at \$88m in 2021, tumbled by 45% (\$39m) to \$49m – its lowest total since 2015.

The rate of decline was less severe for philanthropic funding, which fell by 8.5% (\$71m) to \$767m. This was the lowest level of philanthropic contributions in more than a decade, and left these funders' contributions well below their long-term average.

Private sector funding, on the other hand, increased for the second year running, rising by 3.9% (\$24m) to its second-highest total on record. There were increases in headline investment from both MNCs (up \$18m, 3.2%) and SMEs (up \$6.3m, 11%). Adjusting for significant shifts in survey participation across the private sector, though, shows that while MNC funding remained essentially unchanged, there was a one-third (\$15m) increase in funding from SMEs, which drove the genuine growth in 2022 private sector funding.



Figure 42. Total R&D funding by sector 2013-2022

Public funding

The public sector invested \$2,523m in neglected disease basic research and product development in 2022, the third consecutive decrease since its peak of \$3,055m in 2019. This \$397m (-14%) fall is the largest drop ever recorded, both in absolute and percentage terms.

PUBLIC FUNDING FROM HIGH-INCOME COUNTRIES

Funding from high-income countries (HICs) fell by \$344m (-13%), to \$2,384m, its most significant drop since the inception of the G-FINDER survey. Almost two-thirds (63%) of this decline was the result of reductions in funding from the US government (down \$216m, -10%). Just under threequarters (72%) of this drop in US funding came, in turn, from a fall in NIH investment (down \$155m, -8.1%), with most of the remainder due to cuts from the DOD (down \$42m, -29%) and USAID (down \$19m, -25%). Despite the steep decline in overall funding from the US government, its share of total HIC public funding actually rose, to a near-record high of 81% as most other nations made even deeper cuts.

Despite the big fall in US NIH funding – mostly a result of big cuts in its HIV/AIDs programmes (down \$98m, -9.4%) – its overall contributions remained broadly in line with its long-term average following three years of record and near-record NIH funding. Both the DOD and USAID, on the other hand, saw their funding fall well below their respective long-term averages, with USAID's dropping to a record low. The DOD made deep cuts to HIV R&D (down \$22m, -64%), alongside even greater reductions to its malaria programmes (down \$26m, -71%), especially malaria drug R&D. Instead, the DOD's investments were increasingly focused on platform technologies, which accounted for almost half of its 2022 funding, up from just 3.4% a decade ago. The combined effect of all these US organisations' declining investment saw US public funding for HIV drop by more than \$141m (-12%) to its second lowest level on record.

Funding from the European Commission¹ remained at near-record levels despite a drop from last year's record high (down \$17m, -9.0%). UK government contributions recovered slightly from their record low in 2021 (up \$7.2m, 8.9%) due to increases from Innovate UK, UK DHSC and the UK MRC. However, UK funding remained at less than half the level of the peak it enjoyed in the four years to 2020.

Both France and Germany experienced steep falls in public funding, although some of this was an artefact of missing data from key funders. Even after adjusting for differences in survey participation, though, French funding fell by more than two-thirds (down \$30m) to its lowest level since the first year of the G-FINDER survey in 2007, and German funding dropped by 30% (down \$19m) to its lowest level since 2009.

Almost all other top public governments reduced their investments in 2022, including Australia (down \$15m, -30%), Switzerland (down \$9.3m, -37%) and the Netherlands (down \$17m, -68%). As a result – and for the first time ever – the Czech Republic appeared among the top national funders (the sixth-largest), due to its \$16m core-funding grant from the Czech Ministry of Education, Youth and Sport to establish its new National Institute of Virology and Bacteriology.

FUNDING FROM PUBLIC MULTILATERALS

Funding from multilaterals totalled \$49m in 2022, a significant decline from the previous year's record high of \$88m (down \$39m, -45%). Essentially all of the change was driven by Unitaid (down \$39m, -49%) which ended several of the projects which had driven the spike in its 2021 funding. This dropped Unitaid's share of multilateral investment to 85%, four percentage points below its ten-year average.

PUBLIC FUNDING FROM LOW- AND MIDDLE-INCOME COUNTRIES

Funding from low- and middle-income country (LMIC) governments declined in 2022, dropping \$13m (-13%) to \$91m. After adjusting for some shifts in survey participation, there were substantial drops from both India and Brazil – the top two sources of LMIC funding over the last several years. There were meaningful decreases from both the Indian ICMR (down \$3.2m, -5.7%) and DBT (down \$2.7m, -47%), as well as a Brazilian public pharmaceutical company (down \$3.2m, -80%) and Brazilian FAPESP (down \$1.8m, -21%).

Beyond India and Brazil, contributions from Argentina, Thailand and Mexico also dropped significantly, with each of these nations reporting less than \$1m in 2022 funding. There was also no public funding at all from the Mexican CONCYT in 2022, after it provided a near-record \$3.6m in 2021.

South Africa (up \$2.0m, 30%) was one of the only public funders to increase its contributions in 2022, although this was only a slight rebound from the record low of 2021. Colombian funding also saw a relatively large increase in 2022, with the Colombian Minciencias more than tripling its R&D investments (up \$1.0m, 204%).

Three-fifths of the overall decrease in LMIC governments' funding fell on malaria R&D (down \$8.2m, -33%) due to drops in basic research funding from the Indian ICMR (down \$5.1m, -27%) and vaccine funding from Brazilian FAPESP (down \$1.5m, -89%). Brazil's government also reduced its funding for bacterial pneumonia & meningitis and for dengue – by an overall total of \$3.2m (-76%).

The only notable increase in LMIC funding was in diarrhoeal diseases (up \$1.2m, 28%), which benefited from a \$0.6m increase from ICMR, alongside \$0.2m in first time funding from South Africa's Biovac Institute and the resumption of funding from Colombian Minciencias and BIRAC.

Table 30. Top public R&D funders 2013-2022

	JS\$ (millin	unsi									022 % of tot
Country	2013	2014	2015	2016	2017	2018	2019	2020	2021	2 2022	0.
United States of America	1,820	1,834	1,760	1,931	1,948	2,100	2,182	2,151	2,138	1,918	76
European Union	118	117	141	85	122	128	128	170	194	177	7.0
United Kingdom	119	126	103	113	213	238	231	201	82	89	3.5
India	59	45	51	59	81	72	80	72	68	66	2.6
Germany	46	50	56	50	67	71	85	57	83	45	1.8
Australia	25	38	23	34	27	45	57	51	46	27	1.1
Czech Republic						1.4	1.8	2.0	3.3	18	0.7
Switzerland	18	21	23	20	19	18	17	18	25	16	0.6
France	81	66	66	52	50	43	47	41	44	14	0.6
Brazil	15	8.1	8.2	14	9.7	15	15	12	16	11	0.4
Canada	21	12	8.5	16	16	18	13	14	11	11	0.4
Sweden	6.0	6.0	8.6	15	4.8	16	14	12	11	10	0.4
Subtotal of top 12^	2,359	2,347	2,262	2,415	2,599	2,801	2,906	2,810	2,754	2,401	95
Total public funding	2,484	2,435	2,363	2,559	2,738	2,973	3,056	2,952	2,921	2,523	100

^ Subtotals for 2013-2021 top 12 reflect the top funders for those respective years, not the top 12 for 2022.

Funding organisations from this country did not participate in the survey for this year.

- No reported funding

PUBLIC FUNDING BY GDP

Absolute funding can be a misleading measure of public investment in neglected disease R&D 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 remained the top public funder by share of GDP in 2022, devoting \$7.53 per \$100k of its GDP to neglected disease R&D, down slightly from the previous year. The US was followed by the Czech Republic at \$6.19 per \$100k, up from just \$1.03 per \$100k in 2021. This was more than double the next highest share: \$2.88 per \$100k from the UK.

Three countries outside the top 12 largest funders appear here when ranked by their contributions relative to GDP: South Africa (fourth highest by GDP and fifteenth largest funder overall), the Netherlands (eleventh, sixteenth overall), and Ireland (twelfth, eighteenth overall). India, which also ranks fourth highest overall, was the only other LMIC to rank within the top 12 by GDP.



Figure 43. Public R&D funding by GDP 2022^{*} (A value of 10 is equivalent to an investment of 0.01% of GDP)

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

Philanthropic funding

The philanthropic sector invested \$767m in neglected disease R&D in 2022, contributing 20% of the global total. While this is a \$71m drop from 2021, its share of global funding remained stable, reflecting the widespread nature of the fall in overall funding. Almost all the drop in philanthropic funding was the result of reduced investment from the previous year's top three philanthropic funders: the Gates Foundation, Wellcome and Open Philanthropy.

The Gates Foundation – as in all previous years – was the top philanthropic funder in 2022 with a total of \$624m, though this was a \$39m (-5.9%) drop from 2021, and its third consecutive year of decline. Wellcome – the second largest philanthropic funder in 2022 and every other year – also reduced its funding, by \$20m (-16%) to \$106m, which was its lowest total since 2015. Of the other major philanthropic funders, MSF's funding also decreased (down \$2.0m, -18%) as did funding from Open Philanthropy (down \$10m, -58%). The fall in Open Philanthropy's funding represented the largest proportional drop of any philanthropic funder in 2022, though it was partly an artefact of the front-loaded project funding it provided in previous years.

The drop in funding from the Gates Foundation was concentrated on two areas. First: its HIV drug R&D, which was down \$43m, reversing 2021's sharp increase and taking Gates' HIV funding to a record low. And second: its non-disease-specific R&D which – except for platform technologies – fell across-the-board, by a total of \$31m; though this only partly offset the previous seven years of growth. Conversely, Gates funding for tuberculosis increased by \$28m (up 22%), with the majority going to vaccine R&D. Gates Foundation funding for diarrhoeal diseases also increased, rising by a quarter to \$42m.

Like the Gates Foundation, Wellcome also substantially reduced its non-disease-specific funding (down \$15m, -27%), which was felt across every individual category. This included a (mostly inflation driven) \$6.6m fall across its core funding grants, a \$5.9m drop in multi-disease VCPs and \$3.1m less for Other R&D. Alongside the big reduction in multi-disease spending, there were smaller drops in Wellcome's funding for malaria (down \$4.1m -22%), tuberculosis (down \$2.8m, -29%) and kinetoplastid diseases (down \$2.5m, -20%). This left Wellcome's funding at its lowest level since 2015, well below its long-term average.

The drop in Open Philanthropy 2022 funding was restricted to its malaria R&D (down \$13m), and was entirely due to last year's front loading of a multi-year grant to UC Davis for an anti-malaria biologic. Open Philanthropy's investments in diarrhoeal diseases and helminths both grew, including a doubling of their funding for diarrhoeal diseases. This meant its non-malaria funding actually rose by \$3.4m.

Despite the sharp decline in HIV drug funding, drug R&D continued to receive the largest share of overall philanthropic funding in 2022 (\$188m, 25% of the total). Vaccine R&D was close behind with 24% (\$183m). There was also a large increase in funding going to biologics – part of an overall trend towards increased biologics R&D – which rose \$36m (158%), with the increase coming mostly from the Gates Foundation.

In line with previous years, academic & other research institutions received over half of philanthropic funding (57%). Funding to PDPs declined still further, by another \$16m (-10%), entirely due to additional cuts from the Gates Foundation. Philanthropic funding to MNCs also dropped significantly, almost halving (down \$18m, -44%) following the 2021 spike driven by the Gates Foundation's investment in Phase III HIV clinical drug trials.

This decrease in funding to MNCs contributed to a 40% decline in philanthropic funding for clinical development (down \$76m). Funding for early-stage research, on the other hand, increased by \$21m in 2022.

Ň	15\$ Imillic	nsi								ŋ	022 % of total
Funder	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	/
Gates Foundation	648	642	653	678	631	663	698	674	664	624	81
Wellcome	125	117	91	111	114	126	127	137	126	106	14
MSF	6.1	4.9	6.5	11	12	17	14	14	11	9.1	1.2
Open Philanthropy					9.3	5.0	16	28	17	7.3	0.9
Fundació La Caixa	3.3		3.8	3.7	5.3	3.3	4.8	5.5	4.3	5.1	0.7
Individual donors and foundations										3.0	0.4
Gavi	23		12	7.1	8.7	3.9	4.3	3.2	3.7	1.9	0.2
Leducq Foundation										1.8	0.2
amfAR	2.3		0.2	0.5	0.1	0.8	-	0.8	0.6	1.6	0.2
Children's Investment Fund Foundation (CIFF)						-	1.6	1.7	1.2	1.0	0.1
Anonymous funder						-	0.8	0.4	0.6	1.0	0.1
All other philanthropic organisations	14	11	8.0	6.6	36	32	9.8	14	6.6	5.6	0.7
Total philanthropic funding	821	776	775	819	818	853	877	883	838	767	100

Table 31. Top philanthropic R&D funders 2022

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.

No reported funding

Private sector funding

The private sector invested a total of \$640m in neglected disease basic research and product development in 2022, accounting for 16% of global funding. This represented a slight increase (of \$24m, 3.9%) from 2021, about half of which was due to a marginal net increase in survey participation. As in all previous years, multinational pharmaceutical companies ('MNCs') were responsible for most of this funding (\$577m, 90% of the private sector total), with small pharmaceutical and biotechnology firms ('SMEs') contributing the remainder (\$63m, 10%). The overall increase in private sector funding took industry investment well above its ten-year average (\$583m) and left it at its second-highest level ever.

MULTINATIONAL PHARMACEUTICAL COMPANIES

Investments from MNCs rose by a headline 3.2% (up \$18m). After adjusting for increased participation, though, their funding remained relatively stable (down \$2.4m, -0.4%). MNC funding for the top three diseases – HIV/AIDS, TB, and malaria – decreased overall, falling by \$19m (-4.4%) but still accounted for 72% of the total. Their funding for the WHO neglected tropical diseases reached a record high of \$92m, after increasing by more than a third (up \$24m), mostly via increases for dengue (up \$14m, 49%) and helminth infections (up \$9.8m, 144%). Funding from new survey participants was heavily focused on schistosomiasis, driving the sharp increase in helminth infection R&D.

The most notable shift in MNC investment was a significant swing away from R&D for vaccines (down \$44m, -31%) towards drug R&D (up \$46m, 12% to a near record high) and a historic spike in biologics R&D (\$17m, up from nothing in 2021) – all of which was for hepatitis B.

The drop in MNC vaccine funding was a result of decreases in investment for both HIV (down \$33m, -42%), largely due to the discontinuation of Phase III clinical trials in late 2022, and for bacterial pneumonia & meningitis (down \$8.8m, -85%) as LMIC-based post-registration studies of a 13-valent vaccine ended in 2021. The latter took MNC funding for bacterial pneumonia & meningitis to an historic low of just \$1.6m. Only *Salmonella* infections saw a significant increase in their vaccine R&D (up \$4.8m, 76%), which took MNC *Salmonella* R&D to a record high of \$11m.

Total MNC funding for drug R&D approached 2018's record high, as dengue, malaria, and helminth drug R&D each increased by over \$10m. The increase for dengue drugs (up \$13m, 48%) was spread across early- and late-stage development and was the main driver of MNCs' record high investment in dengue R&D. Most of a \$10m (14%) increase for malaria drugs went to clinical development, while the jump in funding for leprosy drugs, which rose by 183% (\$3.4m), also went entirely to clinical development. The latter took overall MNC investment in leprosy R&D to a record high of \$5.4m.

As in each of the preceding four years, more than two-thirds of MNC investment was for clinical development & post-registration studies, with most of the remainder going to early-stage research (\$113m, 20%). Although MNC funding for late-stage development fell slightly (by 1.8%, \$7.4m), it remained well above its ten-year average.

FINDINGS - FUNDERS

SMALL PHARMACEUTICAL & BIOTECHNOLOGY COMPANIES

Headline SME investment rose by 11% (up \$6.3m), seeming to rebound slightly from its 2019-2020 plateau. Adjusting for a fall in survey participation, though, funding from SMEs actually grew by almost a third (up \$15m, 33%), leaving it roughly in line with its long-term average. This increase was largely the result of the first substantial funding reported from SMEs for platform technologies (up \$15m from less than \$0.1m in 2021), essentially all for first time investments in LMIC-specific paediatric vaccine platforms. In contrast to MNCs, just 11% of total SME funding went to the 'big three' diseases – HIV, TB and malaria. Instead, their 2022 funding favoured bacterial pneumonia & meningitis (\$22m, 34% of total SME investment), non-disease-specific R&D (\$16m, 24%) and Salmonella (\$10m, 16%).

It was *Salmonella* investment which saw the largest disease-specific increase, as its funding grew by 47% (up \$3.2m), all for clinical development of typhoid & paratyphoid fever vaccine R&D.

Like MNCs, SMEs provided record funding in 2022 for dengue, their contributions more than doubling to \$3.7m (110%), essentially all for clinical development of a monoclonal antibody-based therapeutic.

There was a purely artefactual drop in SMEs' drug R&D, caused by a lack of reporting for ongoing Phase III cryptococcal meningitis drug trials – for which actual funding likely increased in 2022 along with the reported ramp-up of trials.

Funding for tuberculosis fell by close to two-thirds (down \$4.8m, -63%), the result of a genuine reduction in funding for an ongoing Phase III vaccine trial (down \$2.6m, -83%), and an artefactual drop in diagnostics (down \$2.1m, 55%) as a first-time participant in 2021 dropped out of the 2022 survey.

Excluding the \$15m in new platform technology funding, the vast majority (87%) of SME funding went to clinical development & post-registration studies, with these funding levels remaining mostly unchanged from last year. The remaining \$5.7m went to basic & early-stage research, which fell by 40% (\$3.8m).

LMIC-based SMEs continued to provide a clear majority of funding, as they have since 2013. They accounted for 85% (\$54m), all of which came from India-based SMEs.

Top funding organisations

As in all previous years, the top three funders of global neglected disease R&D in 2022 were the US NIH, industry and the Gates Foundation. Their combined funding in 2022 was \$3,010m, a record 77% of the global total.

Funding from both the US NIH and the Gates Foundation declined roughly in line with the 8.0% of US inflation (down 8.1% and 5.9% respectively), with the Gates Foundation actually slightly increasing its nominal funding in 2022. The largest drop from both organisations was in their funding for HIV R&D. While NIH HIV funding remained broadly aligned with its ten-year average following an extended peak between 2018 and 2021, this third consecutive drop in the Gates Foundation's HIV funding took it to a record low. Overall funding from industry increased by 3.9%, bringing its 2022 total higher than that of the Gates Foundation for only the second time ever. This increase in industry funding was split across hepatitis B, dengue and platform funding, and masked a drop in private sector support for HIV.

Funding from almost all of the remaining top 12 funders declined in 2022, particularly among the US government organisations. Contributions from the DOD were down almost 30%, the result of large drops in its HIV and malaria funding, while USAID's were down a quarter, to an historic low. Funding from the EC – 2022's fourth largest funder – dropped slightly from last year's record total (down \$17m, -9.0%), alongside a somewhat larger drop from Wellcome (down \$20m, -16%).

Funding from the UK FCDO fell by a further \$3.6m (-8.2%). Combined with last year's record \$86m drop, this left the FCDO's contributions at less than \$40m – their lowest level ever. Outside of the increase in aggregate funding from industry, the only top funder to buck the downward trend was the UK MRC, whose funding increased by \$2.0m (6.5%).

Ň	JS\$ (millic	nsl								0	022 % of tr
under	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	~
US NIH	1,580	1,587	1,555	1,681	1,664	1,857	1,969	1,918	1,900	1,746	44
Aggregate industry	426	511	525	561	612	782	620	539	616	640	16
Gates Foundation	648	642	653	678	631	663	698	674	664	624	16
EC	118	117	141	85	122	128	128	170	194	177	4.5
Wellcome	125	117	91	111	114	126	127	137	126	106	2.7
US DOD	126	119	98	135	149	126	124	143	141	100	2.5
USAID	100	95	90	100	108	86	73	69	77	58	1.5
Indian ICMR	39	37	38	47	71	59	60	59	56	53	1.3
Unitaid	10	19	23	56	59	82	59	55	81	42	1.1
UK FCDO	67	73	58	62	113	129	124	130	44	40	1.0
German BMBF	16	18	26	33	44	47	50	42	50	38	1.0
UK MRC	46	46	39	46	45	40	49	45	31	33	0.8
Subtotal of top 12^	3,358	3,419	3,364	3,594	3,737	4,143	4,081	3,979	3,981	3,657	93
Total R&D funding	3,734	3,723	3,664	3,940	4,169	4,609	4,553	4,375	4,377	3,931	100

Table 32. Top neglected disease R&D funders 2022

^ Subtotals for 2013-2021 top 12 reflect the top funders for those respective years, not the top 12 for 2022.

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 ('Other Intermediaries').

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.

Funding flow trends

Just under three-quarters of total investment in neglected disease R&D was external funding (\$2,917m, 74%), with the remaining 26% spent internally via public intramural funding and private sector self-funding.



Figure 44. R&D funding flows 2022

While these shares were broadly unchanged from 2021 and in line with the funding distribution across the last decade, both totals were down in absolute terms. External funding bore the brunt of overall reductions, falling by \$382m (-12%), while internal funding fell much less steeply, by \$65m (-6.0%). This partly reflects the growth in private sector investment, which was, as always, almost exclusively internal self-funding.

Proportionally speaking, the largest drop was in funding to PDPs (down 27%) – the fourth consecutive year it has declined. There were drops in funding from all of the top PDP funders, most notably the US NIH, whose funding to PDPs almost halved (down \$33m, -47%), and the Netherlands Ministry of Foreign Affairs (down \$16m, -69%).

Funding to non-PDP intermediaries ('Other Intermediaries') also dropped quite significantly, by around a quarter. The most prominent individual reductions were in the EC's funding to EDCTP (down \$15m, -14%) – partly reversing an even bigger increase the previous year – and the Japanese government's cyclical funding to GHIT (down \$16m, -59%).

Funding by R&D stage

In 2022, a bit under half of all R&D funding was invested in basic & early-stage research (45%, \$1,784m), in line with its average share over the previous decade. Another 28% (\$1,097m) went to clinical development & post-registration studies. While the proportions of funding across these R&D stages remained consistent with 2021, the absolute value of each declined by over \$200m, leaving both of them more than \$100m below their ten-year average. The remaining funding was invested in non-disease-specific R&D, including core funding & other R&D (\$322m, 8.2%), platform technologies (\$194m, 4.9%), and funding which did not specify an R&D stage (\$534m, 14%).

Over half the \$203m drop for the basic & early-stage research category was in funding for basic research, which fell to \$766m (down \$118m, -13%) – its lowest level since 2015. The fall was largely driven by declines in US NIH funding, but is also partly an artefact of the lack of 2022 funding data from the German DFG, which explains a little over a quarter of the headline reduction in basic research.

Early-stage product development also fell, almost across the board, by a total of \$85m (-7.7%). Record-high early-stage biologics funding – the only early-stage product area which grew in 2022 – was more than offset by reductions elsewhere, including record-low early-stage vaccine and microbicide funding and a steep fall in early-stage drug R&D (down \$50m), the latter due in large part to cuts from the US NIH and DOD.

Funding for the clinical development & post-registration studies category also fell, by 16% (down \$207m). More than half of this drop was the result of record-low vaccine development funding (down \$107m, -20%), which mostly affected HIV/AIDS (down \$73m) and malaria (down \$24m). Drug clinical development also dropped (down \$61m, -10%), due to declines in HIV and TB investment, though it remained well above its long-term average after last year's near-record high.

The US NIH and the Gates Foundation were largely responsible for the decline in clinical development (both down around \$70m) along with big cuts from Unitaid (down \$26m, -44%). Three diseases – histoplasmosis, leptospirosis, and trachoma – saw their clinical development funding drop to zero after receiving small amounts in 2021. The only area of clinical development to increase in 2022 was investment in Phase II trials, which grew by \$67m (55%) thanks in part to a sharp rise for dengue. Some of this growth, however, was just an artefact of more granular reporting.

The three highest funded diseases – HIV, TB and malaria – bore the brunt of the drops in both early-stage research, and clinical development. Cuts to these diseases explain three-quarters of the net drop in basic & early-stage research, as well as the entire net decline in clinical development funding.

Funding for product development partnerships

Funding to product development partnerships (PDPs) continued to plummet in 2022, dropping by more than one-quarter – its largest fall yet. This took PDP funding from last year's record low to a *new* record low of \$302m (down \$110m, -27%). At this level, funding to PDPs was more than 40% below its ten-year average, and less than half of its 2014 peak of \$642m.

While the previous year's decline was primarily due to cuts in funding from the UK FCDO, several major funders contributed to the fall in 2022, including the US NIH (down \$33m, -47%), the Netherlands Ministry of Foreign Affairs (down \$16m, -69%), the Gates Foundation (down \$16m, -11%), and USAID (down \$12m, -23%).

The drop in PDP funding from the US NIH was almost entirely driven by cuts to FHI 360 for its drugs and biologics R&D as part of the HIV Prevention Trials Network. Despite Gates Foundation funding falling for the fourth consecutive year – to a new low of \$124m – it still remained the top overall provider of PDP funding for neglected diseases. The fall in Gates PDP funding was driven by cuts in its HIV vaccine funding to IAVI (down \$15m, -69%), though this was partially offset by a rebound in support to IVCC (up \$13m, 233%).

Funding from the Netherlands Ministry of Foreign Affairs fell as their PDP III fund came to an end, impacting several PDPs including MMV and IPM. However, overall Dutch funding to PDPs is expected to resume at similar levels under their upcoming PDP IV fund (see box below). The largest proportional drop in funding came from the Australian DFAT, whose funding dropped by more than 75% to \$2.6m (down \$8.5m). As with Dutch funding, this also mostly reflects the winding-down of their current funding cycle, with disbursements under a new DFAT funding cycle set to begin in 2024.

With significant declines in funding for both IAVI (down \$29m, -38%) and FHI 360 (down \$36m, -49%), MMV became the top-funded PDP for the first time ever – despite MMV's own funding also dropping (by 20%, \$14m). Funding to FIND, which had peaked at \$65m in 2020, fell by a further 60% to a record low of \$12m. This was the result of cuts from several of its funders, most notably the UK FCDO, whose funding to FIND dropped to just \$2.7m in 2022 – down from a peak of \$45m in 2020. The only PDPs that meaningfully defied the downward trend were IVCC (up \$9.6m, 50%) and IVI (up \$5.4m, 76%), though even these represented partial rebounds from falls experienced the previous year.

Declining PDP funding accounted for over 30% of the overall fall in support for HIV/AIDS R&D, with HIV investment received via PDPs dropping by nearly half, from \$158m in 2021 to \$82m in 2022 (down \$75m, -48%).

Forward looking funding data

The Dutch PDP IV fund, which will run from December 2022 to December 2027, has announced a budget of €86.3m, with awards to IAVI, GARDP, EVI, FIND and DNDi – a figure broadly in line with the annual average under the previous programme. The German Government's PDP funding is also projected to remain relatively stable, based on its announcement that it will fund five PDPs for a total of €50m under their 2023 to 2028 PDP funding cycle.



Figure 45. PDP funding 2022



Funding for other intermediaries

Funding for non-PDP intermediaries ('Other Intermediaries') fell by 25% (\$52m) to \$161m in 2023 – its lowest level in six years. This reversed 2021's rebound – when funding rose by \$23m to \$214m – and instead marked a continuation of the longer-term downward trend since Other Intermediary funding peaked at \$242m in 2018.

The reduction was driven by cuts from multiple funders, most notably the Japanese Government and the European Commission¹, which collectively accounted for almost 60% of the decline. The fall from the Japanese Government was exclusively the result of reduced funding to GHIT, which dropped to a record low of \$5.6m (down \$16m, -74%) – although Japan's GHIT funding systematically fluctuates from year-to-year within its fixed multi-year funding commitments. The Japanese Government did, however, recently commit \$200m to GHIT for the period from 2023 to 2027, as part of its third five-year funding plan. This represents a meaningful increase over the previous five-year funding plan's total of \$130m.

The EC's \$92m in Other Intermediary contributions went, as usual, almost exclusively to the EDCTP. Although \$15m (-14%) below last year's record high, the EC's contributions to EDCTP remained at their second highest level ever, accounting for a record 57% of Other Intermediary funding.

Alongside reduced funding from the EC, there were also significant falls in funding from Unitaid and the German BMBF. Unitaid's funding dropped for a fourth consecutive year to \$5.7m (down \$8.3m, -59%). Its support to Barcelona's ISGlobal for the clinical development of an endectocidebased malaria intervention fell by more than two-thirds to \$3.2m, alongside its funding to the Clinton Health Access Initiative, which came to an end after five years. The German BMBF's Other Intermediary funding dropped to its lowest level since 2014 (down \$7.0m, -42%) mostly due to cuts to its EDCTP funding, which declined by almost three-quarters to \$2.4m.

In contrast to the downward trend seen across many other funders, Wellcome's Other Intermediary funding rose slightly, driven by increased support to the WHO for snakebite envenoming drug development. Additionally, after a one-year pause in 2021, the UK DHSC restarted its contributions to the EDCTP, though these totalled just \$2.7m in 2022 – a far cry from their \$48m peak in 2018.

After a rise in 2021, the EDCTP's 2022 funding returned to levels similar to 2020 (down \$21m, -18%), to a total of \$98m. This left them with over 60% of Other Intermediary funding, more than four times the amount received by GHIT, which saw a cyclical drop in its funding to \$22m (down \$17m, -43%). Other than the EDCTP, the WHO was the only Other Intermediary to see any sizeable rise in funding (up \$2.3m, 89%); over 60% of the \$4.8m in funding it received went towards malaria, with the remainder for snakebite envenoming.

In line with previous years, more than 70% of the funding provided *by* the EDCTP was targeted at malaria, tuberculosis and HIV/AIDS. The vast majority of the funding it *received*, however, and almost 90% of Other Intermediary funding overall, was provided as untied core funding, with malaria R&D receiving most of the remainder.

¹ The terms 'European Commission' and '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.

Figure 46. Intermediary funding 2022



DISCUSSION

After several years of relative stability, funding for neglected disease R&D fell by 10%

The 2022 fall in global funding left it 4.1% below its average level over the previous decade, and nearly 15% below its 2018 peak. While this may provide an initial warning that attention is beginning to drift in the face of post-pandemic budgetary pressures, or that an increased focus on emerging infectious disease is replacing support for neglected disease R&D, much of the drop was also the result of unexpectedly high inflation in 2022, meaning the medium-term outlook may just be more of the stagnation we saw between 2019 and 2021 rather than further decline. Either way, whether stagnation or decline, this trend will not sufficiently deliver on the growing number of products making their way through the pipeline.

Much of the fall in overall funding was the result of increased global inflation in 2022

While global funding fell by 10% in real terms, the drop in nominal funding, unadjusted for inflation, was just 3.0%. We adjust our funding totals for inflation because we think that buying power is what matters, not just the number of dollars, pounds or euros disbursed. But our chosen measure of buying power – national consumer price indices published by the IMF – is not perfect for determining how much more expensive *R&D* actually became in 2022. Many of the biggest price spikes in 2022 – eggs, used cars, natural gas, olive oil – have little to do with the costs of carrying out R&D. One piece of evidence at least demonstrates that we have probably overestimated the impact of overall prices on R&D-specific costs: the IMF's 8.0% figure for general US inflation is considerably higher than the US NIH's 4.9% estimate of how much *its* average R&D costs rose in 2022.

Although it looks like we have overemphasized the immediate impact of inflation on costs – meaning the overall picture is perhaps a little rosier than the one we paint throughout the report – we still prefer to use general purpose inflation measures to R&D specific values, like the one produced by the NIH. In the medium term, the costs of a labour-intensive activity like biomedical R&D are likely to climb in line with the overall cost of living, and short-term departures from that relationship – caused in 2022 by the statutory cap on wage growth for NIH researchers – probably won't hold in the long term.

How much difference does our decision to adjust funding using the IMF's CPI make to the longterm trajectory of measured R&D? The figure below shows our standard G-FINDER inflation adjusted funding totals (the pale pink line) compared to the nominal totals calculated without taking inflation into account at all (the orange line); and the totals using the NIH's R&D-specific inflation rate (the dark red line).

Our inflation adjustments might, however, not always capture funders' actual intentions, since much of the record fall in public funding is the mechanical result of a reduction in the inflation adjusted value of fixed multi-year grants. In some cases, as with funding from the EC and the US BARDA, we pro rate nominal totals over the life of the grant, and any increase in inflation *automatically* reduces our estimate of funding in that year, even without a change in the number of euros or dollars actually being disbursed.

Tellingly, the growth of private sector funding – which is based on actual hours worked rather than fixed multi-year grants – suggests funders may adjust for inflation once they have had the chance, and that we might experience some level of catch-up growth once they are able to predict how much their grants will actually be worth in their final year. In the short term however, the reduced value of grants does create a real disruption to product developers' ability to fund the R&D they had planned in that year.

It would therefore make sense for funders to better take inflation into account when making investments and grants. While low inflation has been the norm for the last decade, it is not however a law of nature. Funders are understandably hesitant to commit to indexation clauses that may unexpectedly leave them out-of-pocket, but they are probably better placed to take on this risk than researchers.



Figure 47. Neglected disease R&D funding adjusted for inflation

Industry funding was the only sector to increase R&D funding in 2022

Private sector funding rose by 3.9% (\$24m) to \$640m, its second-highest total ever, mostly thanks to increases from smaller pharmaceutical and biotechnology companies.

While multinational pharmaceutical companies invested record amounts in R&D for dengue therapeutics, *Salmonella* infections, leprosy, mycetoma and hepatitis B, smaller companies also provided record high funding for dengue, and contributed the first substantial investments in LMIC-focused vaccine platform technology.

Rising industry investment in areas specifically defined by the absence of commercial opportunities is always cause for celebration; but also a little scepticism. Rather than an upswell in altruism, increased private sector interest can sometimes signal a shift in the market, as pharmaceutical companies begin to target emerging opportunities in higher income countries. The most obvious example of this is vaccines for dengue fever, which were removed from our survey's neglected disease scope in 2013 once we became aware of a robust commercial market centred on endemic upper-middle-income countries, high-income country tourists and the US military.

Record funding from both small and large pharmaceutical companies for dengue R&D – centred on (still in-scope) drugs and biologics – is good news for endemic nations, but also raises concerns that something similar might have happened to dengue therapeutics: that these investments are being made, not *despite* their being unprofitable, but because they no longer are.

US\$ millions

This underlines the conceptual difficulty with trying to celebrate private sector involvement in often unprofitable R&D: success makes us wonder whether we have correctly defined the problem. With climate change causing endemic regions for many tropical diseases and vectors to spread further from the equator, high-income countries will increasingly view investment in neglected disease as an investment in domestic health.

The US was reporting multiple severe cases of malaria, Chagas' disease, Zika and at least one case of the tropical parasite *Leishmania*, from 2019. Since then, shifts in the climate have seen multiple cases of leprosy, apparently transmitted via armadillo wrestling, the spread of the Chagas' carrying triatomine bug, and the rise of the dengue transmitting *Aedes aegypti* mosquito in the southern United States.

If we are to prioritise investment in neglected disease R&D motivated by, and targeted at, the specific needs of LMICs – rather than as spillovers from their spread to high-income countries – we need to reduce barriers to registration and market access in low- and middle-income settings so that even products with small markets begin to look commercially viable. This could include low-cost regulatory transfer regimes for existing HIC-registered products, rapid and reliable market access following successful trials, and policies which encourage testing of repurposed entities against a range of tropical diseases. The latter appears to be the motivation behind last year's record spike in cryptococcosis R&D, which was driven by clinical trials of a new form of the widely-used antifungal amphotericin B, in what would otherwise be an unpromising market for clinical development.

Funding for biologics rose for the fifth year running, making it the only product area to see any growth in 2022

Over the last three years, funding for biologics has more than doubled, leaping from \$70m in 2019 to \$144m in 2022. This represents an 85-fold increase since a lull in biologics investment early last decade, when funding averaged just \$1.7m over a five-year period.

The vast majority of the increase in biologics R&D over the past three years is the result of a boost in investments from the three largest overall funders of neglected disease R&D. Biologics funding from the Gates Foundation is up \$39m since 2019, industry's by \$19m and the NIH's by \$9.3m. The comparatively modest three-year growth in NIH funding comes after a sudden \$27m fall in 2022 from the previous year's record high; in 2021 the NIH spent nearly \$80m on biologics, almost two thirds of that year's global total.

It appears that the ongoing rise in biologics funding – along with the growth in drug funding we profiled in last year's report – represents a shift in efforts to combat infectious disease away from a heavy focus on vaccines and towards therapeutics. Among the funders who supported both vaccines and biologics, there was a very strong correlation (83%) between the increase in their biologics funding and the fall in their vaccine funding over the past three years, as shown in the figure below.

Funders switching some of their vaccine R&D investments to previously neglected therapeutics seems to demonstrate a deeper appreciation that multiple tools are needed to combat infectious disease, and of the potential synergies between biologics and vaccines. The initial, very vaccine-centric R&D response to COVID, for example, highlighted the absence of dedicated champions for therapeutics research who could play the role that organisations like CEPI and FIND did for vaccines and diagnostics. This has been identified as a vulnerability not to be replicated in future pandemics. Increased focus by individual funders on therapeutics – hopefully alongside continued vaccine development – probably reflects some of this wider thinking across the global health sector, and represents a valuable diversification of global R&D efforts.

There are, however, ongoing concerns about ensuring affordable LMIC access to monoclonal antibodies (mAbs), and whether current bioreactor capacity can be expanded to support a truly



Figure 48. Three-year funding shift from vaccine to biologics R&D by funder, 2019 versus 2022*

* This figure only includes funders that have provided funding for both vaccine and biologics R&D within the past three years. Of the funders that fall into this group, only the 15 greatest decreases in vaccine R&D have been included.

global roll-out of novel biologics. Lessons from the relatively poor record of mAbs against COVID offer another possible concern – that widespread use of treatments based on a single mAb could lead to the rapid development of resistance. Indeed several biologics which were initially effective against COVID ultimately had their Early Use Authorisations withdrawn following the emergence of new strains against which they were ineffective.

Set against these concerns is the potential for mAbs and other biologics to provide a dual use technology, offering both prevention – via pre-exposure prophylaxis – and cure. Biologics also typically cause fewer side effects than small molecule drugs, and can demonstrate efficacy – in post-exposure use at least – without the massive trials required for vaccines.

There are now mAbs approved for use in treating HIV, but not yet any record of large-scale use in endemic regions. There is hope that new mAbs specifically designed for LMIC use – such as those against paediatric respiratory syncytial virus, which offer extended duration of action at lower cost than existing alternatives – could offer proof-of-concept for the suitability of biologics in LMIC contexts. Showing that mAbs like this can be distributed at scale even in low resource environments would help demonstrate that biologics can deliver real world impacts to LMIC populations, and allay any concerns about an apparent shift away from vaccines in favour of therapeutics.

The number of products in the neglected disease pipeline has risen by 55% since 2015, with growth across almost all product categories

This year's G-FINDER report includes, for the first time, data on the number and type of products in the pipeline for each disease covered by the G-FINDER survey. This provides valuable context for interpreting funding totals against the actual state of products in development. After adjusting for the expansion in our survey scope since 2015, our <u>pipeline database</u> shows that each product, other than vector control, has seen measurable growth in the number of candidates in development, with the biggest increases in vaccines (up 78 candidates overall, 38%) and biologics (up 57 candidates, 713% since their 2017 inclusion).

There has also there been a maturation of the pipeline for drugs, vaccines, biologics and microbicides, with candidates moving from discovery & preclinical development into clinical trials. Since 2015, there has been a striking inversion in the share of products in discovery & preclinical phases (which fell from 56% in 2015 to 40% in 2023) and those in clinical development (from 44% in 2015 to 60% in 2023). This indicates that, overall, products have been advancing through the pipeline more swiftly than new early-stage candidates have entered.

A decline in preclinical candidates can be the expected result of a maturing pipeline: once enough potential products have been identified, focus and funding shift to finding out which ones work in practice. But the key question is whether there are now enough promising candidates in clinical development to satisfy the wide range of unmet needs for neglected diseases, especially given the high levels of attrition inevitable during clinical stage testing: half of the products in the 2019 pipeline were inactive by 2023 and only 8.0% reached Phase III trials. If we exhaust our current clinical pipeline without finding all the products we need, then not having seeded the early stages of the pipeline with a buffer of new investigational candidates will mean a long delay before the next batch of potential products is ready to progress.



Figure 49. Drug, vaccine, biologic and microbicide candidates by R&D stage

We still lack a clear measure for how much neglected disease R&D funding is 'enough'

It is obviously encouraging when global neglected disease R&D funding goes up, and disconcerting when it falls. Beyond this, though, it can be hard to tell whether or not this year's total of a little under four billion dollars is roughly the right amount for the world to be spending on R&D to combat neglected disease.

One approach is to contextualise this \$4bn figure amongst other kinds of spending. Four billion dollars for all neglected disease R&D starts to look quite modest set against the \$6.5 billion devoted to COVID R&D in 2021 at the peak of the pandemic response. Likewise, it is dwarfed by the annual budget of a single research funder: the US NIH's yearly \$48 billion. Or the \$204 billion in global 2022 Official Development Assistance. Or, more frivolously, the annual \$24 billion on processed food R&D, or even the \$7.7 billion beauty companies spent just on advertising. While this doesn't solve the question of whether this is enough, it does go some way to demonstrate how we currently prioritise our spending, especially in times of increasing fiscal constraint.

We might instead assess our level of spending based on whether it provides value for money. If every dollar we spend on neglected disease R&D delivers impacts worth a hundred dollars or more, then we presumably ought to be spending more. The actual return on investment in global health R&D is an incredibly complex calculation, but our preliminary estimates – through the <u>Evidence for Impact</u> project – suggest that the return on products developed between 1999 and 2022 vastly exceeds their costs, implying that increased global funding would deliver a similarly massive return on investment. Given the persistent mortality and morbidity from neglected diseases, there is therefore a strong argument to be made that four billion dollars is not nearly enough, and that increased investment would offer huge social, health and economic benefits in the medium to long term.



Figure 50. How ND R&D compares to other areas of global spending (US\$ billions)

FORWARD-LOOKING DATA PROGRAMME LAUNCH: AN ALTERNATE LENS FOR ANALYSING R&D FUNDING

The G-FINDER survey is a retrospective look at what happened in the previous fiscal year – here 2022. This delay ensures all data arrives complete, and allows us to be scrupulously accurate, ensuring we are able to share the most precise summary of global funding for neglected disease R&D possible. But it also comes with a time lag. We are shortening this delay by providing earlier access to funding announcements via our new project collecting data in real time. This will include PDP funding announcements and estimates of overall funding in 2023 and beyond for major public and philanthropic funders, with updated forecasts throughout the year as new data becomes available. This builds on our work tracking real-time funding announcements in the early months of COVID; and that experience provides some insights about how – and how not – to use this data.

Following COVID funding as it was announced throughout 2020, for example, gave us a preliminary total of \$9.1bn. A more sober retrospective analysis adjusted this total to just over half that amount: \$4.7bn. Some of this gap reflects the wider reach offered by announcement tracking over asking funders to respond to a lengthy survey – we know a lack of survey participation meant G-FINDER missed some genuine funding which showed up in our announcement data. But much of it also represents the ease of *announcing* new funding compared to *delivering* it. Another consideration is that a ten-year commitment to provide \$300m isn't really a \$300m funding commitment, since inflation will erode its value, a product may fail during early trials, or changing circumstances may render it irrelevant long before its final years – as when long term Ebola funding was repurposed to target COVID in 2020.

Each of these issues is relevant when interpreting our forward-looking data. Announcements may not be entirely new money, or may come with strings attached; projections based on modelled data may not hold up to changes in circumstance; and the headline value of announcements don't take into account the long-term effects of inflation. Nevertheless, our real-time data will provide a valuable interim supplement to our annual G-FINDER reports, helping to forecast trends in a more timely manner.

Access our forward-looking Compass data here.

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