Smart Decisions

The G-FINDER 2024 Neglected Disease R&D report







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Acknowledgements

This is the seventeenth in a series of annual reports published as part of the G-FINDER project. We are very grateful to all of the survey participants who have contributed to this effort. Thanks to their commitment, we are able to continue to provide accurate, up-to-date financial information on research and development for neglected diseases. The patience and engagement of the participating government and multilateral agencies, academic and research institutions, product development partnerships, philanthropic institutions and pharmaceutical and biotechnology companies have made this project possible.

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Introduction

The G-FINDER report

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

This year's report focuses on investments made in participants' 2023 financial year ('FY2023') and 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 <u>online data portal</u>, while interactive pipeline and approved product data can be accessed in our <u>R&D tracker</u>.

This year's report contains an overview of the changes in neglected disease funding in 2023, measured in 2023 US dollars ('US\$'), 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 strategic shifts in the funding landscape.

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).

Figure 1. Filter to determine G-FINDER neglected disease inclusions



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

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, see our neglected disease R&D scope.

Changes to the list of neglected diseases

The G-FINDER scope is reviewed annually. While the recent changes to the survey scope, such as last year's addition of yaws and removal of giardiasis, 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.

Inflation adjustments and aggregation of industry data

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

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

Funding for emerging infectious diseases and women's 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 women's 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 <u>companion reports</u>. However, all available neglected disease, emerging infectious disease and women's health survey data (now including 2023 figures) are available via the <u>G-FINDER data portal</u>.

Funding by disease







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Table 1. Disease and product R&D funding 2023 (US\$ millions)

| 50858 0 area | Basic research | | Vaccines | Biologics | Diagnostics Nicrobicides Oroducts Unspecified | | | | | |
|---|----------------|--------|----------|-----------|---|-------|-------|-------|--------|--|
| | 011.07 | 107.75 | 071.05 | 00.57 | 00.40 | | Ĩ | 00.00 | | |
| HIV/AIDS | 211.27 | 187.75 | 150.51 | 69.57 | 26.46 | 20.97 | | 82.02 | 1,269. | |
| | 174.00 | 350.74 | 147.71 | 0.52 | 82.49 | | 60.00 | 19.35 | 806. | |
| Mataria | 174.89 | 247.73 | 147.71 | 10.04 | 14.39 | | 08.28 | 22.31 | 690. | |
| P. talciparum | 80.47 | 77.47 | 10.11 | 13.04 | 3.33 | | 4.60 | 9.31 | 299. | |
| P. Vivax | 10.55 | 28.55 | 10.11 | 1.70 | 3.42 | | 0.25 | 2.13 | 01.4 | |
| Multiple / other malaria strains | //.8/ | 141.71 | 26.44 | 1.70 | 7.64 | | 63.43 | 10.87 | 329. | |
| | 49.33 | 13.60 | 74.20 | 4.33 | 2.30 | | | 0.14 | 144. | |
| Shigella | 9.25 | 1.04 | 30.11 | 2.77 | 1.10 | | | - | 44. | |
| Cholera | 23.85 | 1.97 | 14.83 | 1.50 | 0.34 | | | - | 42. | |
| Cryptosporialosis | 0.41 | 10.04 | - | - | 0.05 | | | 0.04 | 16. | |
| Rotavirus | 3.62 | | 19.29 | | 0.01 | | | - | - 22 | |
| Enterotoxigenic E. con (ETEC) | 1.55 | | 0.01 | | <0.01 | | | 0.04 | 1. | |
| Enteroaggregative E. coli (EAEC) | 4.00 | 0.54 | - | | 0.01 | | | - | 0 | |
| Multiple diarrhoeal diseases | 4.88 | 0.54 | 3.41 | - | 0.86 | | 0.10 | 0.07 | 9 | |
| Kinetoplastid diseases | 45.78 | /4.80 | 4.42 | 0.88 | 6.38 | | 0.16 | 0.57 | 132. | |
| Chagas' disease | 6.87 | 35.82 | 3.08 | 0.75 | 4.21 | | 0.01 | 0.02 | 50 | |
| Leishmaniasis | 21.87 | 15.08 | 1.08 | 0.13 | 2.13 | | | 0.19 | 40 | |
| Sleeping sickness (HAT) | 13.79 | 10.85 | 0.27 | - | 0.04 | | 0.15 | - | 25 | |
| Multiple kinetoplastid diseases | 3.25 | 13.04 | - | - | - | | - | 0.36 | 16 | |
| Dengue | 20.06 | 81.06 | | 0.67 | 3.31 | | 7.66 | 0.49 | 113 | |
| Helminth infections (worms & flukes) | 39.26 | 32.89 | 5.22 | - | 10.30 | | 0.04 | 6.70 | 94 | |
| Schistosomiasis (bilharziasis) | 9.99 | 13.08 | 4.05 | - | 3.77 | | - | 0.59 | 31 | |
| Lymphatic filariasis (elephantiasis) | 6.40 | 2.67 | | | 1.20 | | 0.02 | 3.95 | 14 | |
| Onchocerciasis (river blindness) | 1.98 | 6.68 | 0.01 | | 2.84 | | 0.02 | - | 11 | |
| Hookworm (ancylostomiasis & necatoriasis) | 1.68 | 1.48 | 0.45 | | | | | 0.25 | 3 | |
| Tapeworm (taeniasis / cysticercosis) | 2.54 | 0.83 | | | 1.05 | | - | - | 4 | |
| Whipworm (trichuriasis) | 1.71 | 0.16 | | | | | | - | 1 | |
| Strongyloidiasis & other intestinal roundworms | 1.82 | 0.06 | 0.01 | | 0.19 | | | 0.04 | : | |
| Roundworm (ascariasis) | 1.75 | 0.26 | | | | | | - | 2 | |
| Multiple helminth infections | 11.39 | 7.68 | 0.70 | | 1.25 | | - | 1.87 | 22 | |
| Salmonella infections | 33.50 | 2.16 | 39.89 | 0.35 | 1.74 | | | 0.07 | 77 | |
| Typhoid and paratyphoid fever (S. Typhi, S. Paratyphi A) | 23.08 | 2.15 | 24.91 | 0.35 | 1.34 | | | 0.07 | 5 | |
| Non-typhoidal S. enterica (NTS) | 3.59 | - | 11.07 | - | - | | | - | 14 | |
| Multiple Salmonella infections | 6.83 | 0.01 | 3.90 | - | 0.39 | | | - | 1 | |
| Snakebite envenoming | 0.74 | 21.13 | | 8.14 | 0.53 | | | - | 30 | |
| | 2.89 | 5.43 | | 14.55 | 1.98 | | | - | 24 | |
| | | 3.05 | 13.41 | | 4.87 | | | - | 21 | |
| Leprosy | 6.97 | 11.50 | 0.24 | - | 0.60 | | | 0.02 | 19 | |
| Bacterial pneumonia & meningitis | 5.59 | | 9.96 | | 2.75 | | | 0.82 | 19 | |
| S. pneumoniae | 3.89 | | 7.65 | | 2.30 | | | 0.22 | 14 | |
| N. meningitidis | 1.70 | | 2.31 | | 0.25 | | | 0.60 | 4 | |
| Both S. pneumoniae and N. meningitidis | | | | | 0.20 | | | - | 0 | |
| Cryptococcal meningitis | | 7.05 | | 0.76 | | | | - | 7 | |
| Rheumatic fever | | | 4 90 | | | | | _ | 4 | |
| Histoplasmosis | 3.60 | 0.09 | 1.00 | | 0.07 | | | 0.04 | 3 | |
| | 0.00 | 0.00 | | | 2.42 | | | 0.01 | 2 | |
| Scables | 0.30 | 133 | | | 2.42 | | | | - 1 | |
| Ruruliuloor | 1.06 | 0.14 | 0.35 | | | | | | 1 | |
| Mycetoma | 0.01 | 0.14 | 0.30 | | | | | | 0 | |
| Vawe | 0.01 | 0.59 | | | - | | | - | 0 | |
| | 0.02 | | | | - | | | - | | |
| | | | - | | - | | | - | 275 | |
| | | | | | | | | | 275 | |
| General diagnostic platform technologies multi-disease diagnostics | | | | | | | | | 83 | |
| Drug-related platform technologies | | | | | | | | | 68 | |
| Adjuvanta and immus and international | | | | | | | | | 00 | |
| Piologica related platform to book | | | | | | | | | 30 | |
| Biologics-related platform technologies | | | | | | | | | 12 | |
| Mutti-disease vector control Core funding of a multi-disease R&D | | | | | | | | | 272 | |
| organisation | | | | | | | | | | |
| Other R&D | | | | | | | | | 100 | |

No reported funding Category not included in G-FINDER

Table 2. R&D funding by disease 2014-2023 ^

| | USS Imillic | unsi | | | | | | | | 2 | 023% of |
|---|-------------|-------|-------|-------|-------|---------|---------|---------|-------|-------|---------|
| under | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | |
| HIV/AIDS | 1,414 | 1,343 | 1,455 | 1,553 | 1,741 | 1,760 | 1,603 | 1,662 | 1,412 | 1,269 | 30 |
| Tuberculosis | 707 | 727 | 743 | 754 | 796 | 834 | 796 | 804 | 737 | 806 | 19 |
| Malaria | 715 | 701 | 729 | 780 | 794 | 742 | 732 | 718 | 631 | 690 | 17 |
| Diarrhoeal diseases | 216 | 197 | 188 | 199 | 212 | 199 | 175 | 155 | 164 | 144 | 3.5 |
| Kinetoplastid diseases | 184 | 154 | 176 | 181 | 188 | 189 | 180 | 149 | 133 | 133 | 3.2 |
| Dengue | 102 | 112 | 135 | 98 | 93 | 94 | 87 | 87 | 84 | 113 | 2.7 |
| Helminth infections (worms & flukes) | 113 | 96 | 93 | 106 | 114 | 113 | 94 | 97 | 109 | 94 | 2.3 |
| Salmonella infections | 80 | 84 | 113 | 98 | 107 | 94 | 90 | 78 | 84 | 78 | 1.9 |
| Snakebite envenoming | | | | | 9 | 14 | 18 | 20 | 22 | 31 | 0.7 |
| Hepatitis B | | | | | 12 | 11 | 19 | 17 | 33 | 25 | 0.6 |
| Hepatitis C | 56 | 42 | 36 | 18 | 57 | 13 | 19 | 18 | 16 | 21 | 0.5 |
| Leprosy | 12 | 13 | 13 | 13 | 10 | 11 | 9 | 10 | 14 | 19 | 0.5 |
| Bacterial pneumonia & meningitis | 90 | 113 | 112 | 88 | 103 | 80 | 75 | 67 | 49 | 19 | 0.5 |
| Cryptococcal meningitis | 6.9 | 6.3 | 7.1 | 14 | 10 | 9.5 | 8.2 | 16 | 7.0 | 7.8 | 0.2 |
| Rheumatic fever | 2.0 | 3.3 | 2.1 | 2.1 | 2.3 | 18 | 25 | 18 | 3.5 | 4.9 | 0.1 |
| Histoplasmosis | | | | | | | 4.8 | 4.0 | 3.6 | 3.8 | <0.1 |
| Leptospirosis | 1.5 | 1.5 | 2.7 | 3.6 | 1.9 | 2.3 | 1.6 | 1.5 | 1.2 | 2.4 | <0.1 |
| Scabies | | | | | | | 1.3 | 2.0 | 1.9 | 1.6 | <0.1 |
| Buruli ulcer | 4.4 | 2.2 | 3.4 | 4.9 | 3.0 | 3.2 | 2.8 | 0.8 | 1.0 | 1.5 | <0.1 |
| Mycetoma | | | | | 0.7 | 1.1 | 0.8 | 0.8 | 0.5 | 0.6 | <0.1 |
| Yaws | | | | | | | | | < 0.1 | < 0.1 | <0.1 |
| Trachoma | 1.7 | 1.4 | 2.7 | 3.1 | 2.2 | 2.1 | 2.1 | 0.7 | 0.2 | - | - |
| Platform technologies | 29 | 45 | 93 | 64 | 81 | 113 | 146 | 166 | 282 | 276 | 6.6 |
| Vaccine-related platform technologies | 11 | 15 | 23 | 16 | 23 | 27 | 27 | 18 | 22 | 30 | 0.7 |
| General diagnostic platforms & multi-disease diagnostics | | | | | | | | 13 | 11 | 12 | 0.3 |
| Drug-related platform technologies | 3.0 | 4.4 | 4.1 | 7.9 | 2.6 | 6.6 | 8.7 | 24 | 107 | 68 | 1.6 |
| Adjuvants and immunomodulators | 12 | 19 | 48 | 35 | 37 | 40 | 54 | 52 | 55 | 81 | 2.0 |
| Biologics-related platform technologies | 3.1 | 5.8 | 18 | 4.2 | 18 | 39 | 55 | 59 | 87 | 83 | 2.0 |
| Multi-disease vector control | | | 23 | 34 | 47 | 74 | 75 | 87 | 65 | 55 | 1.3 |
| Core funding of a multi-disease R& D organisation | 121 | 163 | 183 | 313 | 360 | 351 | 363 | 343 | 268 | 273 | 6.5 |
| Other R&D | 47 | 56 | 43 | 51 | 76 | 45 | 62 | 64 | 77 | 100 | 2.4 |
| Total R&D funding | 3 901 | 3.861 | 4 152 | 4 377 | 4 819 | 4 7 7 4 | 4 5 8 9 | 4 5 8 7 | 4 199 | 4 170 | 100 |

Multi-disease vector control products were added in 2017; the 2016 total was added retros pectively, 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. • Please note that some of the diseases listed are actually groups of diseases, such as the diarrhoeal illnesses and helminth infections.



Funding by disease

How funding for individual neglected diseases changed in 2023

R&D funding remained stable after last year's \$350m drop

Global funding for neglected disease basic research and product development was basically stable at \$4.17bn in 2023, down by less than 1% (\$29m) from 2022 – or by just under 2% (\$70m) if we adjust for a slight net increase in survey participation. This failure to rebound from the big, inflation driven fall in 2022 left global funding nearly \$650m below its 2018 peak, and almost \$150m below its average over the previous decade.

The largest falls, in absolute terms, were for HIV/AIDS (down \$143m, -10%), bacterial pneumonia & meningitis (down \$30m, -61%) and diarrhoeal diseases (down \$20m, -12%), all reaching record lows. Mostly offsetting these were substantial increases for both TB (up \$69m, 9%) and malaria (up \$60m, 9%, partly thanks to new survey participants). Several traditionally less funded diseases enjoyed substantial growth, including record funding for leprosy and snakebite envenoming, alongside near record totals for TB and dengue.

The impact of inflation was much smaller than in 2022, when it was responsible for the vast majority of the decrease in the value of funding. Nominal funding (unadjusted for inflation) rose by a little under 4%, with the effects of global inflation turning that into the very slight decline in real funding. So, while funding increased a little in pure dollar terms, the actual purchasing power of global funding declined slightly – though the size of the decline and the rate of inflation driving it were both significantly lower than in 2022.

In these disease chapters, we occasionally omit some qualifiers for the sake of readability: we might talk about 'funding for malaria', for example, but our funding totals only ever refer only to *R&D* funding – not funding for malaria generally. Similarly, we might occasionally talk about 'this year's funding total' in reference to funding for *2023* – the period covered by this year's G-FINDER survey – and 'last year' therefore refers to 2022.

Figure 2. Total R&D funding for neglected diseases 2007-2023



The 'big three' – HIV, TB & malaria

HIV R&D fell to a record low, while both malaria and TB saw increased funding

The 'big three' diseases – HIV/AIDS, malaria and tuberculosis – remained the top recipients of disease-specific R&D funding in 2023, as they have been, in some order, since the survey began in 2007. Together, they continued to account for 80% of disease-specific global funding, and around two-thirds of the overall total.

Global funding for **HIV R&D** totalled \$1,269m in 2023. This was a decrease of 11% (down \$143m) from 2022, leaving funding at an all-time low, 28% below its 2019 peak, following significant decreases from the two top funders: industry and the US NIH.

As in all previous years, the majority of funding went to vaccine R&D (\$671m, 53%), followed by basic research (\$211m, 17%) and drugs (\$188m, 15%). Funding fell across all product areas except for diagnostics, headlined by a further \$58m (-23%) reduction in drug R&D, which is now down more than \$120m from its 2021 peak.

Essentially all LMIC-targeted HIV drug investment came from just three funders – industry, US NIH and the Gates Foundation. It was steep cuts in industry's drug funding (down \$52m, -32%) that were responsible for most of this year's sharp decline. This reduction in private sector drug R&D followed two years of record-breaking investment,

and was partly due to the discontinuation of a daily oral candidate.

Investment for HIV vaccine R&D also fell, to a record low \$671m (down \$32m, -6%), as industry funding dropped by half following the discontinuation of latestage vaccine candidate after two failed clinical trials. Vaccine funding from the US DOD suddenly dropped to zero (down from \$13m and from \$36m in 2021), overshadowing a substantial increase from the Gates Foundation (up \$11m, 20%) as their vaccine funding to IAVI and industry rose sharply.

FUTURE FUNDING

In 2024 HIV/AIDS drug R&D funding received \$6.9 million under the EC's DOLPHIN-3 project, which studies drug optimization for HIV-positive pregnant women and their infants in low- and middle-income countries.

Funding for microbicide R&D fell steeply again (down \$18m, -46%), dropping to \$21m, well over 90% below its 2008 peak, as the remaining pool of microbicide funders shrank to just three organisations – US NIH, Irish Aid and Grand Challenges Canada. We cover the long-term reduction in microbicide funding, and its partial replacement by multipurpose prevention technologies, in the Discussion, below.

All three of the largest funders of HIV R&D made significant changes in 2023, which collectively contributed to the record low in overall HIV R&D funding. Industry investment fell by a third (down \$75m, -35%), with cuts to both drugs and vaccines, to just over half of its 2021 peak. We consider industry's gradual shift away from HIV vaccine R&D in more detail in the Discussion. Funding from US NIH fell across almost all product categories (down \$55m, -6%), to its lowest level since 2017, while funding from the Gates Foundation rebounded from a historic low (up \$12m, 10%). Higher Gates funding was driven by increased vaccine clinical development (up \$14m, 157%), most of which went to IAVI and the Collaboration for AIDS Vaccine Discovery network (CAVD), and to industry for human cytomegalovirus-vectored vaccines.

PIPELINE SPOTLIGHT

Gilead's twice-yearly injectable lenacapavir demonstrated efficacy and superiority to once-daily oral Truvada for HIV prevention in the PURPOSE 1 and 2 trials, with PURPOSE 1 being the first Phase III HIV prevention trial to result in no infections in the lenacapavir arm. Gilead have signed non-exclusive royalty-free voluntary licensing agreements with six high-volume manufacturers ahead of regulatory approval, meaning low-cost generic versions could be available to LMICs soon afterwards.

Funding for **tuberculosis** rebounded by 9% (\$69m) in 2023 to reach \$806m, restoring it to just above its 2021 level and taking it to its second highest level ever. The overall increase in funding was driven by a \$59m (62%) rise in vaccine R&D, which, building on last year's growth, reached a record \$154m. Diagnostics funding rebounded, rising by \$17m (26%) to \$82m, its second highest level on record.

While the US NIH remained the largest funder of tuberculosis R&D overall – as it has been every year since 2007 – its funding declined for the fourth consecutive year. Meanwhile the Gates Foundation, the second largest funder, increased its funding by \$61m (38%), helping drive the big increases in vaccines and diagnostics. The increases in the Gates Foundation's vaccine funding, which has more than doubled over the last two years, went mostly to the Gates Medical Research Institute (MRI) towards the development of the M72/AS01E TB vaccine through Phase III – forming part of its 3.5-year overall funding commitment for TB (see box). The Gates Foundation's increased investment is offsetting declines elsewhere and emphasises the growing role of private philanthropy in TB research.

TB funding from the NIH is now \$80m below its 2019 peak, with a little over half of the fall coming via reductions in its spending on drugs, and such reduction may slow progress in developing new TB treatments. While NIH drug

funding fell only slightly in 2023, it came alongside substantial declines in funding from the US CDC (no funding in 2023 after averaging nearly \$10m over the preceding decade), the US DOD (down \$2.9m, -76%) and industry (down \$6.3m, -6%) – all partly, but not entirely, offset by record drug R&D funding from the Gates Foundation. Despite the decline in NIH and overall drug R&D from its 2019 peak, drugs continued to account for 43% of 2023's TB funding, more than twice the 19% share going to vaccines.

FUTURE FUNDING

The Gates Foundation has committed \$844m to its affiliated research institute, Gates MRI, with \$400m expected to go to the Phase III trial of the M72/AS01E vaccine. Well over a year into the grant, only around \$133m has been disbursed, implying further increases in TB vaccine funding in the near future.

PIPELINE SPOTLIGHT

The M72/AS01E vaccine, potentially the first new TB vaccine in 100 years, is undergoing a Phase III trial spanning 60 sites across seven countries to assess its efficacy. The five year study will assess protection of adolescents and adults from pulmonary TB, building on Phase IIb results that showed 50% protection after three years.

In 2023, global funding for **malaria** basic research and product development reached \$690 million, reflecting a 9% (\$60 million) increase from the previous year. Almost half of this rise, however, was due to new participants in the G-FINDER survey. Funding from ongoing survey participants grew by a more modest 5% – still an encouraging shift after four years of declining funding. Despite the uptick, funding remains at its second-lowest level in the past decade.

Over 90% of the funding from new survey participants was directed towards the clinical development of *P. falciparum* vaccines. Consequently, measured funding for vaccine R&D rose to its highest level in four years, at \$148m (up \$36m, 32%), partly reversing the downward trend from its peak in 2017. Funding from the Gates Foundation for vaccine R&D also rebounded (up \$15m, 186% from 2022), with the additional funding mainly channelled to the Gates Medical Research Institute. Biologics funding nearly halved to \$15m (down \$12m, -45%) after last year's sudden spike, with both rise and fall also driven by the Gates Foundation. Funding for the remaining product areas remained comparatively stable. Diagnostics received the smallest share of funding (\$14m, 2%), with funding sitting at 60% of its long-term average due to the gradual disappearance of funding from the UK FCDO, DHSC and Gates Ventures.

The US NIH continued to provide the largest share of malaria funding (\$201m, 29%), followed by the Gates Foundation (\$181m, 26%). Despite the increasing spread of malaria in the southern United States, funding from the US CDC fell to a record low of \$0.3m (down \$4.1m, -93%), as did funding from the US DOD, which fell to a low of \$7.0m, down 87% from its 2018 level. Partly due to cuts in funding from the US and, in previous years, UK public organisations, the number of funders providing at least \$10m in malaria R&D funding has fallen from 15 in 2018 to just 10 in 2023.

NEW DEVELOPMENTS

Funding for malaria vector control R&D was boosted by an \$85m grant from the Gates Foundation to IVCC in 2024. This is the largest grant from Gates to IVCC ever recorded, building on \$26m of funding in 2023 and \$16m in 2022.

PIPELINE UPDATES

The Safety of Antimalarials in the FIrst TRimEster (SAFIRE) consortium will conduct a groundbreaking adaptive platform Phase III trial on antimalarial drugs, evaluating their efficacy, safety, tolerability, and cost-effectiveness in first-trimester pregnant women, a group often excluded from clinical research. The trial will begin by comparing pyronaridine-artesunate with artemether-lumefantrine, the WHO-recommended treatment for uncomplicated malaria during the first trimester, which will serve as the control.

Figure 3. Big three – HIV, TB & malaria



Malaria





Multi-disease groups – diarrhoeal diseases, kinetoplastids & helminths

A big fall in diarrhoeal disease funding left all three categories at or near record lows

This section covers funding for the three disease categories we use to capture funding for several smaller (that is: less well funded) pathogens within each family. We have summarized changes at the group level and also any notable changes at the level of individual pathogens. A full list of pathogens under each group is provided in Table 1 at the start of this chapter.

Overall funding for **diarrhoeal diseases** was down in 2023, dropping to \$144m (down \$20m), more than offsetting last year's slight rebound and taking it to its lowest level ever – more than \$100m below its 2009 peak. This significant decline raises concerns about the sustained commitment to combating diarrhoeal diseases globally. This year's reductions in funding fell most heavily on cryptosporidiosis and *Shigella*, while the long-term decline has been in funding for rotavirus (down more than \$52m since 2009) and multiple diarrhoeal diseases (down \$40m). Funding for cholera, on the other hand, rose by a further \$3.2m (8%) leaving it close to its all-time high.

Shigella funding was down for the second year in a row after peaking in 2021. While the drop in 2022 was felt mostly by vaccines, most of the reduction in 2023 was due to a reversal of the big spike in diagnostics funding from both Gates and DOD in 2022. The apparent near-disappearance of industry's vaccine funding is artefactual – reflecting a transfer of a candidate's development to non-participating pharmaceutical companies. This shift may affect transparency and tracking of progress in vaccine development efforts.

PIPELINE UPDATES

Valneva and LimmaTech have announced that their <u>Shigella4V vaccine</u> received US FDA Fast Track designation. This designation will facilitate the accelerated clinical development and review of the vaccine, which is set to be evaluated in two Phase II trials expected to begin by the end of 2024. With no *Shigella* vaccines currently approved, Shigella4V – a tetravalent bioconjugate vaccine – represents the world's most advanced candidate for shigellosis.

Cholera funding was up slightly again in 2023 (\$3.2m, 8%) following a sharp increase in cholera fatalities which continued into 2024. All of this new funding has been invested in vaccine R&D, while basic research has been trending down. Even after years of decline, though, basic research remained the best funded of cholera's product areas. An emerging shift towards vaccine R&D may signal a new emphasis on prevention and control of cholera outbreaks, drawing on prior basic research.

PIPELINE UPDATES

This year saw the progression of two oral cholera vaccines, each with the potential to offer an alternative to Sanofi's Shanchol after it ceased production in 2023. <u>Euvichol-S</u>, a low-cost inactivated vaccine with a simplified formulation for faster production, was <u>prequalified by the WHO in April 2024</u>. Meanwhile, <u>Hillchol</u>, supported by and innovative partnership between Hilleman Laboratories and Bharat Biotech, received approval in India following successful Phase III trials.

While **rotavirus** funding has remained largely unchanged at a little over \$20m in each of the last three years, its long-term decline reflects previous reductions in vaccine funding from the Gates Foundation and from industry. This sustained decrease may impede the development of new vaccines and treatments, potentially affecting global efforts to reduce rotavirus-related child mortality.

Cryptosporidiosis funding experienced the biggest drop in 2023, down \$8.2m (-33%), following four years of relative stability. Cryptosporidiosis saw reductions in funding from each of its three biggest funders, the NIH (down \$1.6m, -14%), industry (down \$3.8m, -40%) and Wellcome (down \$2.7m, -84%) which together fell heavily on drug R&D, which dropped by \$6m (-38%). These cuts to drug R&D were headlined by a sharp, and concerning, reduction in industry and Wellcome contributions to a Phase I drug trial. This decline is likely to threaten the development of new treatments for cryptosporidiosis, a significant cause of morbidity in vulnerable populations.

There was no funding for cryptosporidiosis vaccines in 2023 for the first time since 2007. While funding had been relatively low (averaging \$0.2m in the first six years and increasing to over \$1m in the years since 2014) this represents a worrying development, with dangerous implications in vulnerable infant populations as incidence is likely to increase alongside the increased frequency of heavy rainfall and flooding events brought on by climate change.

Funding targeting **multiple diarrhoeal diseases** was down by \$5.4m (-36%) to \$10m, following a brief rebound in 2022. It remains much lower than pre-2020 levels, when it averaged over \$50m a year. The 2023 fall in multidiarrhoeal disease funding, and much of the long-term decline, was driven by ongoing reductions in funding from the US DOD, which reduced its funding by \$4.1m in 2023 – reflecting a large one-off drug grant in 2022 – and by more than \$13m over the last decade, mostly due to declining vaccine investments. This, and a similar decline in Gates funding to PATH for multi-disease vaccines, may actually signal progress in the pipeline, as products become focused on specific target pathogens as they advance through the development process.

Funding for **kinetoplastid** R&D was almost entirely unchanged at its record low of \$133m in 2023, though this stability partly reflected offsetting changes in underlying survey participation. It also masked some meaningful shifts at the individual disease level, with a big rise in Chagas' disease funding (up \$5.7m, 13%, or more than \$9m after adjusting for participation) and a sharp drop in multiple kinetoplastid R&D (down \$3.8m, -18%, or almost \$6m on a participation adjusted basis).

The near record funding for **Chagas' disease** was mostly thanks to big jump in industry drug funding, which rose by \$5.6m (30%) to \$25m. Industry has now committed almost \$112m to Chagas' drug R&D over the past five years, compared to less than \$60m, total, over the previous twelve. The US NIH, the second largest funder of Chagas' R&D after industry in each of the last five years, also saw its funding rebound after two slightly down years, rising by \$3.2m (25%) to \$16m and offsetting a similarly sized drop in Unitaid's drug and diagnostic funding.

PIPELINE UPDATES

A <u>proof-of-concept study</u> in infants showed the PrintrLab-LAMP test for Chagas' yielded a higher sensitivity than microscopy and almost equal to that of PCR. Combining Eiken's LAMP technique with a 3D-printed DNA extractor, PrintrLab-LAMP has the potential to provide low cost diagnosis with minimal infrastructure requirements, making it suitable for infant diagnosis in low-resource settings.

Research targeting **multiple kinetoplastids**, which is now down more than 70% from its 2017 peak to a new record low, fell due to reduced contributions from the UK FCDO and the German BMBF. The FCDO has been by far the largest funder of multi-kinetoplastid R&D, but reduced its funding by another \$2.4m (-24%) leaving it more than \$19m below its peak in 2017. In contrast to funding for multiple diarrhoeal diseases, there is no evidence of the FCDO, or other funders, shifting their efforts to pathogen-specific products as they advance through the pipeline. Declining funding for multi-disease approaches may undermine the eventual development of products targeting individual diseases currently lacking in advanced candidates.

NEW DEVELOPMENTS

The UK charity LifeArc followed up its initial, 2023, round of global health funding with an increased commitment in 2024, headlined by a £5.9m commitment to FIND to improve diagnostic testing and early access to treatment for visceral leishmaniasis in Kenya. Funding for both **leishmaniasis** (\$39m) and **sleeping sickness** (\$25m, down \$1.8m, -7%) was largely unchanged from last year's record lows, the slight drop in funding for sleeping sickness likely reflecting the recent registration of the drug fexinidazole and a resulting pivot from R&D to access and distribution.

Overall funding for **helminth infections** fell \$15m (-14%) to \$94m in 2023, undoing the previous two years of growth and leaving it just above its 2016 decade low.

A large proportion of this drop was in funding for schistosomiasis (down \$10m, -23%) – though it remained the highest funded disease – and lymphatic filariasis (down \$7.4m, -34%), both of which had surged in 2022. These kinds of fluctuations often reflect the planned frontloading of grants, but, where they do not, they can undermine the forward planning of product developers.

Onchocerciasis funding was also down (-\$3.3m, down 22%), while funding for multiple helminth infections was the only area to see a significant increase (up \$6.7m, 42%). This round of shifts reverses many of the ones we saw in 2022, returning the distribution of funding to one quite similar to that of 2021. The main exception onchocerciasis, which has seen its funding decline each year since peaking in 2018 with the FDA approval of treatment with moxidectin.

The US NIH remained the largest single funder of helminth R&D, a total of \$41m (down \$1.7m, -4%) leaving it responsible for 44% of global funding. There were significant reductions in funding from the other major 2022 funders: the Gates Foundation and industry.

These same three funders – the NIH, Gates and industry – were also mostly responsible for the fall in **schistosomiasis** funding, along with the conclusion of a four-year funding programme from the US DOD. Over half of the drop in schistosomiasis funding was for vaccine R&D, with both the NIH and Gates decreasing their funding in this area by at least three-quarters.

Lymphatic filariasis funding was down a third in 2023 (down \$7.4m, -34%), undoing a similarly sized spike in 2022. Both the 2022 spike and subsequent 2023 drop were due to changes in the German BMBF's funding its TAKeOFF program, which aims to standardise clinical trial procedures for filariasis.

Hookworm funding declined by 20% (\$1.0m). leaving it only a little higher than 2018's record low.

PIPELINE UPDATES

Baylor College of Medicine's Na-APR-1 and Na-GST-1 hookworm vaccine candidates were found to be safe and immunogenic when co-administered in a Phase I trial among children aged 6-10 in Gabon. In a rare move in the neglected disease field, the candidates are being tested in children immediately following completion of Phase I trials in adults, assessing the vaccines in this key target population early in their development. 100

—Aggregate industry —Other funders

Kinetoplastid

diseases

Figure 4. Multi-disease groups - diarrhoeal diseases, kinetoplastids & helminths







Vx: vaccines, Bx: biologics, Dx: diagnostics, VCP: vector control products D/P: discovery and pre-clinical, \equiv Out of scope product for this disease



Diseases with moderate funding – dengue, *Salmonella*, snakebite, hepatitis B & C

Increases for snakebite and dengue left them at or near record highs; *Salmonella* funding was the lowest in more than a decade

This section covers the diseases outside the Big 3 which received more than \$20m in R&D funding in 2023 – an arbitrary threshold which only narrowly excludes leprosy and bacterial pneumonia & meningitis, both of which received more than \$19m and are covered in the section on 'Diseases with little funding'.

Funding for **dengue** R&D jumped by \$29m (35%) to \$113m, its second highest level on record and more than \$20m above its average over the preceding half decade.

The increase was the result of another surge in industry funding, up a further \$26m (56%) from last year's record high. Industry has now provided more R&D funding for dengue in the last three years (\$152m) than it did over the first twelve years of the G-FINDER survey. Industry funding now dominates dengue R&D, with NIH contributions dropping to less than one-third of industry's total in 2023. Funding from the US NIH has slumped in tandem with the rise in private sector investment, falling by a further \$5.7m (-20%) in 2023 and by \$50m (-69%) from its 2016 peak. After being the top funder of dengue R&D every year until 2022, NIH funding fell to less than a third of industry's total in 2023.

The rise in industry funding took dengue drug R&D to \$81m – another record high, up \$33m (66%) since 2022 and more than double its then-record 2021 level. The ongoing rise in drug funding has been accompanied by a gradual decline in basic research, down a further \$2.2m (-10%) in 2023 and by two-thirds (\$43m) from its 2016 peak. This shift from basic research to a mix of early- and late-stage drug R&D mirrors the changing of the guard in leading funders, from the basic research focused NIH to industry's focus on product development.

NEW DEVELOPMENTS

The surge in industry dengue drug R&D will likely taper off a little, following the late 2024 discontinuation of a first-in-class oral antiviral.

In the longer term, though, The Lancet Countdown on health and climate change demonstrates the incidence of dengue is rising due to favourable climate conditions, population mobility, urbanization, and evolving virus serotypes. This ongoing spread, which now includes several high-income countries, has generated a robust commercial market for dengue vaccines, leading us to remove them from our list of neglected areas of research.

Global funding for **Salmonella** R&D fell by \$6.4m (-8%) to \$78m in 2023, though nearly a third of the reduction was an artefact of missing data from the Indian private sector. This drop left *Salmonella* funding at roughly the level it had been in 2021, considerably below its three year peak between 2016 and 2018, when it averaged more than \$100m per year.

Both typhoid & paratyphoid fever (\$15m) and non-typhoidal *Salmonella* enterica ('NTS', \$52m) received slightly less funding in 2023. Typhoid & paratyphoid fever continued to receive more than three times as much funding as NTS, despite NTS funding remaining close to last year's record high.

Reduced funding from the US NIH – still the top overall *Salmonella* funder – was the main contributor to both reduced 2023 funding and the long-term decline since 2016, driving the long term downward trend in basic research funding, which fell for the fifth consecutive year in 2023. The single biggest reduction in 2023 funding, though, was from CARB-X, the antimicrobial resistance-focused nonprofit. CARB-X had tripled its *Salmonella* vaccine funding – across both NTS and typhoid – to nearly \$5m in 2022 before cutting it to below \$1m in 2023 in what appears to be the result of front-loaded disbursements. CARB-X's cuts drove a 9% (\$4m) reduction in vaccine funding, which left industry (down \$1.5m to \$21m) responsible for more than half of global vaccine R&D, focusing on the clinical development of bivalent and trivalent combination vaccines.

Funding for **snakebite envenoming (SBE)** R&D grew for a fifth consecutive year (up \$8.2m, 37%), to reach \$31m in 2023. The ongoing growth enjoyed by SBE contrasts sharply with the overall stagnation in funding for other WHO neglected tropical diseases; but there remain concerns about the sustainability of the increased investment.

Almost all of the increase in 2023 was linked to drug development (up \$8.5m, 68%), with a focus on clinical development (up \$4.8m, 53%). This, in turn, is largely linked to investment in Ophirex's broad-spectrum small molecule therapy, varespladib, which recently completed Phase II trials.

These trials were the beneficiary of both increased funding from the US DOD (up \$ 4.0m, 58%) and first-time selffunding from Ophirex, the developer, as well as the first recorded drug funding from the US NIH (\$0.9m). After four years of growth, Wellcome's SBE investment sputtered (down \$1.1m, -12%) as their long-term funding programme gradually begins to approach its scheduled 2026 conclusion.

NEW DEVELOPMENTS

Biologics R&D for snakebite envenoming received a fresh \$17m, six-year commitment from Wellcome in 2024. The 'Multi-centre Antivenom Trial in Africa' project will run across ten trial sites in sub-Saharan Africa, led by the Liverpool School of Tropical Medicine.

Open Philanthropy have also awarded the Liverpool School of Tropical medicine \$5.5m to take two repurposed drugs to Phase II trials. These are the only three drug candidates currently in the clinical pipeline, all of which have emerged since 2017 – highlighting the speed of development which can be achieved through repurposing treatments with existing safety data

PIPELINE UPDATES

October 2024 saw the release of results from the Phase II trials of varespladib for snakebite envenoming in India and the US that were enabled by the increased 2023 funding. They showed that, while the additional use of oral varespladib alongside antivenom did not definitively reduce the prespecified measure of morbidity, it did show significant benefits for patients receiving treatment within five hours. This highlights the potential for oral varespladib to serve as a field or prehospital treatment, as upwards of 75% of deaths occur prior to hospital arrival.

Funding for **hepatitis B** R&D was \$25m in 2023, down almost a quarter from 2022's record high (down \$7.7m, - 24%), but still the second highest funding total since it was added to the survey in 2018. The entirety of the drop in overall hepatitis B funding was due to a decrease in funding for biologics, the sole recipient of the 2022 increase, leaving 2023 biologics funding still much higher than its average prior to 2022. Both the 2022 increase and 2023 drop in biologics funding were entirely due to changes in industry investment, which was again the leading source of funding in 2023 and which continued to focus exclusively on biologics R&D.

Despite the drop in industry's biologics spending, still more than half of all hepatitis B funding in 2023 was for biologics (59%), with another 22% for drugs and the remainder divided between basic research (12%) and diagnostics (8%). Industry's big bet on hepatitis B biologics demonstrates how radically private sector funding can reshape the product landscape.

The US NIH, which had been the top funder every year prior to 2022, remained in second place, but reduced its funding by \$0.8m (-11%) to \$5.8m, its lowest level since 2019. Of the 28% of 2023 funding reported as going towards clinical development, around nine-tenths went towards the development of biologics, including around half the overall funding from industry and from the EC – the third largest supporter of hepatitis B R&D behind industry and the NIH.

Global funding for **hepatitis C** rose by \$5.0m (30%) to \$21m, the highest total since 2019. This was its highest funding level since 2018, though still just over a third of its peak from a decade ago. This rebound in funding was driven by a record \$17m (up \$2.4m, 16%) in funding from the US NIH – the top funder in each of the last three years – and the resumption in funding from Unitaid, which had been absent in 2022 (\$1.8m in 2023, down from \$2.7m in 2021).

As in each of the past three years, vaccine R&D remained funders' primary focus, rising by \$3.7m (38%) to a record high \$13m. This left vaccines responsible for nearly two-thirds of the total, compared to just 8% a decade earlier. The remaining funding was divided relatively evenly between diagnostics (basically stable at \$4.8m, 23% of the total) and drug research \$3.0m (14%), which rebounded (up \$1.5m, 100%) from last year's record low. The long-term decline in drug R&D is the result of the continued absence of any funding from (traditionally drug focused) industry – which has provided no meaningful hepatitis C funding since its \$40m spike in 2018.

Cuts to industry's drug funding have also driven a steep decline in clinical development, which remained below \$2m, two-thirds of which was for late-stage diagnostic development. This was close to last year's record low, after having averaged more than ten times that amount each year between 2013 and 2018.

PIPELINE UPDATES

The WHO prequalified the first hepatitis C virus self-test, following its recommendation of self-testing in 2021, in a crucial step to expand access to testing and diagnosis. The <u>OraQuick HCV</u> <u>self-test</u>, is an extension of the OraQuick HCV Rapid Antibody Test, which was first prequalified for professional use by the WHO in 2017.



Figure 5. Diseases with moderate funding - dengue, Salmonella, snakebite envenoming, hepatitis B&C





Figure 5 cont. Diseases with moderate funding







Diseases with little funding – leprosy, bacterial pneumonia & meningitis, cryptococcal meningitis, rheumatic fever & histoplasmosis

There was record funding for leprosy and at least some growth for almost all the others; but bacterial pneumonia & meningitis funding fell to a record low

This section covers the diseases receiving between \$2.5m and \$20m in R&D funding in 2023. Together, they received just 1.3% of global funding, or by way of comparison, just over 4% of the funding allocated to HIV alone.

Global funding for **leprosy** R&D reached a new peak of \$19m in 2023, jumping by almost 40% (up \$5.3m) from the previous year in its third consecutive year of growth.

As in 2022, more than 60% of this rise was driven by increased drug R&D funding from industry (up \$3.4m, 60%), focused on the late-stage clinical testing of Bedaquiline, while much of the remaining increase was due to an increase in basic research funding from the Indian ICMR. Over the last three years, industry has provided a total of almost \$17m for leprosy drug R&D, more than triple its overall investment in leprosy over the previous 14 years. In 2023, it accounted for nearly half of all global leprosy R&D funding.

Rising drug funding from industry cemented an overall shift towards drug R&D, which accounted for a record 59% of global leprosy funding in 2023, up from less than half a percent a decade earlier. Industry has also driven a big rise in clinical development funding, which accounted for a little over half (\$11m) of the 2023 total, 95% of it for drugs.

Most of the remaining funding went to basic research (\$7.0m, 36% of the total), which rebounded very slightly (up \$0.5m, 8%) following three years of decline, thanks to a near-record \$3.4m from the Indian ICMR. This trend suggests a promising trajectory for drug breakthroughs but may also raise questions about the balance of investment across other critical areas, such as diagnostics and prevention, which remain essential for long-term leprosy control and eradication.

PIPELINE UPDATES

American Leprosy Missions <u>announced</u> the start of a Phase Ib trial for LepVax, the first vaccine developed specifically for leprosy and the only candidate in clinical development. LepVax is being investigated for both the <u>treatment</u> and <u>prevention</u> of leprosy in trials led by Fiocruz in Brazil.

Global investment in **bacterial pneumonia & meningitis** R&D – a two-disease group covering funding for both *S. pneumoniae* and *N. meningitidis* – totalled just \$19m, dropping by close to two-thirds (down \$30m, -61%). This was the fifth consecutive decrease, and took investment to its lowest ever recorded, at around a quarter of its ten-year average.

Funding for **pneumonia** R&D fell by two-thirds (down \$27m, -66% to \$14m) and investment for meningitis fell by a third (down \$2.6m, -35% to \$4.9m), both reaching record lows. Despite the larger drop in pneumonia funding, it continued to receive around three times as much funding as meningitis.

Pneumonia funding fell across all product areas except for diagnostics, as all six of 2022's top funders reduced their contributions. Industry's pneumonia vaccine funding fell by \$20m (-96%) following the positive conclusion of a Phase III trial in infants of a 14-valent pneumococcal conjugate vaccine. Sharp declines in early-stage vaccine funding from the US NIH (down \$4.8m, -96%) and post-registration studies sponsored by the Gates Foundation (down \$3.3m, -52%) pushed pneumonia vaccine R&D down even further.

Pneumonia diagnostics was the only area to record an increase, jumping 262% (up \$1.7m) thanks to new investments from the Gates Foundation (\$0.9m) and Australian NHMRC (\$0.2m) and the US NIH (up \$0.4m, 70%) including funding for the development of a breath-based test designed for both diagnosis and antibiotic resistance profiling.

The pool of **meningitis** R&D funders fell by half in 2023, leaving just three: the Gates Foundation, the US NIH and MSF, as industry funding fell to nothing (down \$2.8m) following the positive conclusion of a Phase III trial of pentavalent conjugate vaccine. A small drop from the Gates Foundation (down \$0.4m, -24%) also contributed to the record-low funding for meningitis vaccine R&D

The small amount of diagnostics funding for meningitis fell by over a quarter (down \$0.1m, -29%) as MSF, the sole funder, disbursed a smaller amount for the ongoing development of DiaTropix rapid diagnostic tests.

Global funding for **cryptococcal meningitis** drug and biologics R&D was \$7.8m in 2023. This represented only a slight increase from 2022 (up \$0.8m, 12%), with funding from ongoing survey participants remaining broadly in line with its long-term average.

With funding from the UK's NHS and MRC essentially unchanged at a total of \$1.7m, the small increase in funding was due to a rebound in funding from the US NIH, which had fallen in each of the previous three years. The rise in

NIH funding went to drug R&D, which, in line with previous years, represented 90% of both the NIH's contributions (which totalled \$6.2m) and overall global funding (\$7.8m). The net increase in NIH funding was thanks to new funding for a Phase III trial studying encochleated oral amphotericin for the treatment of HIV-related cryptococcal meningitis, contributing to a record \$4.6m (65%) of funding going to clinical development.

Funding for cryptococcal meningitis biologics remained essentially unchanged at \$0.8m, all of which came from the US NIH.

NEW DEVELOPMENTS

Early US NIH cryptococcal meningitis funding data for 2024 show no further funding for the Phase III oral amphotericin trial which drove the 2023 increase following the trials conclusion in early 2024.

This suggests that overall funding fell in 2024, with the potential to rebound in 2025 when new Phase II/III trials are scheduled to begin.

Funding for **rheumatic fever** vaccine R&D – the only product area included in the survey – was \$4.9m in 2023, a 40% increase on 2022, when funding fell by more than 80% to just \$3.5m. The 2022 drop, though, followed a surge in funding between 2019 and 2021 which saw average funding rise to \$21m, compared to just \$2.4m prior to 2019. The end result is a level of funding far below its recent peak, but still safely above its longer-term average.

The high level of 2019-21 funding was mostly driven by major contributions from two organisations: the Australian Medical Research Future Foundation, which invested in the Telethon Kids Institute's Strep A vaccine; and CARB-X, which provided funding to GSK-Bio and Vaxcyte towards their Strep A vaccines. Neither of these organisations have provided any funding over the last two years.

Instead, the partial bounce back in 2023 was thanks to record contributions from the US NIH, which saw its funding nearly quadruple from last year's record low of 0.6m to 2.8m - 57% of the 2023 total. Early indications suggest

that the rise in NIH funding persisted into 2024. Most of the remaining 2023 funding was provided by the Leducq Foundation (\$1.8m, 36%), which began funding rheumatic fever in 2022 via the Telethon Kids Institute.

In 2023, the fourth year of its inclusion in the G-FINDER report, **histoplasmosis** R&D received \$3.8m, a very slight rebound of \$0.2k (6%) from last year's record low.

NEW DEVELOPMENTS

Preliminary 2024 histoplasmosis funding data from the US NIH – responsible for more than 95% of 2023's funding – suggest that its contributions declined in 2024, falling from \$3.7m to an estimated \$2.8m. Without offsetting increases from other funders (or additional grants yet to be recorded by the NIH) this would leave histoplasmosis funding well below 2022's record low. With drug funding again largely unchanged at around \$100k, the small increase was split relatively evenly between basic research and diagnostics. Basic research (\$3.6m in 2023) continued to receive the vast majority of overall funding. This reflects the focus of the US NIH, which again provided well over 95% of global funding and which again directed over 95% of its funding to basic research.

The slight increase in histoplasmosis diagnostic funding – still well below its 2020 peak of \$0.5m – was mostly due to newcomer French ANRS (\$22k) and a resumption in funding from the NIH (\$51k) aimed at aggregating industry efforts to leverage dual-iDDS probe technology.



Figure 6. Diseases with little funding - leprosy, pneumonia & meningitis, cryptococcal meningitis, rheumatic fever & histoplasmosis





Figure 6 cont. Diseases with little funding





Diseases with almost no funding – leptospirosis, scabies, Buruli ulcer, mycetoma, yaws & trachoma

Leptospirosis funding doubled, but to just \$2.4m and Buruli ulcer rebounded slightly, but there was essentially no funding for yaws and none at all for trachoma

This section covers the diseases receiving less than \$2.5m in R&D funding in 2023. Together, they received just \$6.2m, or 0.015% of global funding. Several of these diseases were added to the G-FINDER survey only recently, meaning we lack long term funding data and may have yet to identify some of their sources of funding.

Overall funding for **leptospirosis** diagnostics – the only product area included in our scope – more than doubled to \$2.4m (up \$1.2m), its highest total since its peak of \$3.6m in 2017.

This growth was mostly thanks to \$1.0m from the US NIH, it's first contribution since 2019, and a record high. The only other funding came from the Indian ICMR, which rose by \$0.3m to a near-record \$1.5m. For the first time in five years, there was no funding from the UK MRC (down from \$25k) and once again none from the private sector. There remained almost no leptospirosis funding explicitly devoted to clinical development – just \$37k, though up from none at all in 2022. This suggests a continued reliance on public funding, with critical gaps in clinical development and private sector engagement still unaddressed.

The already low level of funding for **scabies** R&D dropped slightly to \$1.6m in 2023 (down \$294k, -15%), though nearly half of this fall was due to reduced survey participation. Funding from ongoing respondents was down a slightly less concerning \$167k, or 7%.

In 2023, there were just two participating scabies funders: the Australian PDP Medicines Development for Global Health provided \$1.3m, or 82% of the total (up \$0.7m, 84%) and the Australian National Health and Medical Research Council (NHMRC) with \$0.3m (down \$0.3m, -44%). This represents a significant decline from the six funders that reported funding in 2022 and five in 2021 partly due to the absence of data from two of those 2022 funders. The concentration of funding in Australia reflects the prevalence of scabies in Australian indigenous communities, but also the departure of the UK's NHS and DHSC, which together had accounted for 15% of global funding since scabies was added to the survey in 2020.

All funding from Medicines Development for Global Health went towards Phase II clinical trials of the repurposed drug moxidectin. As a result, drug R&D captured over 80% of scabies funding, with its share of funding rising for three years running, up from just 18% in 2020. In contrast, all of the NHMRC's remaining funding went towards basic research, which fell to a record low of \$0.3m, less than one-third of its \$1.0m peak in 2020 and 2021.

Funding for **Buruli ulcer** rebounded again from its record low in 2021 (up \$0.6m, 62%), reaching \$1.5m after two years languishing below \$1m; though it remained less than half of its pre-2021 average.

More than two-thirds of the funding went to basic research, which saw a modest increase to \$1.1m (42%), This makes it the only product category to receive consistent funding since the survey began in 2007, totalling \$26m.

The slight increase in funding was primarily due to the long-delayed resumption of vaccines funding from the EC for the first time since 2013– though it totalled just \$342k. The new EC funding supports the (very) early-stage development of an mRNA-based vaccine and represented essentially all of 2023's vaccine R&D. The only other meaningful increase was from the UK MRC, which contributed a record \$328k (up \$250k, 319%) for basic research. The US NIH, which had been absent for the last two years after committing an average of more than \$1m

a year to drug R&D between 2016 and 2022, also resumed its funding, albeit with just \$62k. While Buruli ulcer again enjoyed a surprisingly diverse funder base, with ten individual funders, there was no funding from the private sector for the third year in a row.

Global funding for **mycetoma** R&D increased very slightly in 2023, rising by \$80k, a 15% increase which still left it languishing well under a million dollars, as it has in four of the five years since we began including it in the survey.

Industry funders accounted for over half of the limited mycetoma funding, modestly increasing their contributions to \$376k – four times the total industry funding received over the previous four years. This reflects private sector investment in the ultimately successful Phase II trial of fosravuconazole, a new oral treatment for mycetoma. Public funding, in contrast, fell by half. This drop was due to the absence of previous UK public funders, the DHSC and the NHS, along with the NIH's lack of contributions for the first time on record. Only two non-industry funders, the Canton of Geneva and the Japan Society for the Promotion of Science, provided any R&D funding for mycetoma in 2023.

The only funding for **yaws** basic research that met our inclusion criteria came from the German DFG, supporting a project by the Kumasi Centre for Collaborative Research in Tropical Medicine to investigate the potential of nonhuman primates as reservoirs for human yaws. The six-year project predates the inclusion of yaws in G-FINDER's data collection and disbursed a total \$106k between 2018 and 2024 – an annualised total of less than \$20k.

There was once again no direct funding for diagnostic development and the funding from the EDCTP we highlighted last year recorded no new disbursements.

PIPELINE UPDATES

The <u>TPHD-LAMP diagnostic</u> fell short of the <u>WHO target product profile criteria</u> for yaws diagnostics when tested in real world conditions, highlighting the importance of assessing novel diagnostics in endemic settings

Funding for **trachoma** vaccine and diagnostic R&D came to a complete halt in 2023, dropping from \$173k to nothing, after having averaged \$2.6m a year over the decade prior to 2021.

The EC's TracVac project had propped up funding, averaging \$1.7m between 2017 to 2021. The EC's exit left NIH as the sole funder in 2022, providing just under \$0.2m for diagnostic R&D in 2022, which did not continue into 2023.

PIPELINE UPDATES

Findings from a Phase I trial of the vaccine candidate <u>CTH522</u> suggest it could provide protection against ocular trachoma and urogenital chlamydia, making it a promising subject for further investigation in Phase II clinical trials.



Figure 7. Diseases with almost no funding - leptospirosis, scabies, Buruli ulcer, mycetoma, yaws & trachoma







R&D for more than one disease – core funding, platforms, multi-disease vector control & Other R&D

Overall multi-disease funding rose slightly, for the ninth year in a row; a fall in multi-disease R&D was offset by a rise in catchall 'Other R&D'

This section covers funding that cannot be allocated to a specific neglected disease. Core funding refers to nonearmarked 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. Multi-disease vector control product captures R&D funding for products that target vectors capable of transmitting several different diseases, often the Aedes aegypti mosquito, which spreads dengue, Zika and Chikungunya. Other R&D captures any remaining grants that cannot otherwise be allocated, including grants targeting multiple diseases for which disease-specific totals are unavailable.

Overall non-disease specific funding increased very slightly in 2023 (up \$12m, 2%). A substantial rise in 'Other R&D' – funding targeting multiple or unspecified neglected diseases – was partly offset by another fall in multidisease vector control, with core funding and platform technologies remaining largely unchanged.

Overall funding for **platform technologies** remained relatively stable in 2023, dropping by just \$6.0m (-2%) following the massive increase in 2022 (up \$116m, 70%). The sudden rise in 2022 and much smaller drop in 2023

result from US NIH funding for drug platforms, which jumped from under \$3m to \$86m in 2022, thanks to a new \$80m programme for antiviral development, before dropping by half, to \$43m, in 2023. This offset growth in NIH platform funding elsewhere, and also the record-high in funding for diagnostic platforms, which grew by 49% (\$27m) to \$81m, leaving it essentially tied with vaccine platforms as the largest recipient of platform funding.

FUNDING COMMITMENTS

In 2024, the Gates Foundation provided \$19.5m to Germany's Schrödinger's to fund use of their computationally-driven molecular platform for drug discovery for use with neglected diseases.

This rise in funding for diagnostic platforms came via multiple new programs funded by the US DOD, as well as new funding from the Gates Foundation – both of which are focused on development of low cost, field deployable, pathogen agnostic diagnostic tools.

PIPELINE UPDATES

Gilead's twice-yearly injectable lenacapavir demonstrated efficacy and superiority to once-daily oral Truvada for HIV prevention in the PURPOSE 1 and 2 trials, with PURPOSE 1 being the first Phase III HIV prevention trial to result in no infections in the intervention arm. Gilead have signed non-exclusive royalty-free voluntary licensing agreements with six high-volume manufacturers ahead of regulatory approval, meaning low-cost generic versions could be available to LMICs soon afterwards

Core funding of multi-disease R&D organisations remained relatively stable in 2023, increasing by \$5m following a \$75m drop in 2022.

Wellcome reduced its core funding by \$17m (-39%) mostly via a sharp reduction in its – historically very consistent – funding to various Oxford University programmes. Funding from the Japanese government to the GHIT fund increased by \$18m in line with its usual two-year cycle. Funding from the Czech Republic Ministry of Education, Youth and Sport – which provided first time funding of \$18m in 2022 – was mostly sustained at \$17m and continued to go entirely to the Czech Institute of Organic Chemistry and Biochemistry. Finally, core funding from the EC to EDCTP (now its sole beneficiary) dropped by \$12m (-12%).

Accordingly, funding to EDCTP was down slightly (though it was still by far the top recipient, with \$100m), and funding to GHIT was up (by \$25m, to reach \$47m).

Funding for **multi-disease vector control** dropped by \$10m (-16%) in 2023, after having dropped by over \$20m the previous year from a peak of \$87m in 2021.

FUNDING COMMITMENTS

USAID's funding to IVCC for multi-disease vector control resumed in 2024 with a \$2m grant to support field testing of IVCC's pipeline of new insecticides

drops it experienced in 2021 and 2022 (totalling \$10m).

While several funders reduced their multi-VCP funding, among the biggest contributors to the drop were the cessation of funding from the US DOD (down from \$6.6m in 2022) and, to a lesser extent, the Australian DFAT (down from \$2.6m). As usual, the US NIH accounted for a large proportion of multi-VCP funding (over half, 56%), its funding rebounding somewhat (up \$4.1m, 15%) from the consecutive

Multi-disease and otherwise hard-to-categorise funding under the catchall category of '**Other R&D**' increased to \$100m in 2023 (up \$23m) growing for the fourth consecutive year, with increases from the US NIH, the Gates Foundation and new funding from the Indian ICMR and DBT. Large Other R&D grants in 2023 included \$4.7m in industry funding for a global health institute, \$3.6m from the Gates Foundation for wastewater-based diagnostic surveillance techniques and \$3.1m from Wellcome for a range of multinational R&D and capacity building activities.

Figure 8. Non-disease-specific funding



Neglected disease funders







impactglobalhealth.org



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Global funding for neglected disease basic research and product development totalled \$4,170m in 2023, a drop of less than 1% on the previous year, or just under 2% once we account for a rise in survey participation. Following on from 2022's much larger fall, this slight decline left funding nearly \$650m below its 2018 peak and 3% below its average over the previous decade.

While overall funding was relatively consistent, there were big changes in who provided it. Public sector funding fell, again, dropping by another \$103m (-4%) to its lowest level since 2015. Private sector funding fell too, dropping by \$52m (-8%) which, after two years of growth, left it roughly in line with its recent average. The substantial drops in both public and private sector funding were mostly offset by a big rise in philanthropic (mostly Gates Foundation) funding, which rebounded by \$125m (16%) to \$929m – its highest total since 2008 and the second highest total ever recorded.



Figure 3. Total R&D funding by sector 2014-2023

Public funding

Governments provided a record low 63% of global funding, mostly due to big cuts from the US that record funding from India could not come close to offsetting

The world's governments invested \$2,622m in neglected disease basic research and product development in 2023. This represented another small drop – of around \$100m, or 4% – after the record fall in 2022 and the fourth consecutive year of declining public funding. This has left the public sector \$580m (18%) below its 2019 peak – 8% below its average over the previous decade – and responsible for a record low 63% of global funding.

Public funding from high-income countries

The decline in overall public sector funding was driven by further drops in contributions from high-income countries (HICs), which fell by another 4% (\$113m) to \$2,465. This left HICs responsible for 94% of global public funding, a little below last year's level (94.6%) and their average over the preceding decade (94.4%).

A sharp drop in funding from the US government, which continued to contribute 80% of the high-income country total, was more than enough to account for the fall in HIC public funding. US public funding fell by 6% (\$120m) to \$1,968m – leaving it more than \$100m below its ten-year average – because of cuts from multiple US government agencies. The DOD's funding fell to an all-time low of \$75m (down \$29m, -28%), with almost half of this drop due to a sudden halt to its HIV/AIDS vaccine R&D (down from \$13m in 2022, and from \$36m in 2021). The CDC's tuberculosis funding also fell to zero, down from \$9.1m in 2022, leaving its overall contributions to neglected disease R&D at just \$0.3m (down \$13m, -98%), a far cry from its yearly average of over \$20m over the past decade. The US NIH's funding fell for a fourth consecutive year, dropping to \$1,827m (down \$76m, -4%), though the NIH alone continued to contribute 74% of total public HIC funding. And neglected disease funding from USAID fell again, albeit by a more modest \$2.6m (-4%) after last year's \$21m drop.

Alongside a drop in funding from the US, there were much smaller cuts from each of the next three largest public funders: the European Commission (EC), the UK and Germany. The fall in EC funding was just \$4.2m (-2%) – much smaller than the cuts it made in 2022. After a rebound in 2022, the UK's funding dropped back to its 2021 record-low of \$88m (down \$7.6m, -8%). While reduced FCDO funding is mostly responsible for the long-term decline in UK government funding, this year's fall was largely the result of record-low funding from the MRC. Funding from Germany declined again, though much more slowly than last year, falling by \$4.1m (-8%) to \$45m – half of what it was in 2021.

There were also large proportional drops in funding from Australia (down \$7.5m, -22%) and Switzerland (down \$5.6m, -33%). Funding from the Australian DFAT dropped to zero in 2023 after it made contributions of \$11m in 2021 and \$2.6m in 2022. Both this year's and last year's declines reflect the gap between the conclusion of its previous round of PDP funding and the commencement of the new one, which will distribute a total of \$75m between 2024 and 2028. The fall in Swiss funding was the result of steep reductions in funding from the SNSF, which fell by more than half to \$5.0m (down \$5.4m, -52%), its lowest level since 2009.

In contrast to the falls in funding from multiple public HIC countries, funding from Japan rose fourfold to \$28m (up \$21m, 314%). This year's rise and last year's slightly smaller decline were both driven by the regular two-year cycles in Japan's core funding to the GHIT fund. France's funding more than doubled to \$29m (up \$16m, 127%), two-thirds of which was due to record funding from the ANR across several diseases.



Public funding from low- and middle-income countries

Public funding from low- and middle-income countries (LMICs) totalled \$113m in 2023, a rise of \$22m (up 24% – or 20% if we adjust for a slight increase in survey participation) which left it just below its peak, and 16% above its long-term average.

Basically, all of the net growth in funding can be attributed to a sudden rebound in India's spending, which rose by \$21m (32%) to a record \$89m after having declined at least a little in each of the past three years. This left India responsible for a record 78% of LMIC R&D funding, compared to an average of 68% over the previous decade. Net contributions from other LMIC governments remained essentially unchanged at \$24m, with a \$2.5m (21%) increase in funding from Brazil – again the second largest contributor – basically offset by a \$2.3m (-29%) decrease from South Africa – the third largest.

The rise in Indian funding was mainly due to jumps in funding from the ICMR (up \$15m, 29%) and the DBT (\$12m, 384%). The ICMR's funding rebounded to \$68m following three years of decline, leaving it just below its 2017 peak. It increased its contributions across almost all its target diseases, headlined by substantial increases for tuberculosis (up \$4.6m, 34%) and kinetoplastid diseases (up \$3.1m, 71%). The Indian DBT's funding also rose to its second-highest level ever, at \$15m, with most of the increase directed to tuberculosis basic research. These rises offset falls from BIRAC (down \$2.1m, -48%) and the Department of Science and Technology (down \$3.5m, -61%).

The one-fifth increase in funding from Brazil (up \$2.5m, 21% to \$15m) was mostly an artefact of improved data collection, though the similarly-sized fall from South Africa (down \$2.3m, -29%) was, sadly, genuine – a result of cuts from both the South African DSI and MRC.

LMIC governments remain much more heavily focused than other funders on basic research, which received 57% of their funds in 2023, compared to just 18% for other funders. In 2023, their funding for basic & early-stage research rose to \$87m (up \$22m, 33%), capturing a record 77% of public LMIC funding. Partly as a result of this focus on basic research, the share of funding they commit to clinical development is much lower than other funders' – 6% compared to 26% across all other sectors. These gaps are smaller but still striking if we instead compare LMIC governments only to those in high-income countries.

| | e Imillic | Ins | | | | | | | | | a ole of to |
|--------------------------|-----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------------|
| ountry | 155 | | | | | | | | | 2 | 025 |
| | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | |
| United States of America | 1,910 | 1,833 | 2,011 | 2,029 | 2,187 | 2,274 | 2,242 | 2,226 | 2,081 | 1,961 | 75 |
| EC | 127 | 153 | 92 | 132 | 139 | 139 | 184 | 210 | 192 | 187 | 7.1 |
| United Kingdom | 135 | 111 | 121 | 229 | 257 | 249 | 217 | 88 | 96 | 88 | 3.4 |
| India | 45 | 51 | 59 | 81 | 72 | 81 | 73 | 68 | 67 | 88 | 3.4 |
| Germany | 54 | 61 | 54 | 72 | 77 | 93 | 62 | 90 | 49 | 44 | 1.7 |
| France | 72 | 72 | 56 | 54 | 46 | 51 | 44 | 35 | 13 | 29 | 1.1 |
| Japan | 9.3 | 12 | 14 | 15 | 28 | 27 | 9.5 | 21 | 6.7 | 28 | 1.1 |
| Australia | 38 | 23 | 34 | 27 | 45 | 57 | 51 | 46 | 27 | 22 | 0.8 |
| Czechia | | | | | 1.6 | 2.1 | 2.3 | 3.9 | 21 | 21 | 0.8 |
| Canada | 12 | 8.5 | 16 | 16 | 18 | 13 | 14 | 11 | 11 | 16 | 0.6 |
| Brazil | 8.7 | 8.8 | 15 | 10 | 17 | 16 | 13 | 18 | 12 | 15 | 0.6 |
| Switzerland | 22 | 24 | 22 | 21 | 19 | 19 | 20 | 28 | 17 | 12 | 0.4 |
| Subtotal of top 12^ | 2,456 | 2,367 | 2,524 | 2,719 | 2,930 | 3,042 | 2,943 | 2,868 | 2,594 | 2,511 | 96 |
| Total public funding | 2,549 | 2,486 | 2,695 | 2,865 | 3,105 | 3,203 | 3,096 | 3,059 | 2,725 | 2,622 | 100 |

Table 3. Top public R&D funders 2014-2023

Funding organisations from this country did not participate in the survey for this year • Subtotals for 2014-2022 top 10 reflect the top funders for those respective years, not the top 10 for 2023.



Funding from public multilaterals

Funding from multilaterals declined for a second consecutive year from their record high in 2021, dropping by a further \$12m (-21%) to \$44m. While this drop was smaller than last year's, it still brought funding to its lowest point since 2015, sitting at two-thirds of its ten-year average and well under half of its 2021 peak.

More than half of this fall was driven by Unitaid (down \$6.8m, -14%) – as always by far the largest multilateral funder, responsible for 95% of the 2023 total. Funding from CARB-X also fell, reflecting cuts to its *Salmonella* and rheumatic fever vaccine programmes. This left CARB-X only narrowly the second largest multilateral funder and took its funding to a low of just \$0.9m in 2023 (down \$4.0m, -81%), just 7% of its 2020 peak. After recent declines, funding from the only two other significant multilateral contributors – the Task Force for Global Health and Grand Challenges Canada – rebounded slightly. However, the World Bank, last year's third-largest multilateral contributor, provided no funding at all for the first time since 2014.

Public funding adjusted for 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 and lower-income countries. For this reason, we also analyse countries' investments as a proportion of their gross domestic product (GDP).

The US remained the top funder by share of GDP in 2023, devoting \$7.07 per \$100k of its GDP to R&D for neglected diseases, down slightly from 2022. They were followed by the UK at \$2.61 per \$100k, with India close behind at \$2.46 per \$100k. Both the US and UK have seen their funding relative to GDP fall over the past few years, the US dropping from \$9.02 in 2020 to this year's \$7.07 per \$100k and the UK from \$6.90 to just \$2.61.

Conversely, there were three countries outside the top 12 largest funders which appear here when ranked by their contributions relative to GDP: Sweden (fourth highest by GDP and thirteenth largest funder overall), South Africa (fifth highest by GDP and seventeenth overall), and Colombia (twelfth by GDP and twentieth overall).



Figure 4. Public R&D funding by GDP 2023^{*} (A value of 10 is equivalent to an investment of 0.01% of GDP)

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

Philanthropic funding

A sharp rebound in funding from the Gates Foundation took philanthropic funding to its highest level in well over a decade

Philanthropic funding rebounded by \$125m (16%) after two years of decline. This growth lifted 2023 funding to \$929m, just above its 2020 total and, narrowly, its highest level since 2008.

Essentially all of this increase (\$125m, 99%) was thanks to an increase in funding from the Gates Foundation – the top philanthropic funder in 2023 and every other year – whose funding was up almost a fifth. This comes after three consecutive years of reduced funding from the Gates Foundation, reversing all of the decline and leaving 2023 funding \$50m higher than when the decline began. This was the most funding provided by the Gates Foundation since 2009 and the third-highest total on record, following a sharp increase in its TB R&D funding (up \$61m, 38%) and smaller rises in its malaria and multi-disease funding.

The only other substantial increase was from Spain's Fundacio La Caixa – now the third largest philanthropic funder – which saw its funding jump by \$8m (up 145%), more than double its previous high. Fundacio La Caixa's spending again came mostly via untied core funding contributions to IS Global, which more than doubled to \$11m, along with \$1.0m in new malaria diagnostics funding to Vall d'Hebron Research Institute.

Contributions from Wellcome – as always, the second largest philanthropic funder – were down just slightly (by \$4.9m, -4.3%), declining for the third year running and leaving them 26% below their 2020 peak. Funding from Open Philanthropy fell by a similar amount (down \$4.7m), though this represented a much larger proportional reduction (-63%). Like Wellcome's, Open Philanthropy's neglected disease R&D funding peaked in 2020 and has fallen every year since. It has now dropped by more than 90%, though preliminary data for 2024 and beyond suggests a significant rebound in Open Philanthropy's neglected disease funding.

The short and long-term declines in both Wellcome and Open Philanthropy's funding reflect declines across a number of disease areas, especially their multi-disease funding. One area that has experienced meaningful growth from both organisations is TB, with Wellcome providing a one-off increase in its funding of nearly \$12m (156%) in 2023 and Open Philanthropy by \$1.3m, a more than tenfold increase.

The rise in Gates funding, along with the declines from Welcome and Open Philanthropy, had driven a big increase in the share of philanthropic funding provided by the Gates Foundation, which rose to 83% in 2023, its highest level since 2015, when Open Philanthropy did not yet exist.

Outside the top few contributors, the number and make-up of philanthropic funders remained relatively consistent. However, 2023 did see almost \$2m in funding from the UK's LifeArc, a new survey participant this year.

Most of the increase in philanthropic funding was invested in the 'big three' diseases – TB, malaria and HIV – and in platform technologies. The single biggest increase was in funding for tuberculosis (up \$72m, 41%, mostly for vaccines), mostly due to the increased investment from the Gates Foundation and, to a lesser extent, Wellcome. Much of this increase was directed to the Gates MRI's Phase II clinical trial of the M72 vaccine candidate.

Philanthropic non-disease-specific funding was up by \$21m, most of which was for platform technologies. Malaria funding was up \$24m, and HIV by \$10m – all mostly thanks to the Gates Foundation.

Over half of philanthropic funding went to academic & other research institutes (\$506m, 54%), followed by funding to PDPs (\$158m), which increased by \$11m after four years of decline. This still leaves philanthropic funding to PDPs more than a third lower than when the most recent decline began in 2018 and over 70% below its 2008 peak. Philanthropic funding to small pharmaceutical companies rose by \$44m (40%) to a record \$152m – more than six times their contributions to big pharma.

Table 4. Top philanthropic R&D funders 2023

| | 155 Imillic | nsl | | | | | | | | 9 | 023°% of t |
|---------------------------------------|-------------|------|------|------|------|------|------|------|------|------|------------|
| under | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | |
| Gates Foundation | 66 9 | 680 | 706 | 657 | 690 | 727 | 702 | 691 | 650 | 775 | 83 |
| Wellcome | 126 | 98 | 119 | 123 | 135 | 137 | 148 | 136 | 114 | 109 | 12 |
| Fundació La Caixa | | 4.1 | 4.0 | 5.8 | 3.6 | 5.2 | 6.0 | 4.7 | 5.5 | 14 | 1.5 |
| MSF | 5.3 | 7.0 | 12 | 13 | 18 | 15 | 15 | 7.0 | 9.8 | 9.2 | 1.0 |
| Individual donors and foundations | 1.1 | 1.4 | 1.3 | 1.8 | 2.5 | 1.9 | 5.1 | 4.2 | 3.3 | 3.7 | 0.4 |
| Open Philanthropy | | | | 9.6 | 5.2 | 16 | 29 | 21 | 7.6 | 2.8 | 0.3 |
| Anonymous funder | | | | | <0.1 | 0.8 | 0.4 | 0.6 | 1.0 | 2.6 | 0.3 |
| Gavi | | 13 | 7.4 | 9.1 | 4.1 | 4.4 | 3.3 | 3.9 | 1.9 | 1.8 | 0.2 |
| Leducq Foundation | | | | | | | | | 1.9 | 1.8 | 0.2 |
| LifeArc | | | | | | | | | | 1.7 | 0.2 |
| Dutch National Postcode Lottery | 0.7 | 2.2 | 3.4 | 2.4 | - | - | - | 4.9 | - | 1.1 | 0.1 |
| All other philanthropic organisations | 13 | 9.0 | 7.5 | 35 | 34 | 12 | 18 | 8.9 | 8.5 | 6.2 | 0.7 |
| Total philanthropic funding | 814 | 814 | 861 | 857 | 893 | 919 | 926 | 882 | 803 | 929 | 100 |

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients and so may be incomplete.
- No reported funding

Private sector funding

Private sector funding fell, partly undoing two years of growth; participationadjusted funding was down for both large and small pharmaceutical companies

The private sector invested a total of \$619m in neglected disease basic research and product development in 2023, accounting for 15% of global funding. As in all previous years, multinational pharmaceutical companies ('MNCs') were responsible for most of this funding (\$541m, 87% of the private sector total), with small pharmaceutical and biotechnology firms ('SMEs') contributing the remainder (\$78m, 13%).

Multinational pharmaceutical companies

Investments from MNCs fell by 11% (down \$66m), undoing about two-thirds of the growth over the past two years and leaving it just above its 10-year average. The top two MNC funders from 2022 both made substantial reductions to their neglected disease R&D from that year's record highs. However, if we adjust for a slight fall in year-on-year survey participation, the overall decrease was a little smaller, at \$60m or 10%.

The share of MNC funding going to the big three diseases – HIV/AIDS, tuberculosis, and malaria – fell seven percentage points to 65%, driven by a sharp reduction in their HIV R&D (down \$80m, -38%), leaving big three funding more than \$80m below its average over the previous half-decade. Also driving this shift was record-high MNC funding for the WHO neglected tropical diseases (NTDs), which grew by more than a third (\$35m), mostly via increases for dengue (up \$30m, 68%), kinetoplastid diseases (up \$7.3m, 24%) and leprosy (up \$3.4m, 60%). MNCs' funding for NTDs has now grown by more than \$60m since 2020, with more than 80% of the increase driven by rising dengue drug funding.

MNC R&D fell across all of their major product areas, headlined by significant decreases in both vaccines (down \$32m, -32%) and drugs (down \$26m, -5.6%), taking their vaccine R&D to a near-record low and just a third of its peak in 2018. There were also proportionally significant decreases for biologics (down \$10m, -55%) – after a record year in 2022 – and basic research (down \$3.7m, -66%).

The drop in MNC vaccine funding resulted from decreases in R&D across all diseases except for tuberculosis, which nearly tripled (up \$4.9m, 286%). The decreases in vaccine development were heavily concentrated in two areas: HIV R&D (down \$28m, -58%), following the discontinuation of a late-stage vaccine candidate after two failed clinical trials, and diarrhoeal diseases (down \$6.4m, -68%). The fall for diarrhoeal diseases is likely to be at least partly artefactual: it represents funding for a *Shigella* vaccine candidate that changed hands to another organisation for which no spending data is available.

Total MNC funding for drug R&D dropped by \$26m (-6%) as investment in HIV drugs fell by a third (down \$52m, -32%). This decrease overshadowed record-high drug R&D investment for studies investigating the treatment and prevention of dengue (up \$30m, 70%), post-exposure prophylaxis for leprosy (up \$3.4m, 62%) and a once-a-week treatment for mycetoma (up \$0.3m, 625%).

The vast majority of the headline fall in MNC R&D was in clinical development (down \$50m, -15%) and post-registration studies (down \$20m, -26%), while their investment in early-stage research rose slightly.

Small pharmaceutical & biotechnology companies

Reported investment by small pharmaceutical companies ('SMEs') rose by a fifth (up \$14m, 22%). After adjusting for a big jump in survey participation, though, SMEs' funding was down by nearly half, with just \$28m reported by ongoing survey participants. These big shifts in participation mean that the headline data on SME funding are a bit misleading; we do our best to pick through the real and illusory changes below.

Funding for the 'big three' diseases – HIV, TB and malaria accounted for an uncharacteristically large 74% share of the SME total, compared to an average of just 24% over the previous decade. This swing, though, mostly reflects

the impact of new survey participants – funding for the 'big three' diseases from ongoing participants made up just 30% of their total, though this was still up from just 12% in 2022.

Also contributing to the swing towards the 'big three' – though also partly an artefact of participation changes – investment for bacterial pneumonia & meningitis fell from \$22m to zero after four years of steady funding as one of only two funders from 2022 reported zero funding and the other was unable to participate in the 2023 survey. Another artefactual drop in SME funding, this time for dengue (down \$3.3m, -88%) was caused by a lack of reporting for still-ongoing clinical trials of pan-serotype monoclonal antibody-based biologics, now being run by a new (and non-participating) corporate sponsor.

A key driver of the (as noted above, mostly artefactual) shift towards the 'big three' funding from SMEs was a big jump in reported malaria investment (up \$25m, 663%), which came mostly from new survey participants and was all for the clinical development of vaccines (\$24m). The \$20m increase in tuberculosis was also mostly an artefact of new participants and went to vaccine R&D to advance mRNA candidates (\$16m, from a low base) and to diagnostics (up \$4.0m, 224%) for a point-of-care blood-based test.

There was also record SME funding for snakebite envenoming, which jumped 307% (up \$4.8m), most of it going to drug development.

SME's investment increased for both basic & early-stage research (up \$8.2m, 141%) and clinical development & post-registration studies (up \$16m, 40%), though the latter was entirely thanks to a new survey participant. Shifts in participation also meant that, for the first time since 2013, HIC-based SMEs provided the majority of funding (\$65m, 83%), as LMIC-based SMEs reported just \$13m (17%), almost all of which came from India.

Top funding organisations

Funding from the US NIH and industry declined, but both remained close to their recent averages; Gates Foundation funding surged; and the DOD's plummeted

As in every other year, the top three funders of neglected disease R&D were the US NIH, industry and the Gates Foundation, whose combined funding totalled \$3,220m, or 77% of the global total.

Funding from both the NIH and industry declined slightly (by 4 and 8%, respectively), in each case, returning funding to its average over the preceding decade. Funding from the Gates Foundation, on the other hand, rebounded sharply after three straight years of decline, rising by almost a fifth (to \$775m) and taking it to its highest level since 2009 and its third-highest total on record.

Funding from most of the other top 12 funders declined, headlined by record low funding from the US DOD (down \$29m, -28%), which ceased its funding for HIV altogether and drastically dropped its funding for diarrhoeal diseases, leaving its overall contributions down by half from their 2017 peak. We consider the sharp reduction in DOD vaccine R&D in more detail in the Discussion, below.

The sole exception to the (mostly slight) general decline was the Indian ICMR. Its funding rose \$15m (29%) to a near-record \$68m with increased funding across a number of diseases.

Funding from the UK FCDO declined just slightly in 2023 (-3%), to a new record low (\$42m), having dropped by \$92m from \$140m in 2020 and by a smaller amount every year since. The long-term decline in funding from the UK MRC has been slower, but its 2023 cuts were more profound than those of the FCDO; its funding was down almost a quarter (down \$8m, -23%) also to a record low (\$27m).

| | cs Imilli | onsi | | | | | | | | | 23% of tota |
|---------------------|-----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------------|
| Funder | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | 0 |
| USNIH | 1,652 | 1,619 | 1,750 | 1,733 | 1,934 | 2,052 | 1,999 | 1,979 | 1,903 | 1,827 | 44 |
| Gates Foundation | 669 | 680 | 706 | 657 | 690 | 727 | 702 | 691 | 650 | 775 | 19 |
| Aggregate industry | 53 5 | 551 | 587 | 643 | 820 | 652 | 566 | 643 | 671 | 619 | 15 |
| EC | 127 | 153 | 92 | 132 | 139 | 139 | 184 | 210 | 192 | 187 | 4.5 |
| Wellcome | 126 | 98 | 119 | 123 | 135 | 137 | 148 | 136 | 114 | 109 | 2.6 |
| US DOD | 124 | 102 | 140 | 155 | 131 | 129 | 149 | 147 | 103 | 75 | 1.8 |
| Indian ICMR | 38 | 38 | 47 | 71 | 59 | 61 | 59 | 56 | 53 | 68 | 1.6 |
| USAID | 99 | 94 | 104 | 112 | 89 | 76 | 72 | 81 | 60 | 57 | 1.4 |
| UK FCDO | 78 | 63 | 67 | 122 | 139 | 133 | 140 | 47 | 44 | 42 | 1.0 |
| Unitaid | 20 | 36 | 79 | 61 | 80 | 66 | 63 | 95 | 49 | 42 | 1.0 |
| German BMBF | 20 | 28 | 36 | 47 | 51 | 54 | 45 | 54 | 41 | 34 | 0.8 |
| UK MRC | 49 | 42 | 50 | 49 | 43 | 53 | 48 | 33 | 35 | 27 | 0.7 |
| Subtotal of top 12^ | 3,578 | 3,531 | 3,778 | 3,911 | 4,330 | 4,278 | 4,174 | 4,172 | 3,914 | 3,862 | 93 |
| Total R&D funding | 3.901 | 3.861 | 4,152 | 4.377 | 4.819 | 4.774 | 4.589 | 4.587 | 4,199 | 4,171 | 10.0 |

Tables 5. Top neglected disease R&D funders 2023

^ Subtotals for 2014-2022 top 10 reflect the top funders for those respective years, not the top 10 for 2023.

Funding flows

Funding for PDPs and late-stage clinical development continued their slow decline

Funding flow trends

In 2023, just over three-quarters of investment in neglected disease R&D – amounting to \$3,176 million or 76% – came from external funding sources. The remaining 24% was spent internally through intramural funding or private sector self-funding. These proportions were broadly consistent with previous years.

However, there were shifts within these categories: external funding increased by \$116 million (up 4%), while internal funding decreased by \$146 million (down 13%). Although industry self-funding declined by 8% (\$55 million – and potentially more when adjusting for increased participation), the majority of the reduction in internal funding was due to a significant drop in public sector intramural funding, which fell by nearly \$90 million or 19%.

This, in turn, was mostly the result of a sharp drop in the NIH's intramural funding (down \$67m, -21%) from last year's record high, alongside smaller intramural funding reductions from the US DOD and CDC.

Most of the increase in external funding went to researchers & developers (up \$105m, 4%), with a smaller – though proportionally more significant – increase in funding to Other Intermediaries (up \$28m, 16%). Funding to PDPs fell by a further \$16m (-5%), their fifth consecutive year of decline.

A large share of the rise in funding to non-PDP intermediaries was the result of a scheduled cyclical increase in funding to the GHIT fund from the Japanese government (up \$18m), while funding from the EC (still the top funder of Other Intermediaries) was down by \$12m (-12%), mostly due to its reduced contributions to the EDCTP.

While funding from Gates – the top funder of PDPs – rebounded slightly, by \$12m (9%) after four years of decline, overall funding to PDPs was still down from 2022, mostly due to a \$17m drop from the US NIH (primarily in its funding for FHI360), as well as a fifth consecutive drop in PDP funding from the German BMBF (down \$6.1m, - 62%). The Gates Foundation's increase was thanks to a \$24m rise in its funding to IAVI, along with a smaller (\$6m) increase to MMV, though these increases were partly offset by drops in its funding to several other PDPs, most prominently FHI360 and IVI.

How funding was allocated across the different stages of R&D

In 2023, a little under three-fifths of the funding allocated to a specific stage of R&D went to basic or early-stage research (58%, \$1,883m), with a third going to either clinical development or post-registration studies (33%, \$1,070m), both broadly in line with the shares across the last decade. The remaining 8.5% (\$276m) was for platform technologies, which had grown rapidly before remaining basically unchanged in 2023. These shares do not include an additional \$569m (14% of the global total) which did not specify an R&D stage (\$569m, 14%) or \$649m (16% of global funding) for non-disease-specific R&D (\$649m, 16%). Funding in the latter category skews much more heavily towards clinical and platform development, suggesting that our 58% share for basic and early-stage research is a slight overestimate.

These figures remained largely unchanged from their 2022 values, with basic & early-stage increasing by \$22m (1%) and clinical development & post-registration down by \$82m (-7%). This was the fifth consecutive year of decreasing funding for clinical development & post-registration studies from its industry-driven peak of \$1,603m in 2018, leaving it reduced by a total of more than half a billion dollars.

Basic research spending was essentially unchanged at \$789m (down 1%). In comparison, the slight rise in earlystage research (up \$31m, 3%) was due to increases in funding for discovery & preclinical drug research and early development of diagnostics. The decrease in clinical development & post-registration studies was felt in both the private sector (down \$54m, - 14%, or by 17% if we adjust for changes in survey participation) and the public sector (down \$80m, -14%, a little over half via the NIH), partly offset by a sharp rise in philanthropic product development (up \$53m, 43%).

Alongside a big fall in clinical development without a specified R&D stage (down \$70m), the drop was concentrated on later-stage product development, including Phase III development (down \$58m) and post-registration studies (down \$30m), reflecting a mix of successful and abandoned late-stage trials. This fall in late-stage development was partly offset by a \$65m increase in funding for Phase II clinical development, much of it for malaria drugs and vaccines. Most of the overall drop in clinical development was in drug R&D (-\$52m), but biologics, VCP and microbicides all experienced a decline.

Funding for product development partnerships

Funding to product development partnerships (PDPs) declined slightly in 2023 (down \$16m, -5%) to a new record low, following a fifth year of consecutive decline. The decline has, at least, begun to slow relative to the previous two years when funding dropped by over \$100m each time. Their cumulative effect still left funding at less than half of its 2014 decade high and more than 60% below its all-time high in back 2008.

The Gates Foundation was again by far the largest funder of PDPs in 2023, accounting for almost half of the total and over \$100m more than the UK FCDO, the next largest funder. While a large proportion of the longer-term decline in funding to PDPs was attributable to declining PDP funding from the Gates Foundation, its funding actually rebounded slightly in 2023, though it remained more than \$100m below where it was in 2018 when the recent decline began – and almost three-quarters below its peak in 2008.

Most of the 2023 increase in Gates PDP funding went to IAVI (up \$24m), though even IAVI's 2023 total was less than it had received from the Foundation in 2018. Gates Foundation's funding to MMV also increased (up \$6m), while its funding to most other PDPs declined, especially in its contributions to FHI 360 and IVI.

The 2023 decline in overall funding to PDPs was primarily due to a \$17m drop in funding from the US NIH – particularly their funding to FHI360 as part of the HIV Prevention Trials Network – and the German BMBF. The BMBF's 2023 funding to PDPs was just \$4m, having peaked at \$22m in 2018, with the BMBF 2023 cuts falling most heavily on DNDi and MMV and its long-term reductions on IPM and FIND. Funding from the UK stabilised at \$40m in 2023, after having dropped by almost two-thirds between 2020 and 2021, at least maintaining its new lower level of funding.

Funding to PDPs from the Netherlands Ministry of Foreign Affairs failed to recover the drop we saw in 2022. However, our forecasts show that with the advent of PDP IV – their new PDP funding round running from 2022-2027 – that total committed funding will remain similar to the previous round, implying an imminent rebound in disbursements. The situation is similar with PDP funding from the Australian DFAT, which was between its PDP funding cycles in 2023, with no funding disbursed before the new, slightly increased, cycle beginning in 2024.

Unitaid was the only PDP funder other than the Gates Foundation to significantly increase their funding – a rise of \$60m (up almost 80%) – which went mostly to MMV. There was also new, first-time PDP funding from the Japanese government, albeit just \$2.6m.

MMV was again the top-funded PDP in 2023, receiving 22% of all PDP funding. The Gates-driven rebound in IAVI's funding left it a close second, with 20% of the overall total. Funding to most other PDPs declined, most significantly FHI 360 and IVI, both of which saw their funding drop by 50% or more, compounding previous declines.

Direct funding to research and developers



Figure 5. R&D funding flows 2023 \$4,170m Global investment in neglected disease R&D in 2023 76% \$3,176m External investment (grants given to others) 64% 7% 5% \$2,675m \$301m \$199m

Funding to PDP's

Funding to other intermediaries

Figure 6. PDP funding 2023



Funding for other intermediaries

Funding for non-PDP intermediaries ('Other intermediaries') rebounded to \$199m, an increase of \$28m (16%), which restored about half the funding they lost in the previous year's sharp dip.

The bumpy path of Other Intermediary funding mostly reflects the two-year cycles on which the Japanese Government makes its disbursements to the GHIT fund; its contributions went from \$21m in 2021 to just over \$5m in 2022, to \$24m in 2023 – generating illusory changes in each year. Amid these cycles, GHIT funding has trended chiefly upward over time, reaching a record \$47m in 2023, thanks to record funding from the Japanese Government and a doubling in funding from industry, which rose from \$5.7m to \$11m.

The other major driver of non-PDP intermediary funding is the European and Developing Countries Clinical Trials Partnership (EDCTP). Though it remained the largest recipient of intermediary funding, the EDCTP saw its funding dip by \$5.5m (-5%) in 2023 to \$101m – its lowest level since it began benefiting from increased funding under the second EDCTP funding round in 2017. The decline in funding to the EDCTP was the result of a second consecutive drop in disbursements

NEW DEVELOPMENTS

In 2024 announced it would join the Gates Foundation and Wellcome in providing core funding to the GHIT funding, promising an initial contribution of \$125k.

from the EC, which fell by another \$12m (-12%) after having dropped by \$16m in 2022. This fall was only partly offset by increased contributions from the German BMBF (up \$3.4m) and the UK MRC (up \$3.7m after a three-year absence).

The only other notable shift was an \$8.5m increase in funding to the Barcelona Institute for Global Health (up \$8.5m), mostly due to increased funding from the Spanish philanthropy Fundació La Caixa.

Figure 7. Intermediary funding 2023



Discussion







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What we learned from this year's data

A high-level view of global funding for neglected disease R&D suggests that the situation has largely remained the same over the last five years. Funding peaked in 2018, and since then, it has experienced a mostly gentle decline – largely due to increased global inflation eroding its buying power.

Beneath the surface, however, much has changed. By integrating funding data from the G-FINDER survey with our pipeline tracking and forward-looking funding announcements from the Compass project, we are gaining a clearer understanding of shifts in funders' priorities and how they align with real-world events.

We see funders adjusting their strategies in response to developments like product approvals, often leading to reduced funding. Sometimes, these shifts are driven by the progress of promising products, such as the M72 TB vaccine, entering their expensive late-stage trials. And other times, as with the rapid rise in private sector dengue drug development, they are due to a literal shift in the global climate making a previously overlooked disease seem much closer to home. With overall funding stagnant or declining, prioritising one area means another will be deprioritised or sometimes even forgotten: after several years of decline, funding for trachoma R&D fell to zero in 2023 after averaging \$2.6m a year in the decade before 2021. It joined yaws and mycetoma on the list of the most neglected of the neglected diseases – those receiving well under a million dollars a year in R&D funding.

Also increasingly neglected is funding for vaccine R&D, its fall driven by successful trials for malaria and unsuccessful ones for HIV.

Some kind of setting priorities is not only wise but, as we argue below, essential. While every area of unmet need represents a valuable investment, not all can be given equal priority. There is no single solution to unlock unlimited – or even sufficient – global funding. Smart choices need to be made.

Below, we try to separate the signal of strategic shifts in global funding from the noise of the random changes in funding we observe every year. We show how the pipeline helps explain some, but not all, of what funders are choosing to focus on and argue that priority setting needs to be backed by the right data to maximise its impact.



Funding moves on after a new product is approved

One area of R&D that has experienced a significant long-term decline is vaccine development for *S. pneumoniae* and *N. meningitidis* ('pneumonia and meningitis'). Vaccine funding for both pathogens is down by more than 90% from their respective peaks, falling from a total of \$136m in 2013 to less than \$20m in 2023.

Broadly speaking, this shift makes sense. New conjugate vaccines for both pneumonia and meningitis have been launched over the last 15 years, which <u>our modelling</u> credits with averting more than 138 thousand disability-adjusted life years (DALYs) through to the end of 2024. These new vaccines remain vulnerable to the rise of resistant serotypes, leading to an arms race of multi-valent vaccines targeting an ever-changing list of dominant variants. As a result, there is still some ongoing development of whole-cell-based and non-conjugate-protein-based vaccines, which would limit the virus's ability to select for resistant strains.

However, compared to the world before the new conjugate vaccines, the burden from both pneumonia and meningitis is substantially lower. Death rates from meningitis fell from <u>4.66 per hundred thousand people</u> in 2010 when MenAfriVac began widespread distribution to <u>2.71</u> in 2021. It makes perfect sense that funding for a now much smaller problem has declined, shifting to ensuring access to those new products or to other areas with a relatively greater untreated burden.

Malaria vaccines show a similar, if less striking, response to the success of new products. While early-stage research continues on vaccines that could supersede R21 and RTS,S by delivering higher efficacy or disrupting transmission, malaria vaccine R&D has fallen sharply from the peak associated with those vaccines' late-stage trials. This, too, seems like broadly good news – provided the displaced funding is allocated wisely. Production and distribution of R21 remains a barrier to reaching its full potential, with <u>current plans</u> accounting for only around 25 million doses, compared to the 200 million needed to maximise its <u>impact</u>.

Another area where funding is understandably down is onchocerciasis drug R&D, which peaked in 2016 with trials of the repurposed drug moxidectin before falling steeply once it was approved.

Shifts in funding following product launches or unsuccessful trials



Less obviously explicable is the long-term decline in microbicide funding for HIV prevention, which has dropped by over 90% from its peak. Unlike other areas of long-term decline, however, this downward trend began well before the launch of any approved product; funding was already far below its peak by 2021, when the WHO recommended the dapivirine ring, still the only regulatory-approved microbicide.

Some of the missing microbicide funding has shifted into multipurpose prevention technologies (MPTs). These are products which act as contraceptives while also protecting from sexually transmitted infections, including HIV. This shift reflects an emerging consensus that MPTs deliver more impact than single-purpose microbicides, offering users better options for pre-exposure prophylaxis and reducing their need to interact with the health system. However, while some funders have explicitly shifted their microbicide budgets towards MPTs, there has been nothing like enough MPT funding to account for the more than \$200m decline in annual microbicide spending. One culprit might be the failed 2022 Phase III trial of the MPT candidate EvoGuard, which may have dented funders' enthusiasm – hopefully only temporarily.

Funding for HIV vaccines has fallen alongside microbicides, albeit much more slowly. Unlike pneumonia, meningitis, and malaria – where reductions follow successful product launches – this drop reflects multiple late-stage setbacks, forcing a move back to less costly early-stage R&D as part of an overall shift away from HIV vaccine research. Since 2018, HIV vaccine funding has fallen by nearly a quarter of a billion dollars, across both early- and late-stage research – reaching a record low in 2023. As with microbicides being replaced by MPTs,

some of this dip may reflect the success of alternative product categories, including improved HIV diagnostics and the long-acting injectables which have significantly reduced the burden of HIV even without a new vaccine.

The net effect of all these shifts is that global vaccine funding has trended gradually down since its peak in 2009, with one major exception, tuberculosis.

Outside of TB, funding for vaccines has repeatedly declined



Figure 9. Vaccine R&D funding, TB vs other diseases 2007-2023 (participation adjusted for 2023)

While reported vaccine funding rose slightly in 2023, this reflects funding from new survey participants (which we excluded from the graph above) and, more importantly, a second consecutive leap in funding for TB vaccines. The share of global vaccine funding going to TB has risen from just 5% of the global total in 2018 to 12% in 2023, rising sharply as vaccine R&D for most other diseases has fallen. As shown below, these falls are headlined by the \$250m (27%) reduction in HIV vaccine funding and the even larger proportional falls for malaria (down by 33%), diarrhoeal diseases (down by 43%) and especially pneumonia & meningitis (down by 89%), most of them reflecting one or more product launches.

Figure 10. Change in vaccine R&D between 2018 and 2023 by disease



Can the M72 vaccine help eliminate TB?

The single biggest strategic shift in the funding landscape over the last two years has been the near doubling of spending on TB vaccines, with the vast majority of the new funding being directed to the Gates Medical Research Institute for late-stage trials of the M72 vaccine.

M72 is the most advanced of the 16 different TB vaccine candidates currently in the pipeline. In Phase IIb trials, M72 has demonstrated <u>around 50% efficacy</u> in preventing disease in children – a small but meaningful improvement on the existing BCG, which offers roughly 45% protection. The small number of actual infections observed during the trial, though, means there is significant overlap in the confidence intervals for M72 and BCG's efficacies: we can't yet be sure that M72 will improve on the existing standard of care.

The scale and epidemiology of TB infections are such that even a 5% increase in efficacy would avert millions of deaths and tens of millions of cases over the next 25 years: as many as two million deaths and almost 13 million cases in India alone.

M72 offers a significant opportunity to drastically reduce the global burden of TB and slow the rise of extensively drug-resistant strains. Its development reflects a big bet by its philanthropic backers, the Gates Foundation and Wellcome, who plan to invest a significant share of the neglected disease funding in hopes of a successful trial result. Practically, though, all this funding for M72 has come at the expense of other neglected diseases: both major funders have reduced their non-TB expenditures over the past two years. Evaluating whether this gamble is worthwhile – accounting for the roughly 30% chance that M72 might demonstrate lower efficacy than BCG – requires careful consideration of where the money is coming from.

The calculus for investing in TB R&D looks very different if M72's efficacy proves to be high enough to make elimination of the disease a realistic goal. The prospect of eliminating TB, rather than merely controlling it, ought to push funders towards an 'all of the above' TB R&D strategy, including improved diagnostics and therapeutics to detect and treat the cases where the vaccine fails and improved public health measures to control its spread while the other measures take effect. These other approaches all remain valuable investments even if – as seems likely for a vaccine with roughly 50% efficacy – M72 can't form part of a realistic elimination strategy; but they are much

less valuable if elimination is off the table; and less valuable than they were in a world with no M72 and more cases of TB, despite the obvious medical synergies between vaccines, diagnostics and therapeutics. If M72 doesn't reduce TB's prevalence, and with it the likely impact of a novel TB drug, we should not be spending \$500m testing it.

In a world where funding for neglected diseases is – mostly – fixed, big bets like M72 require big sacrifices somewhere else. Not everything can be prioritised, as we discuss further below.

How much of the year-to-year change we observe is random?

Each year, we carefully catalogue the most significant changes in funding over the previous year and try to explain why, for example, private sector investment went up. Sometimes, that same trend reverses itself the following year, and we are left explaining why private sector funding went down again. This sort of variation *can* represent two real and opposing trends, both worthy of explanation, or it might just be random variations in companies' year-to-year spending as their trials ramp up or wind down.

One way to avoid being drawn into building complex explanations for simple randomness is to restrict ourselves to long-term trends: the declines in vaccine or microbicide funding have been going on far too long to be written off as mere blips. The downside of only writing about long-term trends, though, is that we need to wait years for them to emerge from the data, and we miss big new shifts as they happen.

Another way to avoid talking about randomness is to understand the processes that generate funding totals: we know, for example, that Japanese public funding to GHIT follows a two-year cycle, and that Australian PDP funding runs for five years. When we see these anticipated cyclical changes, we avoid getting too worried. But, despite our best efforts, we often don't have any ability to determine when funders have changed their strategy – bad news about future commitments to neglected disease is unlikely to make it into a press release.

As a result, we are trying to develop an understanding of how random neglected disease R&D funding has been in the past so that we can separate the genuinely surprising shifts from the sort of transitory changes we observe all the time.

The graph below represents an attempt to use 'autoregressive integrated moving average' (ARIMA) modelling to explain past changes in overall funding and to forecast its future direction. This is a 'dumb' model: it doesn't know anything about global funding, including the specific cyclical shifts in GHIT and PDP funding identified above. It treats funding as a sequence of numbers over time and tries to build a model to fit the observed data.



Figure 11. Observed and Forecasted Funding, Totals



What the model suggests is that overall global funding follows a comprehensible trajectory – the model is able to produce values that fit closely with the real ones. It also suggests that the slight drop in funding we observed in 2023 was a little unexpected. Based on its past behaviour, the model 'expected' funding to rise a little in 2023 and it forecasts that funding will continue to rise over the next two years. This suggests that the drop in funding we observed is perhaps more significant a departure from previous trends than the rest of the report acknowledges, but also that the observed level of funding is not hugely different from what an uninformed observer, armed only with trend data, would have predicted.

Looking instead at funding specifically for vaccines, we see a slightly different picture:



Figure 12. Observed and Forecasted Funding, Vaccines

The larger gap between actual and predicted funding implies that vaccine funding is harder for the model to explain than overall funding, which aggregates more individual decisions and disbursements, balancing out some of its random variation.

Second, the observed trend to date suggests (to the model) that vaccine funding will continue to fall; the model is 'surprised' by the slight uptick in vaccine funding we saw in 2023. We know, though the model doesn't, that the very small rebound in reported vaccine funding reflects new survey participants, and secondly, that funding would



have fallen sharply were it not for the big increase in TB vaccine R&D. So, the model is telling us that these events do represent a break from the existing trend – they are worth explaining and probably won't disappear in next year's data.

Public funding from the US is sputtering

Funding from the US government dropped sharply for the second year in a row, with big cuts from almost every major funder: the NIH, the DOD, the CDC and USAID. Overall US public funding is now closer to its level prior to the 2009 pre-American Recovery & Reinvestment Act than to its extended peak between 2018 and 2021, when it averaged more than \$2.2bn a year.

The broader decline in U.S. funding for neglected disease R&D highlights the importance of making a compelling case for continued U.S. engagement. As outlined in last year's *Doing Well by Doing Good* report, emphasising the domestic as well as global benefits of such investments is critical. At the same time, diversifying funding sources is essential to reduce reliance on the shifting priorities of US defence and basic research funding, which often reflects the interests of America's soldiers and scientists, rather than the burdens faced by LMICs.

Climate change is expanding the range of tropical diseases

Alongside the direct health impact of rising global temperatures and their accompanying extreme weather events, climate change will increase the range of many tropical diseases and provide new habitats for the insects and other vectors that carry them.

A key part of adapting to the impacts of climate change will be preparing naïve populations and inexperienced health systems to deal with the threat from diseases previously confined to countries closer to the equator. A <u>2021</u> <u>systematic review</u> of links between climate change and tropical disease found that several neglected diseases had already spread to new areas and predicted significant further increases in both range and incidence as warming continues. This is particularly true of vector-borne diseases like dengue, which it predicted would spread to coast cities in Eastern China and Japan, alongside a 40-fold projected increase in cases in existing endemic areas like Dhaka, Bangladesh.

These predictions would prove prescient. In 2024 incidence of Dengue exploded across the globe, leading to an <u>estimated 3,000 deaths</u>, including several major outbreaks across parts of Pakistan previously considered outside its range. In this context, both the surging private sector investment in dengue drug R&D – which leapt to a second consecutive record high in 2023 – and their earlier focus on vaccines (see graph below) is both easy to understand and likely too little, too late to address the ongoing rise of dengue infections.



Figure 13. In-scope private sector dengue R&D funding, by product*

* Dengue vaccine funding was excluded from the G-FINDER survey post 2012 following strong commercial funding growth.

The rush to create viable treatments for dengue should serve as a reminder of all the other climate-sensitive G-FINDER neglected diseases – such as malaria, helminths, diarrhoeal diseases, leishmaniasis, and Chagas – that will spread across a warming world.

Neglecting these kinds of diseases was never a good policy, but climate change will transform funding from a question of providing neighbours with development assistance to one of health security at home.

Funders need to set priorities

Impact Global Health has consistently called for increased funding for neglected disease R&D. The Impact of Global Health R&D report we published in May 2024 demonstrates that funding for neglected disease R&D delivers a massive return on investment – more than 400 to 1 – and argues that funders of all kinds should be spending more money on securing even more of these gains.

We reiterate those sentiments here: funding for neglected disease R&D is a good investment, and the world should be doing more of it.

But after nearly two decades of urging funders to increase support, it's clear that simply calling for "more money" rarely prompts a drastic shift in priorities. To meaningfully expand the pool of funding for neglected disease R&D, advocates will actually have to make the case that it represents a good use of funders' limited resources.

The good news is that we have strong arguments on our side:

The first of these is the sheer scale of R&D's global impact, mostly measured in the value to society of lives saved and DALYs averted.

The second is that conducting R&D delivers tangible economic benefits to the nations where it takes place, including more than 15,000 jobs and €30bn in economic activity in Europe alone.

The third, which we make above, is that neglected disease R&D can and should be viewed through the lens of climate abatement and health security. A stockpile of products to deal with a distant disease can rapidly transform from a tool for vaccine diplomacy to a means of keeping one's population safe. From the point of view of the private

sector, diseases can go from rare and unprofitable to endemic and lucrative much faster than candidates can advance through the pipeline.

No matter how persuasive our advocacy, there will inevitably be more unmet needs than funding to address them. While working to increase the size of the funding pie, funders and developers must also ask two questions: how to turn a fixed budget into as much R&D as possible, and how to maximize the impact of that R&D.

In an ideal world, funders would estimate the full cost of building a pipeline designed to meet every unmet need, incorporating the risks of failure and evolving disease burden. In practice, we have something in the order of \$4bn to work with each year, and the question funders face is not 'what is the optimal number of late-stage trials to guarantee a vaccine by 2030?' but instead 'could the cost of a late-stage vaccine trial deliver more health impact if spent on other things?'. Assessing 'what we need' in light of what we actually have means funders need to know not only what a given outcome is likely to cost, but also develop a triage strategy to ensure their limited resources deliver the greatest possible impact.

If R&D costs less, we can afford more of it

The first of those two goals, lowering the costs of conducting R&D, deserves more detailed consideration than we can provide here.

As we discuss <u>elsewhere</u> in the context of EID product development, trial protocols and – especially – benchmarks of statistical certainty designed for peacetime use in rich country health systems often fail to strike the appropriate balance between risk and cost in poorer nations struggling with an ongoing health crisis. Critics of the FDA argue that the costs and delays involved with a gold standard review are hard to justify, even in the case of expensive drugs for mild problems in rich countries. They are much harder to accept for something like a repurposed therapeutic with a known side effect profile being used against a communicable or potentially fatal disease.

Clinical trials account for an <u>estimated 68 per cent</u> of the cost of bringing a new product to market, peaking with the late-stage trials designed to demonstrate the product delivers a meaningful benefit. Given this distribution of costs, the <u>decision</u> by the governments of Ghana, Burkina Faso and Nigeria to begin using the R21 malaria vaccine based on its promising Phase IIb trial results is almost certainly the right one. This approach could form the basis of a more general trend towards approving products once they have been proven safe, based on suggestive but inconclusive evidence of efficacy, and then substituting real-world data collection for late-stage clinical trials. This would require developers (and the regulators who control their market access) to weigh the trade-off between distributing a product earlier, and at perhaps half the R&D cost, against the costs and risks of approving a product which ultimately proves to be harmless, but useless. Proceeding on the basis of incomplete data may not often be the right decision, but sometimes it will be.

The costs of clinical development can also be brought down by building trial capacity in LMICs. Something like the UK's COVID-era RECOVERY trial, which tested ten different interventions across 48 thousand patients at a cost of just <u>\$20m</u>, is obviously partly an artefact of the pandemic, and of the UK's National Health Service and its investment in <u>clinical research facilities</u>. But the concept of lower cost platform trials drawing on a pre-identified patient population ought not to be inherently more expensive when performed in, say, Nigeria instead of the UK.

Finally, and more generally, conventions regarding "certainty" and "significance" in clinical trials are not immutable; they are norms grown up around historical accident – including, notably, the calculations of an Irish beer scientist. When a clinical trial concludes that a medicine is worthless because the data show a 6% chance it has no effect, this reflects a deliberate choice. Evaluating whether this choice is the right one requires consideration, not just of the probability of being wrong (in this case, 94%) but also of the potential consequences of abandoning a working product. It is vanishingly unlikely that a statistical threshold originally designed to optimise the purity of Irish beer would be perfectly suited to determining the approval of a vaccine in Nigeria.



We can't set the right priorities without the right data

Above, we consider the evidence that funders are rationally responding to their successes and failures when deciding where to spend their money. Two new malaria vaccines don't obviate the need for different and better vaccines in the future, but it makes them less of a priority than a decade ago. A still-unproven late-stage TB vaccine doesn't mean we should abandon early-stage research on other candidates, but, at the margin, it probably means we should be spending less. The second approved therapeutic for onchocerciasis will probably provide less impact than the first.

Are funders striking the right balance between maintaining long-term commitments and responding to emerging priorities? While we certainly hope so, the reality is that we don't truly know – and we strongly suspect that funders themselves may not know either. Deciding how much funding to allocate to TB vaccines versus Chagas diagnostics, for example, is an incredibly complex optimisation challenge. This is further compounded by the fact that individual funders often make these decisions without a clear understanding of how much other funders are investing in each area.

We like to think that G-FINDER provides funders with part of that picture by helping them monitor what others have spent, are spending, and will spend on a particular area; and by helping them identify other candidates and where they sit in the pipeline. However, knowing how much is being spent is only a starting point. Leading funders like Wellcome and the Gates Foundation refine their decisions by weighing each candidate's probability of success, likely impact on clinical practice, and alignment with existing pipelines. Peer review and expert panels also shape funders' priorities, though repeatedly relying on the same voices can introduce biases.

Estimating how many lives a yet-to-be-developed vaccine might save is daunting, but focusing on impact rather than just regulatory approval helps to keep the interests of patients at the heart of R&D decisions. As with the M72 TB vaccine, looking at a product's role in actual communities can guide not only how much funding it deserves, but how well it complements or replaces other tools, ensuring resources genuinely improve lives where they're needed most.

Prioritisation is a particularly fraught debate in global health because almost everything we could be researching is, in some sense, incredibly worthwhile. When the average return on R&D funding is more than 400 to 1, even our least promising ideas will deliver health improvements worth ten times what we spend on them. Inevitably, though, some ideas will be more promising than others. Funders need robust data – not wishful thinking or guesswork – to identify the most promising opportunities and ensure each investment has the strongest possible impact.

Figure 14. Projected DALYS averted, by product, 2024-2040



As funders strive to build complementary portfolios that maximise impact, it is vital that they regularly revisit past allocations with the benefit of new evidence. In that light, it is encouraging to see funders actively redirecting their efforts in response to changes in burden, and in the product landscape, to where past successes and failures point them next, making smart choices to drive future breakthroughs in global health.