

POLICY CURES RESEARCH.

Neglected Disease Research and Development:

The status quo won't get us there

EXECUTIVE SUMMARY

Each year since 2007, the G-FINDER project has provided policy-makers, donors, researchers and industry with a comprehensive analysis of global investment into research and development of new products to prevent, diagnose, control or cure neglected diseases in developing countries. This is the fifteenth annual G-FINDER report, presenting data on investments made in 2021.

OVERVIEW OF 2021 NEGLECTED DISEASE FUNDING

Funding for neglected disease R&D in the second year of the COVID-19 pandemic looked a lot like it did in the first. Overall funding was almost unchanged at \$4,137m, with most of the apparent fall of \$44m resulting from the absence of Indian funding data.

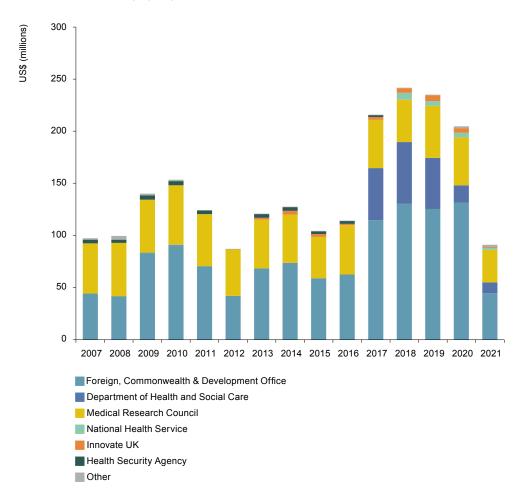
Clinical development and private sector funding, which had begun to raise concerns following consecutive drops in 2019 and 2020, rebounded. Funding to Product Development Partnerships (PDPs) fell, again, to another record low. Research and development continued its long-term shift away from vaccines and towards drugs and biologics. Investment in the WHO neglected tropical diseases (NTDs) continued to languish, with a disproportionate share of their funding again provided by the US National Institutes of Health (NIH).

Global funding remained highly concentrated: the NIH, Gates Foundation and pharmaceutical industry accounted for almost three quarters of the total. The same top ten funders who provided 88% of total funding a decade ago still accounted for 88% in 2021; organisations that began their funding over the last ten years accounted for just 2%.

There was at least one big, worrying development in 2021: funding from the United Kingdom government fell by more than half. This was a drop of nearly \$114m, which coincided with the UK's departure from the EU – reflected in the cratering of its contributions to the European & Developing Countries Clinical Trials Partnership (EDCTP) – and its implementation of a lowered target for official development assistance (ODA). Alongside the sudden near-absence of contributions to the EDCTP, the UK also reduced the neglected disease funding it provides directly to low- and middle-income countries (LMICs), as well as its R&D funding for COVID, for non-COVID emerging infectious diseases, and for sexual & reproductive health.

Even with big cuts from almost every UK funding agency, it was still, depressingly, the second largest national funder of neglected disease R&D – behind the United States – underscoring how dependant funding remains on potentially volatile commitments from a few big investors. There is some room to hope that this particular change will prove temporary: the UK's previous, more generous ODA target has been restored as a matter of policy (though not yet in practice); and adapting its funding mechanisms to the realities of Brexit will presumably get easier with time. But, for now, it is extremely worrying that one of the major drivers of global funding growth since 2017 seems to be considering giving up the fight against neglected disease.

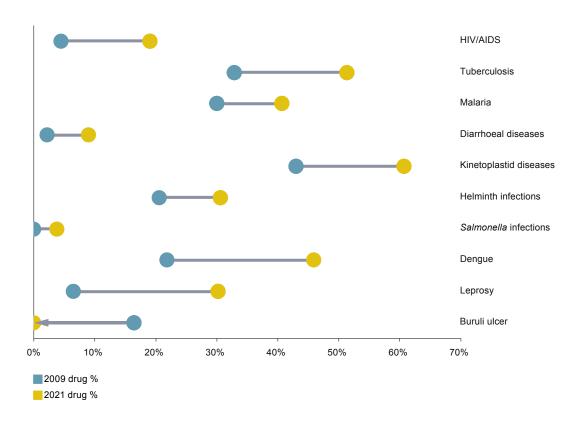
UK funding by organisation 2007-2021



The UK aside, whether three years of relative stasis in global funding represents pleasing consistency or disappointing stagnation is very much in the eye of the beholder. The 'glass half full' view is that funding remains historically high, even in the face of a pandemic. The pessimistic response is that growth is stalled, actual progress insufficient and the real threat to funding just around the corner – likely in the form of post-pandemic cuts to public funding. The optimist could point out that we gave the same warning last year.

Mostly, though, 2021 represented an emphatic continuation of the ongoing trends. Funding for drug R&D, for example, finally overtook funding for vaccines. This was the culmination of a gradual trend, one which saw vaccines go from receiving \$850m more than drugs in 2009 to \$12m less than drugs in 2021. This rise in drug funding could just reflect increased funding directed to diseases for which vaccines are out of scope (like dengue) or impractical (like snakebite). But, for the most part, it doesn't. Instead, almost every disease with drug funding in 2009 has since increased its share of overall funding going to drug R&D. The share of TB drug funding, for example, rose by 18 percentage points since 2009, HIV's by 15 and malaria's by 11.

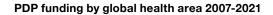
Share of disease funding for drug R&D, 2009 versus 2021

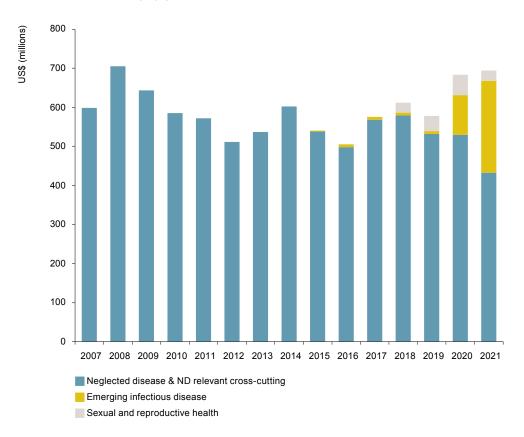


There's no single, obvious explanation for the shift in global R&D funding away from vaccines in favour of drugs (and, in recent years, biologics). Some of it is because earlier vaccine funding has led to successful product launches, or, conversely, ended in high profile failure. The remaining shift is – we hope – the result of individual funders making sensible decisions based on the available investment opportunities. But it still seems a bit odd. Partly because individual vaccines typically cost a lot more to trial; partly because it comes alongside growing concerns about microbial drug-resistance; and maybe also because it doesn't at all resemble the R&D response to COVID, which spent four times as much on vaccines as it did on drugs.

Unrelated, but also somewhat mysterious, are the ongoing falls in funding to PDPs – punctuated this year by a new record low. PDP funding has now fallen from a peak of more than \$700m in 2008 to \$433m, a drop of nearly 40%. This year's fall was mostly due to \$87m in cuts from the UK's Foreign, Commonwealth & Development Office (FCDO), which headlined the sweeping cuts to UK funding. But the overall post-2008 downward trend is a result of ongoing reductions from USAID – down by \$44m, or 51% – and especially the Gates Foundation. Overall neglected disease R&D funding from the Gates Foundation is down about 15% from its peak in 2008. But its PDP funding has fallen by more than 60% – dropping in 11 out of the last 13 years, by a total of \$270m.

While we can point to the biggest shifts in PDPs' funding – PATH's is down \$76m (52%) since 2008, IPM's by \$52m (73%), Aeras and OneWorld Health have both wound-up – we don't have a firm explanation for *why* funding keeps falling. At least some of it, as illustrated below, seems to be a reallocation of the funding given to PDPs away from neglected disease R&D toward sexual & reproductive health (SRH) and emerging infectious diseases (EID), especially COVID-19.





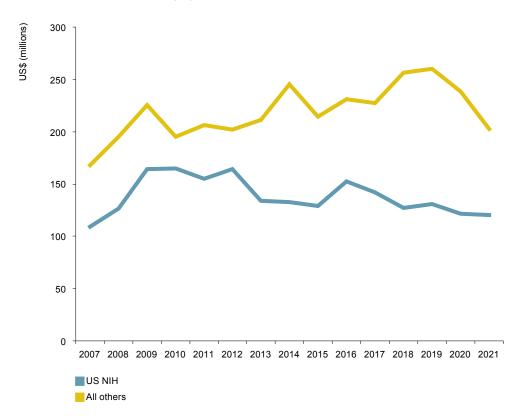
It's hard to know whether this represents a complete explanation of the longer-term decline, because we only began collecting this data relatively recently: since 2014 in the case of EIDs and 2018 for SRH. But it does suggest that our headline neglected disease figures exaggerate the fall in PDP funding – that there may have been a shift in focus rather than a loss of relevance. Perhaps inevitably, we want to see more data before drawing any concrete conclusions.

There was one last mystery in the 2021 data: how was clinical trial funding able to rebound in the second year of COVID? The data from 2020 presented a relatively straightforward, if worrying, conclusion: clinical development was down sharply because the pandemic was disrupting clinical trials, and private sector development was down most of all because companies report actual money spent, not just funding disbursed to product developers that year. Then, in 2021, clinical development (and private sector funding) bounced back, to basically 2019 levels. This is obviously good news; and a reminder not to spend too much time interpreting the fluctuations of something as inherently lumpy and unstable as clinical trial expenditure. But it's also a little unusual. Global hours worked bounced back in 2021, but remained significantly below where they were pre-COVID; but clinical trial funding (and as near as we can tell, actual spending) was close to its pre-pandemic level. Our best guess is that measured funding rebounded without necessarily achieving a complete restoration in actual R&D, as was the case in many sectors of the pandemic-hit economy. With luck, the effect of a pandemic on neglected disease R&D remains an historical curiosity, and we continue to enjoy a return to (near-record) pre-COVID levels of clinical development and private sector funding.

One area where the status quo clearly *wasn't* ok was funding for the WHO neglected tropical diseases, which has stagnated for more than a decade. Here, sadly, things got worse. Funding for the WHO NTDs fell by more than 10%, to their lowest ever share of global funding.

Since growing rapidly between 2007 and 2009, funding for the WHO NTDs has trended down at a little under \$1m a year, despite the addition of several new diseases. The sharpest downward trend has been for kinetoplastid R&D, falling by an average of \$1.5m every year. In 2021, both trachoma and Buruli ulcer saw their (participation-adjusted) funding fall by more than two-thirds, each dropping to well under \$1m for the first time. Kinetoplastid funding also reached a record low, while funding for leprosy fell to its lowest level since 2007.

WHO NTD funding by NIH and all others 2007-2021



The long-term stagnation of NTD funding, punctuated by brief periods of intense funder disinterest, reflects a world where almost every disease is heavily reliant on the NIH, and the NIH has been gradually reducing its funding for more than a decade.

But, during the pandemic, the world demonstrated that given enough funding, it's possible to create novel health technologies very quickly indeed. The US Biomedical Advanced Research and Development Authority (BARDA) – the largest single funder of COVID R&D – devoted a total of \$265m to the successful development of 25 different COVID diagnostics, based on 14 distinct technologies. This puts the total cost of rapidly developing a novel diagnostic – by far the cheapest area of product development – at somewhere between \$11m and \$19m. By contrast, if we look at all the areas of unmet need across each individual neglected tropical disease, the median annual contribution to each of these unfilled product categories is just \$0.8m. This is less than one three-hundredth of what a single funder spent on COVID diagnostics, and implies a multi-decade timeline for the development of even the least expensive new technologies.

Optimism about directing sufficient attention to diseases which are, by definition, neglected, is hard to come by. There has been a slight uptick in industry investment (still just \$69m across all NTDs in 2021) and a related increase in clinical development (averaging over \$90m in the last four years compared to \$45m a year over the preceding decade). NTD funding also looks slightly better if we consider disbursements from intermediary organisations – particularly the EDCTP – which we don't include in our headline figures to avoid double counting the funding they receive. But we don't currently seem to have a credible pathway to meeting the unmet needs of populations burdened by NTDs. Beyond annual pleas to the same ten or twenty funders to – please – provide more funding, real progress requires a way of upending a status quo that allows these diseases to fester, destroying lives and crippling development, year after year.

The remainder of this document provides a brief summary of the other headline findings from the full G-FINDER report – available at https://www.policycuresresearch.org/2022-g-finder-neglected-disease/

A Need for Novel Diagnostics: Meeting the Moment

FUNDING BY DISEASE

Most of the \$44m headline decrease in global funding for neglected disease R&D was due to a small net drop in survey participation, particularly the absence of funding data from India's ICMR and BIRAC, who collectively accounted for nearly \$64m in 2020. Higher inflation and the depreciation of most currencies against the US dollar (which we use to aggregate global funding) also depressed the measured total by more than \$25m – although some of this was probably artefactual rather than a genuine fall in buying power. In real terms, total funding was almost unchanged from 2020.

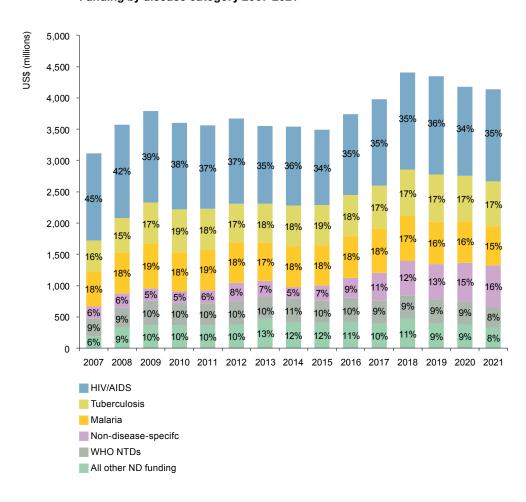
The survey's scope was likewise almost unaltered, with the only substantive shift being the introduction of a standalone category for biologics-related platform technologies, funding for which had previously been captured under other platform categories.

At the disease level, HIV/AIDS, tuberculosis and malaria received the largest shares of funding, as they have every year, accounting for just over two-thirds (68%, \$2,815m) of reported global investment. Funding for HIV/AIDS increased while malaria saw a substantial decrease, and funding for tuberculosis remained basically unchanged.

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

Funding for the WHO neglected tropical diseases (NTDs) covered by the G-FINDER survey totalled \$323m, down \$37m (-10%) from 2020. This marked two years of decline from their short-lived peak in 2019, which itself followed a decade of near stagnation.

Funding by disease category 2007-2021



FUNDERS

As in all previous years, the lion's share of public funding came from high-income country (HIC) governments (\$2,561m, 95% of public funding, and 62% of the global total), with the balance split between multilateral organisations (\$79m, representing a record-high 2.9% of public funding) and low- and middle-income country (LMIC) governments (\$45m, 1.7%).

HIC public funding fell by \$70m (-2.7%) after three years of record and near-record funding. The US government continued to be the largest public funder, at \$1,963m, accounting for over three-quarters of total HIC public funding. The EC became the second largest contributor for the first time since 2015, as its funding increased to a record \$202m (7.9% of HIC public funding), while disbursements from the UK government – previously the second largest funder since 2016 – fell by more than half to \$91m (down \$114m, -56%).

The steep headline fall in LMIC funding is a result of the near-total absence of funding data from India – the top LMIC funder every year since 2008 and provider of nearly three-quarters of 2020's LMIC funding. Public LMIC funding from ongoing survey participants increased slightly (up \$3.1m, 9.7%), though this change is liable to be swamped by any 2021 shifts in the (currently missing) Indian funding data.

Multilateral funding rose by \$22m (39%) following two years of decline, contributing a record 1.9% of global funding and a near-record \$79m – just below its 2018 peak. This is thanks to Unitaid, which has built its investment from just \$0.4m in 2012 to \$75m in 2021, giving it a 95% share of multilateral funding.

Philanthropic organisations again provided a fifth of global funding (\$842m), a drop of \$22m (-2.5%) which still left it at its third-highest level ever. An increase from the Gates Foundation and substantial cuts from 2020's other top funders reversed some of the recent diversification in philanthropic funding.

Private sector funding rose to \$608m, rebounding to 2019 levels and making up nearly 15% of the global total. Multinational pharmaceutical companies ('MNCs') continued to provide most of the private sector R&D funding (\$552m, 91% of the private total), reaching their third-highest level ever. This was a result of increased support for late-stage drug R&D, particularly for HIV/ AIDS and tuberculosis. Small pharmaceutical & biotechnology firms ('SMEs') accounted for the remaining \$56m. The headline increase in SME investment was a result of a new participant reporting the first ever investment in cryptococcal meningitis by an SME, with funding from consistent survey participants down by \$3.1m (-6.6%).

FUNDING FLOWS

A little over three-guarters (76%, \$3,149m) of all funding for neglected disease basic research and product development in 2021 was directed externally via grants or contracts, while the remaining 24% (\$988m) was spent internally via intramural or self-funded R&D. This is broadly in line with last year's shares.

External funding fell for the third straight year. The entirety of the \$42m drop was in funding to PDPs (down \$97m, -18%), driven by an \$87m drop in funding from the UK FCDO. The decline in PDP funding was partly offset by a \$33m (17%) increase for non-PDP intermediaries - predominantly from the EC to the EDCTP - and a \$22m (0.9%) rise in funding directly to researchers & developers.

Reported internal funding was relatively stable. After adjusting for the absence of intramural funding data from the Indian ICMR, though, it actually increased by \$46m (5.0%), thanks to a \$70m rise in self-funding from MNCs.

Funding to PDPs hit a record low of \$433m in 2021 (an 18% decrease from 2020). Some of this fall reflects the shift of funders' contributions to emerging infectious diseases - as outlined earlier - alongside the longstanding downward trend in funding to PDPs as intermediaries for neglected disease R&D. This particular fall was driven by UK FCDO, previously the second largest funder of PDPs, as it reduced its investments by two-thirds (down \$87m, -66%).

Funding to basic & early-stage research fell by 8.2% (down \$159m), reversing the growth seen since 2017 and leaving it just above its 2016 level. Investment in clinical development & post-registration studies rebounded by 9.1% after two years of decline, with much of the \$106m increase concentrated on drugs (up \$149m, 35%) and biologics (up \$4.0m, 7.8%).

Additional analysis of the 2021 funding landscape is provided in the full G-FINDER report, available at https://www.policycuresresearch.org/2022-g-finder-neglected-disease/. The underlying data can be viewed using our data portal at https://gfinderdata.policycuresresearch.org/

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