

Neglected Disease Research and Development: The higher cost of lower funding

EXECUTIVE SUMMARY

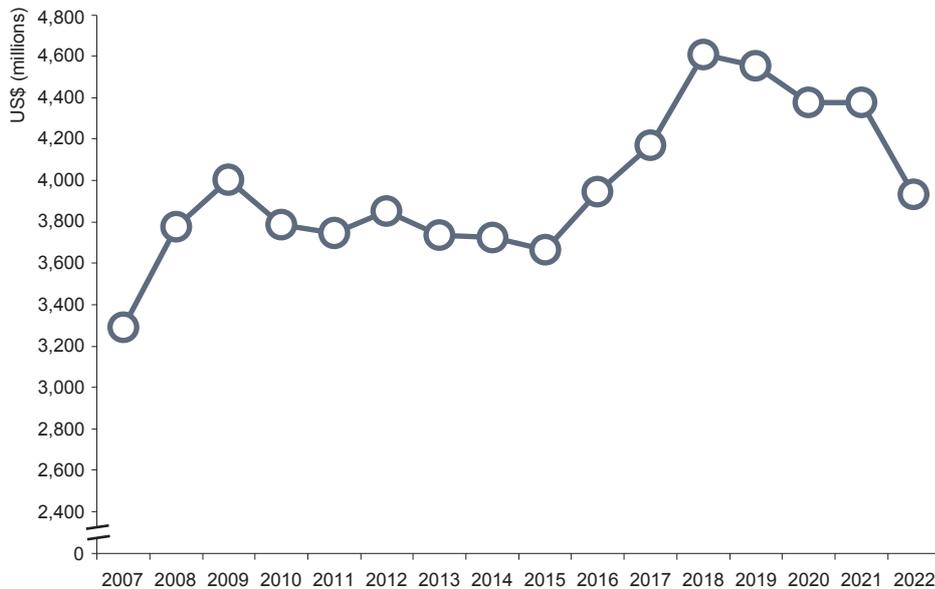
Each year since 2007, the G-FINDER project has provided policymakers, donors, researchers and industry with a comprehensive analysis of global investment into research and development of new products to prevent, diagnose, control or cure neglected diseases in low- and middle-income countries. This is the sixteenth annual G-FINDER report, presenting data on investments made in 2022.

KEY TAKEAWAYS

- **Global funding for neglected disease R&D fell by 10% in 2022, mostly due to increased inflation reducing its buying power.** Although less concerning than a policy choice to reduce funding, this still impacts product developers' ability to plan and conduct R&D. Funders should consider indexing the value of long-term grants to inflation.
- **Funding from industry rose to its second highest level ever, including record highs across several diseases.** This is good news, but highlights tensions within our definition of 'neglect', which requires the absence of commercial incentive. Even if some of this funding is spillover from increasing concern about tropical diseases spreading to high-income countries, we should still aim to lower barriers to market access in LMICs and foster incentives for industry investment, so that even small markets become commercially viable.
- **Biologics R&D more than doubled in the three years to 2022, with key funders reducing their funding to vaccine R&D over the same period.** Biologics could represent a valuable part of the toolkit for fighting neglected diseases, but have yet to prove they can be distributed at scale in low resource settings. New monoclonal antibodies for RSV could provide proof of concept for using biologics in LMICs.
- **The neglected disease pipeline has increased in size by 55% since 2015 and has matured significantly.** The share of products in clinical trials rose from 40% to 56% in that period. But with high attrition we may not have enough candidates in the pipeline to meet the product needs across the neglected disease landscape.
- **We still lack a good measure for how much funding is 'enough', but all indications are that we should be spending more.** We can compare neglected disease R&D funding to other sources of global funding, but it's more informative to look at the actual health impact delivered by new products. The early returns from this investigation point to over a hundred dollars of return on R&D spending for every dollar invested.

OVERVIEW OF 2022 NEGLECTED DISEASE FUNDING

Total R&D funding for neglected diseases 2007-2022



After three years hovering just below its 2018 peak, global funding for neglected disease R&D fell sharply to \$3.93b in 2022, a drop of 10%, or \$446m – mostly concentrated among public and philanthropic funders.

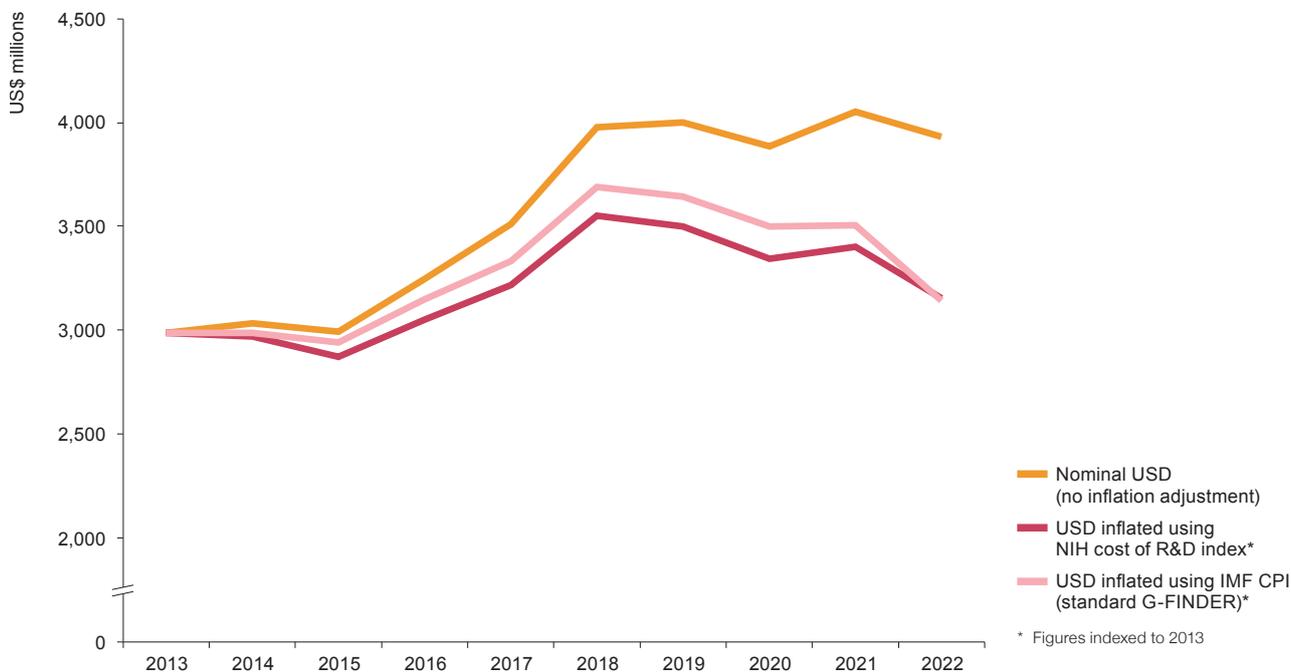
Mostly, this big drop was due to rising global inflation. Funding in dollar terms was down, but only by about 3%. The rest of the reduction was because of how we index disbursements every year to reflect changes in their estimated buying power – what economists call ‘real’ funding.

How worried should we be about a drop in funding that’s mostly just inflation?

That depends on whether we’re doing a good job measuring how changing prices actually affect the buying power of R&D funding. We use an index of consumer prices (the ‘CPI’), but product developers aren’t ordinary consumers, and they buy different things – more lab coats and many fewer used cars. The US NIH deals with this problem by creating its own price index for the things it buys, and this NIH index – the darker red line in the graph below – shows that R&D costs went up less than other parts of the economy, by 4.9% compared to the overall 7.0% consumer price inflation in the US. So the drop in real NIH funding was probably a bit smaller than we’ve calculated, and that might well be true of other funders in other nations as well.

Why didn’t we just use the NIH price index, then? Mostly because it’s pretty specific to the NIH. It turns out that most of the change in R&D costs is not lab coats, it’s researchers’ wages. And the amount the NIH could pay its researchers in 2022 was fixed by a law that doesn’t apply to other funders, and probably won’t be enough to hold down the cost of recruiting and retaining scientists in the long term. So, for now at least, we’re more comfortable tying our measure of buying power to changes in the overall cost of living.

Neglected disease R&D funding adjusted for inflation



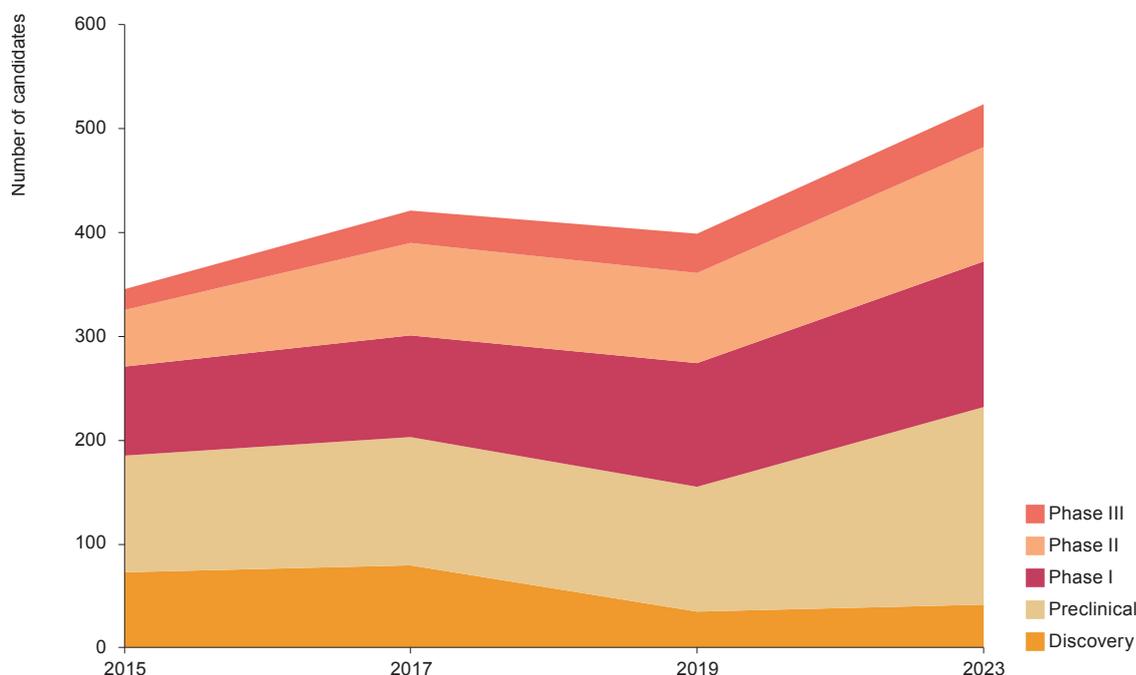
With that in mind, one comforting way to interpret a drop in funding from unexpected inflation is that funders mostly didn't really *decide* to cut their funding. It was something that happened to them, not something they chose. When the UK sharply cut its public funding while leaving the EU in 2021, it looked like a policy choice, one that would need to be reversed if funding was to return to previous levels. This time, though, the number of dollars, pounds and euros being disbursed fell only a little, but we calculated that these mostly fixed value long term grants were *worth* less, because they bought less actual R&D.

If this means that reported public and philanthropic funding rebounds in 2023 once funders begin taking higher prices into account (our new [Compass](#) real time data updates mean we'll know soon), we can hopefully breathe a sigh of relief. But it would still mean a year of reduced progress and disruption as product developers struggled with fixed grants that were no longer enough to pay for the things they were supposed to. In a world where inflation seems substantial and unpredictable, it might make sense for funders to index the value of their long-term grants to future changes in the price level, so these kinds of unplanned cuts don't devalue their investments.

One piece of evidence indicating that the record drop in public funding could be just transitory is that funding from the private sector – where we measure hours worked, not the annualised value of long-term grants – *didn't* fall. Instead, industry funding rose, by \$24m (3.9%), to \$640m – its second highest level ever. Big pharma companies invested record amounts in dengue therapeutics, *Salmonella* infections, leprosy, mycetoma and hepatitis B, and smaller companies also provided record high funding for dengue, and made their first substantial investments in LMIC-focused vaccine platforms.

Increased funding from industry is great news, and lines up with the progress we've seen in the product pipeline over the last few years. The actual number of products captured in our newly released [pipeline database](#) has risen by more than half since 2015, with the shares of products in preclinical development and clinical trials switching: from 56% preclinical and 44% clinical development in 2015, to 40% preclinical and 60% in clinical development in 2023.

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



Now that much of the necessary basic and early-stage research has been done, in many cases the torch is being passed to the private sector to take products through clinical development to registration and roll out. One concern is that we could end up running out of investigational candidates before we get to that point, and having to restart the process from scratch. But provided there are enough promising candidates to survive the inevitable attrition during clinical development, and that we eventually see a similar rise in late-stage clinical trials (only 8% of pipeline products have made it as far as Phase III), we could be poised to benefit from a faster rate of product launches and greater involvement from the private sector in taking those candidates to market.

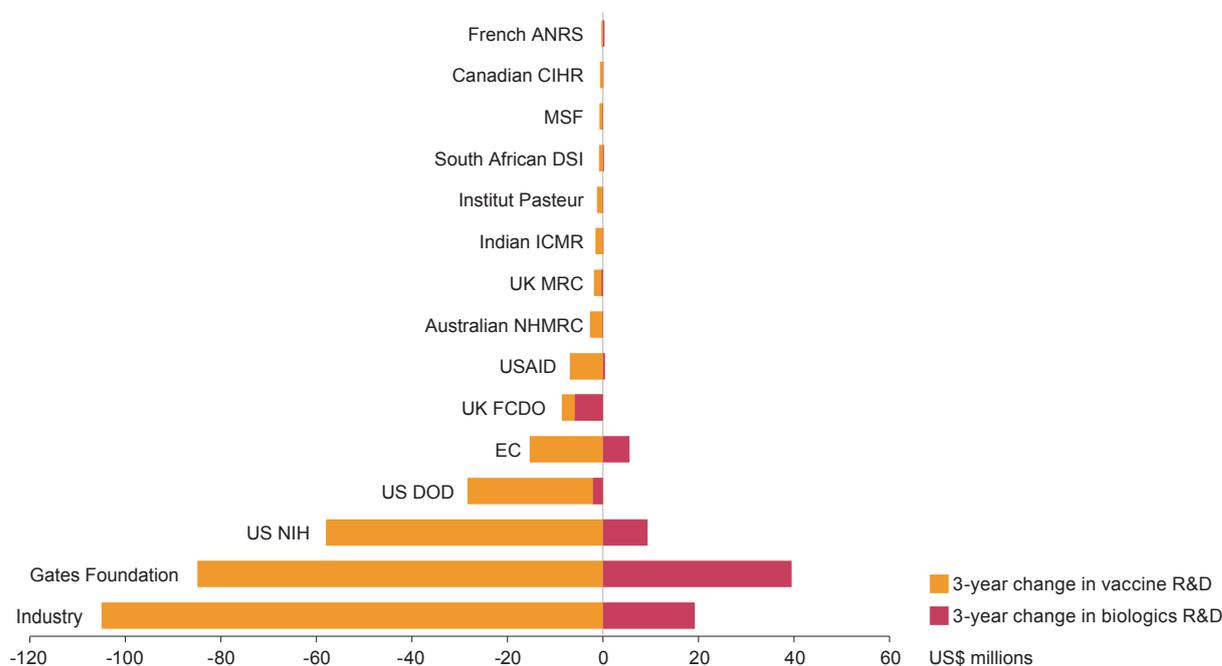
'Market', though, is a bit of a loaded term when talking about neglected disease. We generally assume an area of unmet need qualifies as 'neglected' only if it lacks enough commercial incentive to create a working market. Sometimes, an area like vaccines for dengue fever receives significant private investment, because there is demand in higher income countries – or from tourists, or the military – alongside unmet need in LMICs. In those cases, we usually conclude that that particular area is no longer neglected, and remove it (and all of the associated spending) from our survey's scope.

So record funding from both small and large pharmaceutical companies for dengue R&D – centred on (still in-scope) drugs and biologics – is good news for low-income nations where dengue is endemic. But it does also make us worry that something similar to dengue vaccines might be happening to dengue therapeutics: that these investments are being made not *despite* their being unprofitable, but because they no longer are.

This highlights the delicate balance in celebrating increased private sector R&D in diseases where, by definition, there is insufficient incentive for private sector R&D: success makes us wonder whether we have correctly defined the problem. With climate change causing many tropical diseases to spread further from the equator, and diseases like Chagas', dengue, malaria and even leprosy experiencing community transmission in the US, high-income countries will likely start viewing investment in neglected disease as an investment in their domestic health.

As for the rest of the neglected diseases: how *do* we encourage commercial markets for issues and in places that can't support one? Part of the solution is probably just acknowledging that (fortunately) the list of areas that are genuinely neglected will shrink as (unfortunately) their diseases spread to the rich world. The other part is by trying to make small, underfunded markets more profitable, by making them more attractive, cheaper and easier to enter. This means incentives like encouraging multi-arm trials, especially of repurposed products already making money in other areas, advance purchase commitments, and making sure registration and market access for proven products is quick and reliable.

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



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

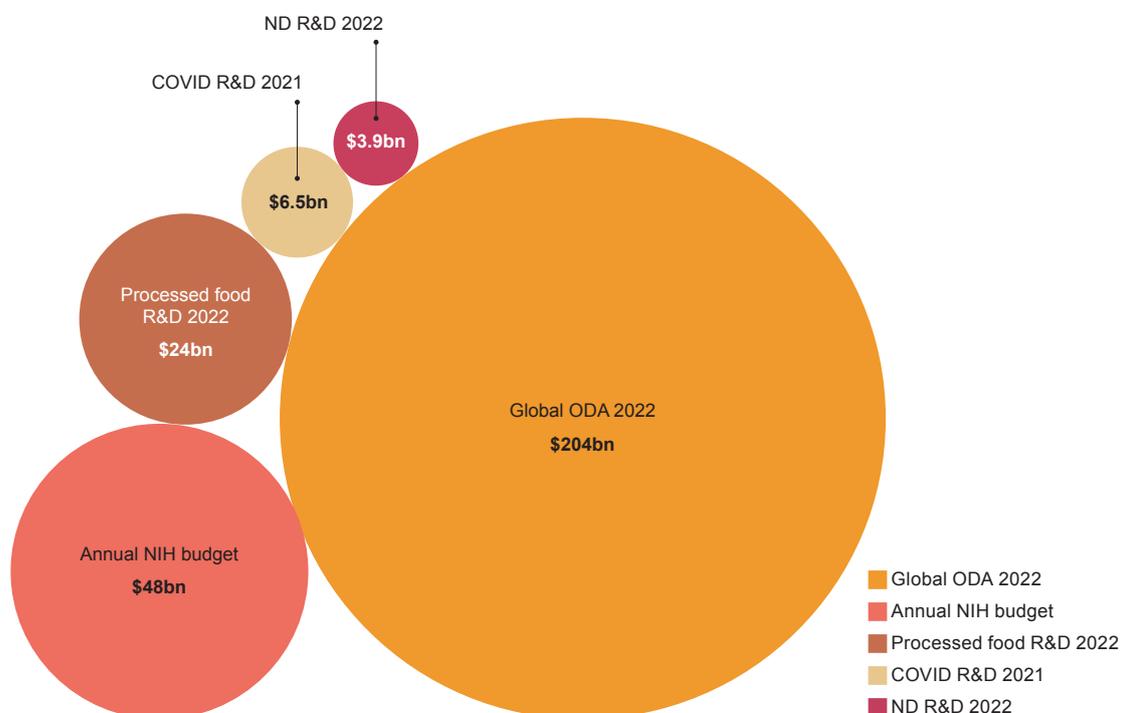
Some of the rise in private investment looks like this – products already registered elsewhere or for other diseases being trialled against neglected diseases because the costs of entry are low enough to justify chasing even a small market, like that for cryptosporidiosis – which has been the subject of trials using a general-purpose antifungal. But much of the growth in global funding over the last three years has been in next generation large molecule biologics, mostly monoclonal antibodies ('mAbs'). Funding for these biologics has more than doubled over three years, leaping from \$70m in 2019 to \$144m in 2022 – and rising by a factor of 85 from early last decade. Biologics funding from the private sector, in particular, rose more than fivefold in 2022, to a record \$23m.

These large molecule treatments are quite the opposite of low-cost repurposed therapeutics. They rely on much newer technologies – as evidenced by their rapid growth – can be finicky to produce and distribute at scale, and are vulnerable to the emergence of variant strains– all reasons why the impact of (costly) biologics on COVID was relatively limited compared to (cheap) repurposed small molecule therapies like dexamethasone. Big increases in biologics funding over the past few years has assisted the development of mAbs that can be used against malaria and HIV, but has also left questions about whether the resulting products can be adapted to LMIC needs. This matters a great deal, particularly since the data show individual funders – and their programmes for individual diseases – shifting their funding away from vaccines and towards biologics.

One area where biologics could provide helpful proof-of-concept for use in LMICs is with new products like nirsevimab, mAbs for use against paediatric respiratory syncytial virus, which offer extended duration of action, hopefully at lower cost than existing alternatives. A successful roll-out showing that mAbs like these can be distributed at scale, even in low resource environments, would help demonstrate that biologics can deliver real world impact in LMICs – and make us worry less about funding seemingly being diverted from vaccine R&D.

Beyond the types of products which deserve more investment, though, is the overarching question of how much R&D funding is ultimately 'enough'. We would obviously rather live in a world where there was no trade-off between money for vaccines and money for biologics, but we recognise that funding will never be unlimited. Constantly calling for 'more' needs to be accompanied by some indication of when we would be satisfied.

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



The G-FINDER survey allows us to look at how global funding has evolved over time; and our new [Compass](#) forward looking data collection gives us some idea of what might happen in the near future based on funding announcements – including a slight rebound in PDP funding and a big Gates Foundation investment in TB vaccines. But neither gives us any normative basis for judging whether funding is, has been, or will be sufficient for LMIC’s needs.

One option is to compare neglected disease R&D to other, vaguely similar pots of money, or to frivolous things industry spends its money on. Although this gives a sense of scale and of global priorities, it doesn’t really answer the question either.

Instead, we might look at whether current levels of investment provide value for money. Our [Evidence for Impact](#) project, which is working to estimate the impact that investment in technologies we invested in between 1999 and 2022 have had, and will have, on global health, offers a good starting point. But determining how many lives were saved by new technologies launched over that time is a complex, messy calculation. Figuring out the future impact of the products still in the pipeline is even harder. And putting a dollar value on those gains is a philosophical challenge as much as a mathematical one. The early returns, though, are extremely promising: our early estimates show that every dollar spent on neglected disease R&D yielded more than a hundred dollars’ worth of impact – in lives saved, morbidity treated or averted, and reduced burden on the health system.

It’s fair to say, then, that we ought to be spending much more on neglected disease R&D: we are passing up an opportunity to turn every extra dollar we spend into hundreds of dollars’ worth of impact. In ten year’s time, instead of talking about stagnation or decline, it would be nice to look back on a decade-long flood of funding into neglected disease R&D, and be able to say that we finally found the resources, and the will, to take advantage of opportunities to make the world a much better place at a relatively trivial cost.

FUNDING BY DISEASE

Global funding for neglected disease R&D fell by \$446m in 2022. Funding from continuing survey participants fell by the same percentage as overall funding and a slight net decrease in survey participation made almost no difference to the headline change.

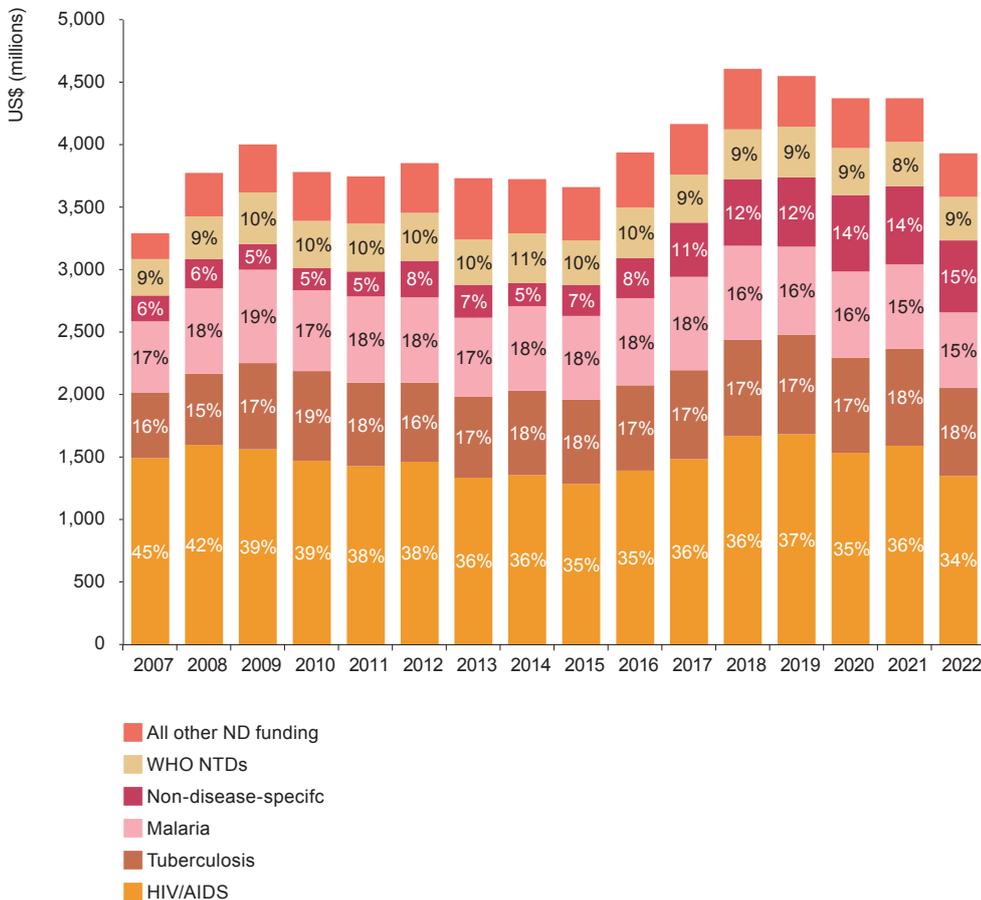
Increased global inflation in 2022 was the main driver of the overall fall in funding, which eroded the real value of R&D funding even as nominal dollar amounts remained relatively stable. In the absence of any inflation, global funding would have fallen by only 3.0%, far below the inflation-adjusted decrease of 10%.

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

Most individual disease areas saw reductions, with several – including Buruli ulcer, trachoma and kinetoplastid diseases – experiencing record lows. Even non-disease specific funding, which had grown every year since 2014, fell (down \$52m, 8.2%) as a result of reduced core funding to multi-disease R&D organisations.

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

Funding by disease category 2007-2022



FUNDERS

As in all previous years, the lion's share of public funding came from high-income country (HIC) governments (\$2.38b, 94% of public funding, and 61% of the global total), with the balance split between low- and middle-income country governments (\$91m, 3.6% of public funding) and multilateral organisations (\$49m, 1.9%).

Funding from HIC public funders fell by a record \$344m (-13%), with almost two-thirds (63%) of this decline the result of reductions in funding from the US government (down \$216m, -10%). Despite this, the US government share of total HIC public funding actually rose, to a near-record high of 81% as most other nations made even deeper cuts.

Funding from multilaterals saw a significant decline from the previous year's record high of \$88m (down \$39m, -45%), driven by Unitaid (down \$39m, -49%) which ended several of the projects that had driven the spike in its 2021 funding.

Funding from LMICs fell to its lowest level since 2015, dropping 13% (down \$13m) to \$91m in 2022. After adjusting for changes in survey participation, there were substantial drops from the top funders, India and Brazil. Contributions from Argentina, Thailand and Mexico also dropped significantly, with each of these nations reporting less than \$1m in 2022 funding.

Philanthropic organisations again provided a fifth of global funding (\$767m), albeit after a drop of \$71m (-8.5%). Almost all of the decline was the result of reduced investment from the previous year's top three philanthropic funders: the Gates Foundation (down \$39m, -5.9%), Wellcome (down \$20m, -16%) and Open Philanthropy (down \$10m, -58%) – though the fall from Open Philanthropy was partly an artefact of front-loaded project funding in previous years.

Private sector investment rose to \$640m, to its second-highest level ever, making up 16% of the global total. Multinational pharmaceutical companies ('MNCs') continued to provide most of the private sector R&D funding (\$577m, 90% of the private sector total). Their funding for the WHO neglected tropical diseases reached a record high of \$92m after increasing by more than a third (up \$24m) – mostly for dengue and helminth infections. Small pharmaceutical & biotechnology firms ('SMEs') accounted for the remaining \$63m. Adjusting for a fall in survey participation, though, funding from SMEs actually grew by almost a third (up \$15m, 33%), leaving it roughly in line with its long-term average. This increase was largely the result of the first substantial funding reported from SMEs for platform technologies (up \$15m from less than \$0.1m in 2021).

FUNDING FLOWS

Just under three-quarters (\$2.92b, 74%) of total investment in neglected disease basic research and product development in 2022 was directed externally via grants or contracts, with the remaining 26% (\$1,014m) spent by organisations internally via intramural funding or self-funded R&D. Though this was broadly in line the last decade's shares, funding fell for both, with external funding down \$382m (-12%) and internal down \$65m (-6.0%).

Funding to PDPs fell for the fourth consecutive year (down \$110m, -27%) to its lowest level ever. This was driven by decreased funding from all top PDP funders, most notably the US NIH, whose funding to PDPs almost halved (down \$33m, -47%), and the Netherlands Ministry of Foreign Affairs (down \$16m, -69%). Funding to non-PDP intermediaries also dropped, by a quarter. The most prominent individual reductions were in the EC's funding to EDCTP (down \$15m, -14%) – partly reversing an even bigger increase the previous year – and the Japanese government's cyclical funding to GHIT (down \$16m, -59%).

Funding to basic & early-stage research fell by 10% (down \$203m), driven by the lowest funding for basic research since 2015, and record-low investments in early-stage vaccine and microbicide R&D. Funding for clinical development & post-registration studies also fell, by 16% (down \$207m), as a result of record-low vaccine clinical trial funding (down \$107m, -20%) and a sizable drop for drug clinical development (down \$61m, -10%).

Additional analysis of the 2022 funding landscape is provided in the full G-FINDER report, available at www.policycuresresearch.org/2023-neglected-disease-g-finder-report.

The underlying data can be viewed using our data portal at <https://gfinderdata.policycuresresearch.org/>

Our R&D pipeline tracker is available at <https://www.policycuresresearch.org/pipeline-database/>

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