The high return of investing in R&D for neglected diseases
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The question behind this project was a fundamental one: Are we doing the right thing by investing this money in R&D for poverty-related neglected diseases?

Certainly, those of us involved think so, but is it true? And if it’s true, can we quantify it? This deceptively simple question leads to further questions, revealing the staggering complexity of the task: what types of impact are important to different stakeholders, and how do we define them? How do we measure the impact of R&D for global health? And how do we assert the return on investing in R&D? Where does that return accrue? And for whom?

We started from the very beginning: defining impact. With our partners and community of experts, we debated the relevance and suitability of hundreds of output, outcome and impact measures related to investing in global health R&D. We elevated the top priority measures to form a first-ever global health R&D impact measurement framework and, from that, designed a methodology for assessing the impact of investment. With a validated approach in hand, we embarked on data collection, one of our specialities. We gathered a wealth of robust, foundational evidence on the landscape of funding, game-changing products, pipelines, and priorities for neglected disease R&D. This data served as the basis of our modelling efforts and impact analysis and has made the development of this report possible.

I won’t give away the key findings here, but I can safely say that the scale of the health, economic and wider societal impact identified in our analysis makes an ironclad case for investing in R&D for global health. No matter how you cut it, the return on investment to the communities impacted by these diseases and to our society as a whole is astounding, as are the broader, knock-on benefits that investing in R&D delivers.

As we look ahead, we recognise that the coming two decades are pivotal. You will see that much of the impact we estimate in this report will be delivered in the next 15 years and is predicated on a global ecosystem that can bring health innovations to scale, as well as one that continues to advance the pipeline and deliver the breakthrough technologies of the future.

Decision-makers will always face competing interests and budget pressures, but recent years have underscored the increasing burden of proof we face as a community to keep global health R&D on the agenda while grappling simultaneously with issues of climate change, financial crisis, war, and racial injustice. May this report serve as a key piece of evidence and insights to help meet that call.

I am invigorated by the potential contained in our findings but humbly acknowledge that there is still much work to be done. Where you may be inclined to think of Policy Cures Research as the stalwart, behind-the-scenes data folks, let this report serve as the harbinger of a new, more vocal role for PCR in the global health R&D community, conducting research and developing tools to inspire change.

Dr. Nick Chapman, CEO
Policy Cures Research
Impact highlights: 2000-2040

- 40.7m lives saved
- 2.83bn DALYS averted
- $49.7tn of net economic benefit generated
- $405 societal ROI
- 183 global health innovations
The insights in this milestone report, drawn from comprehensive literature reviews, sophisticated modelling, and extensive consultations with experts and stakeholders, underscore the considerable societal gains achieved through investments in global health R&D. Key findings include:

- **Millions of lives saved:** Between 2000 and 2040, at least 40.7m lives will be saved, and 2.83bn DALYs averted thanks to biomedical products for poverty-related neglected diseases. Most of these lives will be saved in low- and middle-income countries (LMICs) where populations are most affected by these diseases.

- **High societal return:** Every $1 invested in neglected disease R&D generates a return of $405.

- **Trillions of economic and societal benefits:** Averting 2.83bn DALYs generates $49.7tn in net societal benefit.

- **Many gains will occur in the future:** More than 70% of the health and economic impact is modelled to occur between now and 2040. If this benefit is to be realised, there must be sufficient ongoing investment in R&D to progress the pipeline and deliver the next generation of breakthrough global health products, as well as sufficient programmatic and health systems investment to scale up existing and new tools.

- **Successful product and candidate development:** 183 products targeting neglected diseases have been approved by a regulatory agency or prequalified by the World Health Organization (WHO) since 1999. Moreover, there are 752 active candidates in the neglected disease pipeline and sustained investment is expected to deliver another 182 lifesaving products by the year 2040.

This figure reflects the retrospective and prospective impact of products that have come to market in the last 20 years, as well as the anticipated impact of entirely new innovations that are expected to emerge from the pipeline between now and 2040. Continued prioritisation and expansion of investments in health innovation and solutions for neglected diseases will be essential in the coming years to realise the full extent of this gain.
With a clear, quantifiable and highly compelling picture of the health, economic and societal impact of investing in global health R&D, the R&D community can strengthen efforts to:

1. **Pursue collaborative mechanisms for financing global health R&D.** Funders, product developers and researchers must collaborate to explore new mechanisms for investing in R&D. This entails fostering more equitable power-sharing and resource allocation while leveraging policy to shape investment opportunities and regulatory strategies. Additionally, innovative financing models should be explored to ensure sustainable support for R&D initiatives.

2. **Focus on portfolio investment for greatest returns.** Attributing success in global health R&D can be challenging. However, continuing to coordinate priorities for the global health R&D agenda and promoting strategic diversification across various technologies, product types, and research avenues can mitigate risks and maximise impact.

3. **Optimise regulatory and access pathways to reduce the time from product approval to scale-up.** Use data and evidence to implement more streamlined clinical trial and regulatory approaches, enhance capacity in LMICs, ensure efficient product approval timelines, and plan access strategies at the earliest stages of product development. All of these require deeper collaborations across the entire R&D ecosystem to safely traverse the intricate investment-impact relationship, especially in areas prone to market failures.

4. **Recognise the strategic value of investing in impact assessment.** With a cohesive understanding of the nexus between funding, products and impact, all stakeholders in the R&D ecosystem will be better placed to develop impact-driven agendas and policies. Focusing attention on better demonstrating the impact of key challenging product types (e.g. diagnostics, vector control products) could accelerate investment and product development in these areas.

5. **Strengthen collaboration between R&D and access.** Ensure that the continuum of product development is aligned with efforts to improve access to healthcare, fostering synergies between research, development and implementation strategies. This entails integrating considerations for affordability, availability and accessibility throughout the R&D process, ultimately optimising the impact of innovations on global health outcomes.

Every $1 invested in neglected disease R&D generates a societal return of $405
Introduction

Global health R&D is one of the cornerstones upon which progress in global health and increased life expectancy have been achieved. New technologies and innovations have the potential to save and improve lives, drive economic growth, and strengthen health security.

According to the G-FINDER survey, over $63.5bn has been invested in R&D for neglected diseases between 2007 and 2022. Although neglected disease R&D represents a mere 1-2% of global spending on all health-related R&D, significant progress has been achieved during this period, generating hundreds of new products and a rich pipeline with the potential to save millions of lives around the world (1). This progress, coupled with major world events of the past five years, has accelerated stakeholders’ understanding of the significant impact and importance of this sector while shedding light on the complexity of the ecosystem and its shortcomings.

At the same time, there have been limited attempts to assess the full health and economic impact of the R&D investments made to date. A clear, quantifiable picture of the return on investment in R&D is essential for building the case for the next generation of funding to advance new breakthrough products and technologies. Policy Cures Research (PCR), with funding from the Bill & Melinda Gates Foundation, Open Philanthropy, and Wellcome, in partnership with Anthologie, Avenir Health, the African Population and Health Research Center (APHRC), the Center for Global Development (CGD), and the Stanford Innovative Medicines Accelerator (IMA), has worked since 2022 to assess the health and economic impact and return on investment (ROI) of funding in global health R&D under the umbrella of the Evidence for Impact (E4I) project.

In this report, we present the health, economic and societal impact of products that have launched since 1999 to tackle neglected diseases (as defined by the G-FINDER scope for neglected diseases (3)), as well as the anticipated impact of entirely new innovations that are expected to emerge from the pipeline between now and 2040. This included a rigorous modelling exercise, conducted in partnership with
Avenir Health, to estimate the lives saved, cases averted, and Disability-Adjusted Life Years (DALYs) averted between 2000-2040 thanks to these products.

Of note, the products in the G-FINDER scope are developed with R&D investment for diseases that suffer from poverty driven market failures. This means that, for example, for HIV/AIDS the G-FINDER scope only includes LMIC-specific costs for label-expansion clinical trials of new drugs and reformulations for LMIC use (e.g. paediatric or slow-release formulations; fixed dose combinations; low dose drug formulations for prophylaxis; long-acting injectables for treatment or prophylaxis).

We went a step further to calculate the net financial benefit of averting DALYs, growing the economy, investing in R&D, and transforming the health systems in endemic countries. Leveraging our in-depth knowledge of the historic R&D funding landscape, we also calculated the ROI of the funding responsible for advancing this product and pipeline landscape. We benchmarked this breakthrough ROI finding against other existing studies, providing valuable comparative insights and reflecting on the broader societal benefits that stem from investment in R&D.

Underpinning this modelling work is a suite of valuable data and tools which we have made available to the global health community for conducting ongoing R&D policy research and analysis. This includes a comprehensive database of products approved for neglected and emerging infectious diseases since 1999 (4), an updated database of the current R&D pipeline for neglected and emerging infectious diseases (including key attributes and organisations involved in their development), and a library of consensus R&D priorities mapped against pipeline candidates. We also delivered a global health impact measurement framework that can be used to track and assess the impact of investment in global health R&D going forward. This M&E/impact assessment framework (5) is made up of a diverse and consensus-driven set of key indicators (6), consisting of the most important and compelling measures of success of investment in global health R&D. It served as the basis for developing the impact narrative of this particular report and it is our hope that it will be used widely for ongoing impact assessment work in the future.

Demonstrating impact is necessary to justify continued funding of R&D. The impact framework provides a pathway for informed discussions on how to collectively articulate shared impact of different R&D investment streams and, ultimately, strengthen the progress in global health R&D activities.

We conclude the report by exploring the implications of our findings for shaping the future of investment in global health R&D and calling for collective action to accelerate the transformation of the R&D ecosystem to meet the needs of the most vulnerable populations.
Neglected disease R&D landscape

We first mapped the landscape of products and pipeline candidates (4), how they have evolved as a result of the past 20 years of investment in neglected diseases R&D, how these align with current R&D priorities and what product launches we might expect between now and 2040 based on the state of the pipeline. These findings served as the basis of the health and economic impact modelling and ROI calculation to follow.

Products

183 diagnostics, drugs, vaccines, microbicides and vector control products (VCPs) targeting neglected diseases have been approved by a regulatory agency or prequalified by the World Health Organization (WHO) between 1999 and December 2023. Figure 1 provides a granular breakdown of the approved products by product type and approval date.

Over the last decade, there has been an increase in product approvals for neglected diseases. 67% (123) were approved between 2013 and 2023, compared to just 33% (60) products from 2001 to 2012. We have also seen launches in entirely new product classes for neglected diseases in recent years, including:

- Biological vector control products like the “Friendly” mosquitoes – which target the Aedes aegypti mosquitoes that spread dengue fever, and
- Microbicides like the dapivirine vaginal ring – designed to reduce the risk of HIV/AIDS infection.

Biologics – large molecule therapeutics including monoclonal antibodies (mAbs) like those used in treating COVID-19 – have yet to breakthrough with marketed indications for neglected diseases within our scope, but a number of candidates are active in the pipeline and show significant promise such as those in clinical testing for malaria.

Of the 183 products approved for neglected diseases, 46% (85) target just three disease areas:

- 26% (47) malaria
- 11% (20) diarrhoeal diseases
- And 10% (18) tuberculosis (TB).

The remaining 54% (89) is split across 12 different neglected disease areas, though with a heavy focus on:

- 7.7% (14) leptospirosis
- 7.7% (14) hepatitis C
- 7.1% (13) HIV/AIDS
- 6.6% (12) helminth infections
- 6.6% (12) kinetoplastids
- And 6% (11) hepatitis B.
It should be noted that diagnostics and vector control products have been grouped by technology type to avoid counting similar ‘me too’ tests and painting an inflated picture of the product landscape. Even after this aggregation, however, far more diagnostics have been approved than any other product type. Many diagnostics are relatively simple and far cheaper to develop than drugs and vaccines. Furthermore, trials sizes necessary to demonstrate sensitivity and specificity are usually far smaller than those powered to show therapeutic or vaccine efficacy, so some tests can go from conception to approval in less than one year. Most diseases now have at least one approved diagnostic; the exceptions being histoplasmosis, hookworm, trachoma and scabies.

The 51 approved drugs for neglected diseases make up just more than a quarter of the total product landscape and represent more than three times the number of approved vaccines (16). While most disease groups now have at least one approved drug, just four have approved vaccines. Alongside the sole approved microbicide (for HIV/AIDS), 23 chemical vector control products have been approved – all targeting malaria-carrying mosquitos.

Over the last 20 years, game-changing products have significantly lowered the global burden of neglected diseases. However, there remain notable product gaps. Among them are vaccines for 11 of the 15 neglected disease areas, including HIV/AIDS, tuberculosis and rheumatic fever, drugs for Buruli ulcer and diagnostics for P.vivax malaria. These gaps and others should be borne in mind, especially as we discuss the pipeline, expected product launches and R&D priorities in subsequent sections.
**Pipeline candidates**

As of 2023, the neglected disease pipeline had 752 active candidates, representing 27% growth since 2019 (a net increase of 159 candidates after accounting for product launches). The most significant area of growth was in malaria vaccine candidates, which rose from 42 in 2019 to 65 in 2023. This is followed by diagnostics for helminths (an increase of 19 candidates), hepatitis B biologics (16), first captured in the pipeline in 2023, dengue diagnostics (15) and drugs (13), and diarrhoeal vaccines (12).

Currently, half of the neglected disease pipeline (376 candidates) is made up of candidates for three major diseases:

- 20% (151) malaria
- 15% (114) tuberculosis
- 15% (111) HIV/AIDS.

This broadly aligns with the allocation of R&D funding, where 71% of investment between 2007 and 2022 went to those three diseases. Most of the remainder are candidates for:

- dengue (44)
- hepatitis B (34)
- *S. pneumoniae* (27)
- leishmaniasis (24)
- and hepatitis C (23).

Despite significant growth in some areas, more than a third of the included neglected diseases have 10 or fewer candidates in the pipeline across all product areas combined. In many cases, this barren pipeline is coupled with a lack of approved products and persistently low levels of R&D funding. Most of these diseases clustered at the bottom of Figure 3 are among the WHO’s list of Neglected Tropical Diseases (NTDs), which have collectively seen a decade of stagnating R&D investment.

*Note: the ‘other diarrhoeal diseases’ category includes Shigella, cryptosporidiosis, and enterotoxigenic & enteroaggregative E. coli. Italicsed diseases are among the WHO Neglected Tropical Diseases*
Promisingly, 32% (182) of the vaccines and therapeutics pipeline has reached Phase II and III trials. The high cost of late-stage trials, and the 143 additional candidates still in Phase I, underscore the need for significant funding over the coming years to realise the potential for new product launches.

In contrast to the approved product landscape, which is largely made up of diagnostics and drugs, vaccines make up the most significant proportion of the pipeline:

- 37% (280) vaccines
- 28% (209) drugs
- 23% (172) diagnostics
- Microbicides and VCPs represent less than 2% each.

One notable area of growth in the neglected disease pipeline is in biologics. Six years ago, only a handful of biologics were in development, but there are now 65, representing 8.6% of the overall pipeline and nearly 25% of therapeutics. Over half of all biologics are monoclonal antibodies which are being developed for HIV/AIDS, dengue, malaria, hepatitis B and diarrhoeal diseases (shigella and cholera). There are also several biologic-based therapeutic vaccines for tuberculosis. Biologics are increasingly seen as a valuable complement to vaccines and drugs but must overcome a reputation for high costs and difficulties in large-scale manufacture and distribution to become an accessible tool for people with neglected diseases.

### Table 1.
Breakdown of diseases with limited pipelines

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pipeline</th>
<th>Approved products#</th>
<th>Annual funding average (USD)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buruli ulcer</td>
<td>4 diagnostics, 3 drugs, 3 vaccines</td>
<td>1 diagnostic</td>
<td>$1.9 million</td>
</tr>
<tr>
<td>Histoplasmosis</td>
<td>4 drugs</td>
<td>1 drug</td>
<td>$4.0 million</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td>7 drugs</td>
<td>No approved product</td>
<td></td>
</tr>
<tr>
<td>Leprosy</td>
<td>3 drugs, 1 vaccine</td>
<td>No approved product</td>
<td>$9.6 million</td>
</tr>
<tr>
<td>Mycetoma</td>
<td>3 drugs</td>
<td>No approved product</td>
<td>$0.7 million</td>
</tr>
<tr>
<td>Scabies</td>
<td>1 drug</td>
<td>1 drug</td>
<td>$1.7 million</td>
</tr>
<tr>
<td>Trachoma</td>
<td>4 vaccines</td>
<td>No approved product</td>
<td>$1.4 million</td>
</tr>
</tbody>
</table>

# Only includes products registered between 2000-2023

* Funding average based on last five years (2018-2022) of R&D funding

^ Only three years of available data (2020-2022)

Modelling the launch of future products

The Portfolio-to-Impact (P2I) model (7) utilises standardised assumptions around the cost, duration, and probability of technical success of different clinical development phases for neglected disease products and can be used to estimate the timing and minimum cost of future products launches based on the current state of the pipeline. With the help of P2I, the review of the pipeline we did, and our own informed assumptions of how we anticipate the pipeline changing in the coming years (particularly the entry of new, early-stage candidates), we have modelled the landscape of products we expect to emerge and be approved in the future.

This modelling predicts an estimated 182 additional product launches by the year 2040. In line with the distribution of the existing pipeline and of global R&D funding, almost 46% (84) of these predicted launches are for either tuberculosis (23%, 41), malaria (16%, 30) or HIV/AIDS (7.1%, 13), with no other diseases expected to receive more than 10 new products.

1 Diagnostics and VCPs do not proceed through R&D phases in this way and so are excluded from this analysis.

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Less than a quarter (23%, 42) of expected product launches will be for the WHO Neglected Tropical Diseases. The vast majority of these new NTD products are predicted to be diagnostics (79%, 33), largely due to the model’s treatment of diagnostics as quicker to develop and enjoying a higher probability of success. The remaining NTD product launches are mostly expected to be drugs (19%, 8) and vaccines (2%, 1). Based on current assumptions, there could be more than 20 new vaccine launches by 2040 across all disease areas in the neglected diseases scope.

While this model has its imperfections, it represents a reasonable estimation of how products will ultimately transition from the pipeline to approval. To the extent that it is somewhat overoptimistic about the technical and regulatory difficulties candidates will face before launch, that optimism is offset by the relatively small range of products included in our modelling at the narrow range of impacts we are able to model – see the following chapter of this report for details.

**How does the pipeline fit with global R&D priorities**

While the recent growth in the pipeline is good news, it is crucial to see how well it measures up to identified areas of R&D priority. Focussing on those that are WHO-endorsed or which show other elements of global consensus-driven development, we have captured a total of 45 documented R&D priorities for neglected disease products.

When we compare the current pipeline against these priorities, only the R&D landscape for malaria vaccines and malaria drugs shows strong alignment. Just over half of the tuberculosis vaccine candidates align, but only a small fraction of tuberculosis drug candidates.
The lack of alignment between the pipeline and stated R&D priorities across most disease areas is in sharp contrast to the malaria pipeline’s clear alignment with a wider set of TPPs produced by the Medicines for Malaria Venture (MMV) as well as those from the WHO. Malaria is the only sector where we have included consensus R&D priorities from outside WHO: namely TPPs produced by Medicines for Malaria Venture which are widely accepted and used. Many reasons may explain this clear alignment in the malaria space, but the observation suggests that the malaria R&D community is coalescing around global R&D priorities in a way that other disease areas are not, and lessons should be learned from this sector.

In many cases, the pipeline can’t be compared to a consensus list of R&D priorities because they don’t yet exist. The lack of consensus on R&D priorities is an issue as these are critical for developers to understand unmet need and funders to make informed investment decisions. In some cases, such as HIV/AIDS vaccine development, a lack of R&D priorities may reflect a genuine lack of consensus, encouraging wide-ranging exploratory R&D to narrow down the potential options. However, for some diseases, like dengue, there are no WHO TPPs yet available. In the face of ongoing outbreaks in Latin America and Southeast Asia, articulating priorities for which products would be most useful could help streamline and accelerate R&D.
Health impact of R&D funding

We modelled the retrospective and prospective health impact of a range of products launched between 1999-2023, as well as those projected to be launched between now and 2040, to produce estimates of lives saved, DALYs averted, and, where possible, cases and infections averted globally.

The disease-product categories included in the modelling were selected based on the availability of reliable data on the burden and epidemiology of the disease, as well as historic and projected future product reach and uptake. Due to insufficient data or evidence of significant incremental improvement over existing products or treatment pathways, a number of disease and product areas had to be excluded altogether. The aim of the analysis was not to provide modelling of specific products but instead to model product-disease classes (e.g. HIV/AIDS diagnostics, tuberculosis drugs, malaria VCPs, etc.) and provide an aggregated, macro level view of the portfolio-level impact. See Table 2 for a list of all disease-product categories included in the modelling. The modelling methodology details can be found in the accompanying methodology summary document.

Impact on lives saved

A total of 40.7m lives are estimated to be saved for the period 2000-2040 (see Figure 6). Of these, 8.3m have already been saved to date. As with the distribution of R&D funding and pipeline products, the gains are heavily concentrated in HIV/AIDS, malaria and tuberculosis, with nearly 72% of the total lives saved due to reductions in mortality from these ‘big three’ diseases.

This reflects the flow-on effects of improved treatment and control options that become available following early diagnosis. Following HIV/AIDS are malaria (a total of 22% of the total across a range of interventions), tuberculosis (20%, also mostly thanks to improved diagnostics), and vaccines for pneumonia (14%) and rotavirus (5%).

When looking instead at Years of Lives Lost (YLL), a measure of premature mortality that takes into account both the number of deaths averted and the age at which it occurs, the largest single impact comes from a new vaccine for bacterial pneumonia since its focus on preventing childhood mortality means saving many more years of life for each averted fatality.

The largest single impact comes from improved diagnostics for HIV/AIDS, which account for 30% of the projected lives saved.
Examining the various modelled scenarios over time, it appears that improving diagnostics for HIV/AIDS will continue to provide significant benefits, steadily increasing alongside improved rollout and population growth in endemic regions. Product development in other diseases such as tuberculosis and malaria, and vaccines for rotavirus are expected to begin delivering their impact over the coming years, if there remains a global commitment to the continued investment and innovation required to allow the products that are currently in the pipeline to progress through to approval and introduction. Only if funders continue to back the completion and scale-up of these blockbuster products can the huge future gains implied by our models be fully realised.
The geographical distribution of lives saved

Consistent with where the burden of neglected disease falls most heavily, the overall health impact predicted in our models is concentrated in sub-Saharan Africa and South and Southeast Asia.

Over 75% of averted deaths globally occur in sub-Saharan Africa, primarily due to improved diagnostics for HIV/AIDS and the gradual rollout of new malaria vaccines. These sit alongside smaller gains from other new products for tuberculosis and malaria, and new vaccines for *S. pneumoniae* and rotaviruses.

In South and Southeast Asia, the largest impact will likely come from innovations for the diagnosis and treatment of tuberculosis, as well as malaria prevention and vaccines for *S. pneumoniae*, rotaviruses, and typhoid fever.

These variations in impact highlight the importance of interventions tailored to the needs of specific regional health systems and disease burdens.

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**Figure 8.** Lives saved by region, 2000-2024

![Diagram showing lives saved by region](image)

Key

- **Sub-Saharan Africa**: 77%
- **South Asia**: 15%
- **Southeast & East Asia, Oceania**: 4%
- **North Africa & Middle East**: 2%
- **Latin America & Caribbean**: 1%
- **Central & Eastern Europe, Central Asia**: 0.7%
- **High-income countries**: 0.2%

Efforts to integrate innovations into the existing standard of care and deliver to currently underserved populations in regions with high disease burden typically require a multi-pronged strategy. This strategy should ideally begin alongside a product’s clinical development rather than kicking into gear only upon approval. Such a strategy needs to aim at improving healthcare infrastructure, strengthening healthcare systems, and enhancing accessibility to healthcare services through universal health coverage policies.

Establishing supportive regulatory frameworks and policies is essential for facilitating adoption and scaling up delivery from trial sites to the entire population at risk. This includes establishing pathways for expediting regulatory approval for new products, providing incentives for innovation, timely revision of intellectual property mechanisms, and ensuring compliance with quality and safety standards.

**Impact on cases averted**

Not all the epidemiological models used to estimate the reduction in burden of illness directly calculate averted cases as an intermediate step. This means that, in many cases, including for malaria and tuberculosis, cases are imputed from burden calculation and may be less accurate than the figures for fatalities and DALYs presented elsewhere.

Based on the available data, new malaria products (taken together, 75% of the total) and vaccines for rotavirus (14%) deliver a very significant proportion of the total number of cases averted, together accounting for more than 85% of the total.
As with lives saved, a clear majority (83%) of the impact on cases for which data is available is predicted to occur in sub-Saharan Africa—a projected total of 4.2bn cases averted by 2040. The remaining averted cases are mostly split between South Asia (8%, 427m cases) and North Africa & Middle East (6%, 307m).
Impact on disability-adjusted life years (DALYs)

Between 2000 and 2040, a total of 2.83bn (undiscounted) disability-adjusted life years (DALYs) are predicted to be averted via the deployment of new pharmaceutical products. To date, 598m DALYs have already been averted.

These DALYs are a composite measure of overall disease burden, capturing the number of years of life lost (YLL)\(^2\) together with the number of year-equivalents lived with disability (YLDs). Together, YLL and YLD yield a measure which, unlike 'lives saved', places value on how many years of life are saved and on reductions in morbidity as well as mortality. Children count for more in years of life saved calculations.

Where multiple products had the potential to reduce the burden of a single disease we have selected the single intervention we judged to be most likely or to account for the largest share of the likely impact. This is to avoid double counting. A full list of the interventions we included is available in Appendix I.

While almost 600m DALYs are estimated to have been averted as of 2022, nearly 80% of the 2.83bn total DALYs are still to come – driven by the ongoing rollout of and benefits from products already approved and by the new products predicted to launch over the next several years.

Figure 11. DALYs averted by intervention, 2000-2040

Key

- Cholera - Emergency Reactive OCV
- Cholera - Targeted Preventative OCV
- Rotavirus - New Vaccine
- S. pneumoniae - New vaccine
- TB - Vaccines
- Typhoid - TCV Introduction
- HIV - Ring PrEP
- Other malaria - Improved insecticides/nets
- P. falciparum - ACTs
- P. falciparum - SMC
- HIV - CAB PrEP
- HIV - Improved Diagnostics
- TB - Diagnostics
- TB - Drugs
- Typhoid - TCV/iNTS combination vaccine
- N. meningitidis - New vaccine
- P. falciparum - Vaccines

2 Relative to an ideal global lifespan, not current national life expectancy – see next section for details
Over 28% of the overall benefits come from various interventions targeting falciparum malaria: seasonal malaria chemoprevention, artemisinin-based combination therapy and age-based distribution of malaria vaccines. A further 7% come from the use of improved insecticides and treated bed nets against other strains of malaria. Gains in controlling HIV/AIDS make up another 23%, primarily from improved diagnostics. The remainder come from new pneumonia vaccines and various measures against tuberculosis, again primarily diagnostics.

Geographically, the gains once again centre on sub-Saharan Africa, especially West Africa.

Importantly, it should be noted that while DALYs provide a useful measure of the years of life saved, they capture solely the impact on health and not the broader impact of diseases on societies or the full extent of co-morbidities experienced by different populations.

**Figure 12.**
DALYs averted by region, 2000-2040

While 2.83bn DALYs averted is vast health impact, it likely underestimates the true scale of morbidity averted when we think of impacted communities through a sex and gender lens. Disease affects women and girls differently and often disproportionately, and more nuanced gender- and sex-related impacts should be explored in the future.
Economic impact of R&D funding

Investment in global health R&D delivers tremendous economic impact for societies.

Measuring the economic value of improved health

The epidemiological modelling led by our partners at Avenir Health projected cases and deaths averted by the introduction of new products between 2000 and 2040. Avenir then used these measures to estimate the resulting number of life years saved and the amount of nonfatal disability avoided. In turn this enabled an estimate of the number of disability-adjusted life years (DALYs) averted by the introduction of these new products.

To calculate the ultimate rate of return on the financial investment in R&D we need to calculate the dollar value of these health gains. In the past, this was typically done using the ‘human capital’ measure of improved health which measures the value of saving a life based on the value of additional labour during the extra years of life. The emerging consensus (8), though, is that lives, and good health, have value beyond their ability to deliver additional goods and services, and that it is better to value health gains in line with the value placed on them by society as a whole.

Societal value of averting DALYs

To capture the societal value of a DALY, we used the ‘value of a statistical life’ (VSL). This method assigns a monetary value to lives based on individuals’ willingness to pay for a reduction in mortality risks. Typically, this valuation is derived through stated-preference surveys (‘how much would you be willing to pay for an additional year of healthy life?’) or revealed-preference methods (how much more do workers in dangerous occupations earn than those in similar, but safer, jobs?).

In the United States, the most recent estimate places the VSL at $12.3m in 2022 dollars (9). However, the extra pay demanded to take on a dangerous job, and the trade-off between health and other forms of consumption more generally, will vary with national income; and few attempts have been made to replicate these US-specific estimates in LMICs. So, following the rough consensus of the economic literature⁶, we have taken the US figure for the societal value of a life as our starting point, and adjusted it based on differences in gross national income (GNI) in the nations where our modelling shows DALYs being averted.

Many experts believe that the average value nations place on saving lives responds disproportionately to changes in national income (10). This means that citizens of a country with a 50% lower national income might place only 40% as much value on lives saved. The exact level of this ‘income elasticity’–how sharply the VSL drops in response to much lower national income–is debated and has a huge influence on how we value the DALYs averted in LMICs. The highest estimate of elasticity widely used is 1.5, suggesting that a 1% increase in income leads to a 1.5% increase in the value placed on statistical lives (11).

Based on our review of the literature, and on the income profile of the nations where our projected health gains occur, we have chosen 1.2 as the income elasticity for our economic impact assessment. This is at the lower end of the range recommended in the Reference Case Guidelines for Benefit-Cost Analysis in Global Health and Development (11). This adjustment yields a value of a statistical life of approximately $550,000 for our sample of countries, equating to roughly $19,985 for each statistical life year. Given the significant

$19,985
FOR EACH STATISTICAL LIFE YEAR

See the end of this section for a brief justification for this choice. The sensitivity analyses have been conducted to test how our results are influenced by this decision.
sensitivity of the value of a statistical life year (VSLY) and consequently the overall return on investment to our choice of elasticity, we also provide a sensitivity analysis using other commonly proposed values.

We discount the value of DALYs averted at 2% per year, in line with the latest guidance from the US government, but at the low end of the 3-5% range used elsewhere (see the sensitivity analyses in Appendix I). This turns our raw total of 2.83bn DALYs into a 2022-equivalent of 2.47bn, but at the low end of the 3-5% range used elsewhere (12) (see the sensitivity analyses in Appendix I).

In practice, our modelling showed that the extra costs of distribution dwarf the savings to the health system. This is due to the extremely limited treatment provided to affected populations in LMICs before the introduction of these new products. In many cases, health systems had limited or no other treatment or prevention pathway available under the preexisting standard of care. As a result, there were few health system expenditures to displace by the introduction of these breakthrough technologies. The value of new products is mostly due to the lives they saved. As a result, the net cost impact on health systems was negative and should be subtracted from the overall estimate of gains to arrive at the overall return on investment.

One thing missing from these calculations is the wider costs imposed on health systems by the burden of illness. Even if, for example, limited health system resources mean spending on individual cases of tuberculosis is low, additional cases may still end up placing a burden on other parts of the healthcare system. These costs will not be captured as healthcare costs specific to tuberculosis, but a lower number of cases will still tend to reduce the overall demands on health system resources in a way not captured by our disease-specific modelling.

All lives should be valued equally and our estimated value was selected with the aim of reinforcing an equity centric approach to this economic impact assessment. However, our decision to vary the value placed on life years based on the income of the nation where they are saved can be controversial. One way to justify it is as an attempt to chart a conservative path between very high measures based on a universal VSL, on the one hand, and very low ones based on the widespread 'human capital' approach to valuing a life based only on the market value of its production, on the other. Alternatively, we can justify valuing lives differently based on the genuine differences in trade-offs faced by people in different income settings, which result in different stated preferences around the monetary value of the chance at a longer life. We discuss these arguments further in the next chapter and in Appendix I as part of our sensitivity analyses.

Estimating the net cost impact on health systems

However, there is more to the story than just the health benefits gained from new products such as vaccines, treatments and diagnostics. The introduction of these technologies often triggers significant ripple effects within hospitals and healthcare systems. The impact of new technologies can cut both ways: while vaccines and diagnostics may curb transmission, reducing the number of infections and the cost of treating the resulting illness, they also cost the health system additional money to distribute in the first place.

When multiplied by the estimated value of $19,985 per statistical life year, the resulting figure (discounted) is $49.4tn in societal return between 2000 to 2040.

The total (discounted) health system cost of rolling out these products amounts to $213bn, the vast majority of which (84%) came from the cost of providing access to new products for HIV/AIDS and tuberculosis.
Healthier populations drive economic growth

Beyond the value to the individual of averted death and disease, the benefits from improved health ripple through the economy. Depending on the structure of a nation’s labour market and its society, a single illness can generate a tremendous amount of disruption, pushing economic development off track and forcing families into multi-generational poverty.

Some sources (13, 14) suggest that the wider gains from improved health such as reduced absenteeism, a larger, stronger labour force, reduced demands on carers, and improved opportunity for education amount to as much as an additional 50% of the value of the gain to the individual who avoids falling ill. This would mean the wider benefits from new treatments delivered almost $25tn in additional value to the societies and economies where they took place.

We have opted for a significantly more conservative estimate of these wider gains. Instead of trying to value all the different ways one person’s better health might improve the lives of others, we have focused on the additional ‘frictional’ cost of illness based on the temporary disruption caused for families and employers. Following examples in the literature (9), we treated each averted fatality as avoiding a total of 15 days of lost productivity, valued at the average level of per capita GDP in the nations where cases are averted. This total can be thought of as a hybrid of the various effects of untimely death due to illness, including the delay in finding a qualified replacement worker, the cost and interruption of a funeral, and the time spent caring for and/or quarantining from the victim.

For averted non-fatal cases we used the lower figure of five days, which mostly represented temporary absence from or reduced performance at work.

Given the conservative nature of these estimates, we did not restrict them only to the share of cases likely to have affected people in the labour force. Instead, we assumed that there would be roughly comparable levels of cost and disruption from cases affecting stay-at-home carers, the unemployed and - importantly, given their large share of averted impact - children, who we assume required additional care and/or missed out on valuable educational opportunities.

Multiplying these values by the number of cases and fatalities averted yields an estimate of $269.8bn in wider economic benefits from improved health, or just over 1% of the $25tn figure we have identified as a potential high-end estimate.

Today’s investment in R&D provides the foundation for tomorrow’s innovations

Conducting research and development also benefits the economies where it takes place by generating additional knowledge, which then forms the basis for future beneficial innovations.

We estimate the size of these benefits based on the academic literature, which suggests that each dollar spent on basic research goes on to generate an additional 43 cents in valuable basic science the following year and every year thereafter (15). We discounted this endless stream of these future benefits at 5%, which is higher than our discount rate for future health gain on the assumption that the value of basic research decreases more quickly. We therefore suggest that the $17.6bn of R&D funding which was directed to basic research will go on to generate a discounted total of $262bn in flow-on benefits for future R&D. This value is captured in the improved set of scientific tools and insights provided to future researchers.

Note that this estimate entirely excludes the possibility of future benefits from product-specific R&D (nearly 80% of our total), which may be less likely to generate transferable insights than basic research but which will no doubt still contribute to future product development. In our case studies, we outline how research on vaccines for HIV/AIDS, for example, went on to provide the basis for many of the early COVID-19 vaccines, delivering a substantial global return not captured in our figures. If we look at the net benefit to date, this already amounts to $10.96tn generated to society.

Net economic benefit

Based on all these considerations, we conclude that investing in global health R&D is conservatively expected to generate a net benefit of $49.7tn between 2000 and 2040. This is the total dollar value of the benefits of lives extended, disability avoided, and enhanced scientific knowledge, slightly offset by the net cost of rolling out the health interventions.
Determining global health R&D funding levels, 1994-2040

To calculate the return on investment, the total R&D investment for the period of analysis had to be calculated for all diseases in scope for the G-FINDER survey. While G-FINDER data on neglected disease R&D investment is available from 2007 onwards, we needed to estimate the R&D funding that preceded 2007 and helped to provide the foundation for products launched from 1999. To estimate these funding levels, we analysed historical investment from three major funders for whom pre-2007 data is available: the Bill & Melinda Gates Foundation, the US National Institutes of Health (NIH), and the European Commission. Based on how the share of these organisations’ funding relevant to neglected disease R&D evolved between 2007 and 2022, we projected or ‘backcast’ the amount of their total announced funding likely to have gone to neglected disease R&D from 2006 back to 1994. This is the earliest year for which all three funders reported historical investments. We used the estimated pre-2007 totals for these three funders, together with the time trend in the share of global funding they have accounted for, to estimate each year’s global neglected disease R&D spend.

To test the accuracy of this projection, we also estimated disease-specific funding for malaria, HIV/AIDS and tuberculosis, cross-referencing our estimates with sporadically published projections of global R&D for each disease.

After adjustment for inflation and discounting at 2%, we calculate a total of $97.9bn4 in R&D funding for neglected diseases spanning the years 1994-2022. This represents a substantial overestimate of the costs of completing the specific products included in our analysis, since it also includes: R&D funding for all neglected disease and product areas in the G-FINDER scope (even those excluded from the impact modelling); all potentially relevant basic research; funding for products which would ultimately fail to launch; the final stages of funding for products launched immediately prior to our 2000 cutoff; and possibly the early funding for candidates we don’t project as resulting in approved products until after 2040.

What this figure doesn’t include, though, is the funding necessary to complete products still in the pipeline. We have adopted a conservative approach to the required future funding, including only the estimated Phase-specific costs necessary to move the specific products we have identified through the pipeline to launch. The Portfolio-to-Impact Model (P2I) gives us an estimate of $24.8bn between now and 2040.

Accounting for the broad estimate of relevant historical funding from 1994 to 2022 and the narrower estimate of future funding necessary to complete the products already in

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4 Based on FY 2022 US dollars

impact.policycuresresearch.org
the pipeline, the relevant net present value of investment in global health R&D is $122.7bn.

The high societal returns of investment in global health R&D

We conservatively estimated the net economic benefit provided by current and future neglected disease products at $49.7tn. That's the dollar value of lives extended, disability avoided, and benefits of enhanced scientific knowledge, slightly offset by their net cost impact on global healthcare systems. That huge amount is 405 times the $122.7bn we have and will spend developing these products.

Another way of framing the overall returns from R&D is that for a net total cost of $336bn, including both the costs of carrying out the R&D and the net costs of product distribution, we will ultimately avert a total of 2.83bn DALYs. This represents a cost of just $136 per DALY averted, even if we discount the health gains based on the year they are projected to occur. This is an order of magnitude below the roughly $50,000/DALY threshold used for judging the cost-effectiveness of high-income countries' health spending, and safely below even the $326/DALY figure for the most successful oncology studies of the past 50 years (16).

How our economic impact assessment compares to other studies, and why it differs

A return on investment of 405:1 is, by any standard, extremely high. It compares very favourably to the mean 14:3 ROI from high-income country public health interventions (17), for example, and higher even than the 201:1 ROI from switching to bed nets treated with a novel class of insecticide (18). The following should be considered when reflecting on the scale of this number:

1. Many studies are wary of converting health gains into monetary values, preferring to quote a cost per DALY averted, such as the $136/DALY figure above. This avoids some of the technical and philosophical complexity of putting a dollar value on human life. However, this figure ends up comparable only to other health interventions rather than all the other things funders may consider investing in.

2. When other studies do value health gains, they often assign each DALY a relatively low value based on per capita GDP, implicitly assuming that the value of a life is equal to the value of the goods and services it would yield. Our methodology instead starts from the well-studied preferences of US workers, who act like people who value their lives more than just their wages. We recognise, and adjust for, the fact that the amount a person needs to accept an increased risk of dying rises with their income. It rises by a factor of 2.4 when income doubles. This is controversial, since it varies the value of lives according to national income, rather than adopting a single, global standard for how much health is worth. A global standard would however yield an even greater return on investment.

3. We have adopted a long-term approach to modelling the impact of R&D, rather than insisting that all the benefits of funding be realised within ten or twenty years. In line with the recent shift in the US government’s approach to thinking about the future (12), we have adopted a discount rate of 2% which is lower than most previous studies (3-5%). These decisions impact our measured ROI, since nearly 80% of our projected benefits occur after 2022, peaking in 2040. Simply changing our discount rate from 2% to 5% would increase the present value of R&D funding by nearly 40%, and the value of DALYs averted by 14%. R&D takes a long time to deliver benefits, and the returns on investment are heavily influenced by the patience of funders.

4. Our figures for years of life saved are optimistic as we assume that people who would have died without
pharmaceutical intervention go on to live a life in line with the global ideal lifespan. This assumes the absence of other unusual health problems in the future, rather than the number of years of life currently projected for people of that age in that country. This is due to the difficulty of projecting far future life expectancies in LMICs, particularly as those life expectancies are influenced by large-scale healthcare innovations. It does decrease the bias against saving lives in LMICs implicit in our income-dependent valuations of years of life saved. There may eventually prove to be a substantial difference between our idealised life expectancies and the number of years a Nigerian 5-year-old whose life will be saved in 2040 will ultimately live, but we hope not.

Set against these arguably optimistic assumptions are the places in which we’ve been conservative in our approach:

1. Our accounting of the cost of R&D departs from many similar studies in refusing to cherry-pick only the successful innovations. Instead, we have included all the funding for neglected disease R&D between 1994 and 2022, including basic research, failed products, products for which health/economic impact modelling was impossible, and products launched before or after our 2000-2022 window.

2. We conservatively estimate the non-health benefits of R&D. We treat the wider economic impact of an untimely death as equal to a one-off loss of 15 days’ wages. We exclude the boost R&D funding provides to general economic activity, and model averted health system costs based on today’s very low levels of healthcare spending, rather than the higher values that might prevail in the future.

3. Our epidemiological modelling covers only the countries where the largest impact is likely to have been achieved and only the subset of products where data was available and for which modelling was feasible within the resources available to the project.

It is our belief that we have adopted broadly offsetting conservative and optimistic assumptions in various places, and that an overall 405:1 ROI is both tremendously high and approximately accurate. Investing in global health R&D pays off for societies.

Investing in R&D for neglected diseases delivers high societal return even with very distinct assumptions and methodologies

We have benchmarked our results against a variety of other widely accepted methodologies. More details on this can be found in Appendix I. These methodologies have delivered ROIs ranging from 65:1 when using the Human Capital Approach to 2,563:1 using a universal DALY valuation of $100k. The numbers are clear and consistently reinforce our key finding: investing in global health R&D delivers very high societal returns.

The scale of this high return is driven by the 2.83bn DALYs averted. We made a range of assumptions about how to convert these DALYs into dollars. Some of these, particularly our decision to use the full societal value of a life year rather than just the dollar value of what a person could have produced, push our estimated ROI higher; but under any plausible methodology, averting 2.83bn DALYs by spending $123bn on R&D is going to look like a great investment. So how did we end up with so many DALYs? We deliberately began this project with a wide lens, considering the impact of every product, across every nation, over a 40 year time horizon. These choices, particularly the last one, mean that we were able to capture a broader, longer-term picture of how R&D gradually but permanently lowers the burden of neglected disease.
Estimating the monetary value of all the different impacts R&D can have on society is challenging. In some cases there are identifiable benefits from R&D to which we can point but not assign a realistic monetary value. We therefore present a series of case studies which investigate the ways in which today’s R&D can help to deliver future benefits which fall outside our formal models.

Technology transfer and vaccine development: mRNA vaccine

The mRNA vaccine technology used in COVID-19 vaccines, such as those developed by Pfizer-BioNTech and Moderna, had been under development for use in a potential HIV/AIDS vaccine for decades before the pandemic (19-21). The repeated failures of mRNA-based HIV/AIDS vaccine candidates ultimately laid the foundation for the first wave of high-efficacy COVID-19 vaccines.

This success was built on a series of failures: AIDSVAX B/B; AIDSVAX B/E; Merck STEP; RV144; HVTN 505; Uhambo (HVTN 702); Imbokodo (HVTN 705); and Mosaico (HVTN 706) HIV/AIDS vaccine trials. The knowledge acquired from these unsuccessful clinical trials helped the wider scientific community prepare for the development of mRNA-based SARS-CoV-2 vaccines. As pointed out by Harris, “when the candidate vaccine fails, all the competitors in the vaccine field – not just the patent holder – learn from the mishap. The patent holder can reap the rewards of success, but it cannot fully capture the gains from its mistakes. We thus have a positive externality, specifically a knowledge spillover.”(21)

As of 2019, gradual improvements in mRNA stability, delivery, and expression fostered by the series of failed HIV trials had made it the focus of vaccine research in other areas, including early-stage trials for influenza, Zika and Ebola virus vaccines (19, 20).

The travails of HIV/AIDS vaccine developers also provided the world with valuable lessons on how to adjust SARS-CoV-2 vaccines to tackle immune escape from emerging variants. The findings from the AIDSVAX trials highlighted the potentially key role of cellular immunity in the prevention of HIV/AIDS infection (21). This led to the idea that an HIV/AIDS vaccine might not entirely prevent infection but could permit transient infection while being cleared by the cellular immune system, which is referred to as infection-permissive immunity. This idea was later extended to the cellular immune response to SARS-CoV-2. Some COVID-19 vaccines induced a cellular immune response that helped mitigate the severe consequences of the disease without necessarily blocking acute infection.

Today, the spillover benefits from early mRNA R&D have come full circle, with the mRNA technology behind successful COVID-19 vaccines accelerating the development of a vaccine against HIV/AIDS, along with other diseases such as influenza, respiratory syncytial virus (RSV), dengue fever, malaria, rabies, tuberculosis and cancer (22). Ongoing mRNA-HIV/AIDS trials include the HVTN 302 trial launched in March 2022, which is assessing whether any of the three experimental HIV/AIDS mRNA vaccines are safe and can induce an immune response (23, 24). Moderna is also conducting two trials in partnership with the International AIDS Vaccine Initiative, NIH, and the Bill & Melinda Gates Foundation, leveraging the mRNA technology for an HIV/AIDS vaccine (25).

Knowledge transfer of R&D funding mechanisms: product development partnerships and pull mechanisms

The pharmaceutical sector faces complex, time-consuming and costly development processes for new products, with estimates of the cost of developing new treatments ranging from $43.4m to $4.2bn (26). To encourage R&D investment, pharmaceutical companies are typically granted 20-year patent protection. However, limited market potential in LMICs due to low ability-to-pay and sub-optimal health systems, discourages investment in R&D for diseases that primarily affect these regions.

Alternative business models have emerged to address this market failure. These include the establishment of product development partnerships (PDPs), with approximately twenty founded in the early 2000s to stimulate R&D into medicines for neglected diseases (27, 28). PDPs are non-profit organisations that foster collaboration among academic institutions, governments, industry, and philanthropic entities to drive R&D for drugs, vaccines, diagnostics, and other health technologies targeting unmet health needs. These partnerships are typically funded by public and philanthropic
sources and do not conduct R&D activities in-house but rather operate as ‘system integrators’ that coordinate several partners who actually undertake R&D (28). PDPs are able to adopt a portfolio strategy, simultaneously pursuing a range of different approaches to increase the chance of at least one success (29, 30), including several of the products modelled in this report.

The R&D benefits provided by the PDP model are increasingly replicated in health areas outside neglected disease, such as antimicrobial resistance, with the establishment of the Global Antibiotic Research and Development Partnership (GARDP) (31). PDP models in the R&D response to COVID-19 have also accelerated the development of health technologies and innovations. For example, the Foundation for Innovative New Diagnostics (FIND) successfully developing three approved COVID-19 diagnostics and playing a key role in the Diagnostics Pillar of the Access to COVID-19 Tools Accelerator (32). As part of an increased focus on pandemic preparedness, Medicines for Malaria Venture and DNDi have jointly launched the Pandemic Response Box, providing researchers with free access to 400 diverse compounds to accelerate the discovery of new treatments against a novel pathogen (33).

PDPs have not been the only models to deliver spillover benefits in other areas of R&D. Various ‘pull’ mechanisms designed to incentivise private sector investment, including the priority review voucher (PRV) and the advance market commitment (AMC), initially designed for neglected diseases, have been used to address other disease areas. The PRV, first introduced in the US in 2007 to incentivise R&D for neglected tropical diseases, was expanded in 2012 to encompass rare paediatric conditions, leading to the issuance of over 20 vouchers (34). Similarly, the use of the advance market commitment (AMC) by Gavi in combating COVID-19 drew inspiration from its previous implementation for pneumococcal vaccines in 2009 (35). Pull mechanisms initially theorised for neglected diseases, such as transferable exclusivity vouchers and subscription models, are now being advocated as effective tools to combat antimicrobial resistance (36). The evolution of these tools highlights the potential for even systems of conducting R&D to be repurposed and deliver benefits to the wider research community.

**Investment in R&D through public-private partnerships promotes capacity building in sub-Saharan Africa: the EDCTP**

Investing in R&D capacity building in sub-Saharan Africa is crucial not just for healthcare but also for driving economic development and advancing local scientific knowledge and expertise. As scientists become better equipped to conduct R&D for neglected diseases, they also gain the capacity to conduct other types of biomedical research. This accumulated scientific knowledge can lead to the development of locally-relevant healthcare solutions, such as new treatments, diagnostics and preventive measures that address prevalent diseases and challenges in the region but which fall outside our model’s specific focus on neglected disease (37). Additionally, as African researchers and scientists contribute to the global body of knowledge, it not only enriches the global scientific community but also empowers them to take ownership, make informed decisions and take part in policy making. A robust R&D ecosystem also stimulates innovation and drives economic growth. By investing in capacity building, African nations can cultivate local entrepreneurship and foster a culture of innovation, resulting in the establishment of new downstream industries, businesses and the creation of job opportunities in areas where they may otherwise be limited, potentially also reducing the ‘brain drain’ of talented scientists and researchers (37).

Product-development partnerships (PDPs) and other intermediary organisations, through their ongoing investment in R&D, represent powerful models to build R&D capacity in low- and middle-income countries. The European & Developing Countries Clinical Trials Partnership (EDCTP) serves as an illustrative model in this context. Originally established in 2003 to combat HIV/AIDS, tuberculosis and malaria in sub-Saharan Africa, the EDCTP’s support for clinical studies and capacity development initiatives fosters international collaborations as the basis for grant applications. EDCTP prioritises capacity development in clinical trials and product-oriented implementation research capabilities, thereby placing a significant emphasis on local capacity building at the research sites (38).
Launched in 2014, the EDCTP2 program has been instrumental in promoting and fortifying human capital and institutional capabilities in 39 sub-Saharan countries, involving 238 African institutions, to conduct high-quality clinical research (38). Up until the year 2020, EDCTP had provided support to 171 fellows and 232 postgraduate trainees. Moreover, EDCTP’s short-term training initiatives have benefitted 9,628 researchers and medical personnel (38). Additionally, EDCTP funded four regional Networks of Excellence in sub-Saharan Africa to promote collaboration within the region (South-South) and with countries outside (North-South), benefitting 42 institutions in 27 African countries (38). These networks provide platforms for research capacity building in areas such as infrastructure development, training and mentoring, resource sharing, and harmonisation (39).

Investment in R&D through product-development partnerships can help to close the gender gap

Investment in R&D through product-development partnerships and other intermediary organisations like the EDCTP can foster clinical trial capacity in low- and middle-income countries. In addition, R&D investment from PDPs can play a key role in closing the healthcare gender gap.

Firstly, PDPs can promote gender-focused research. Collaborative R&D partnerships can allocate resources specifically for research that explores gender-related issues and challenges, including gender-specific health concerns, economic disparities, or social barriers. To name a few concrete examples, DNDi is investing in gender-sensitive research, enhancing capacity, and facilitating the involvement of women of childbearing age in clinical trials (40, 41). While there has been a reluctance to involve women susceptible to becoming pregnant in clinical trials because of the potential risk of exposing the foetus to investigational drugs, DNDi is working to ensure that there are available data to support the safety and efficacy of the treatments for these women and their babies (41).

In 2017, the EDCTP launched a call for proposals valued at $38m to accelerate the adaptation and/or optimisation of treatment and prevention products for poverty-related diseases for use with pregnant women, newborns and/or children. TB Alliance, a PDP, contributes to closing the gender gap by enrolling women in all its clinical trials aimed at evaluating new tuberculosis treatments. This approach allows for an assessment of gender differences in treatment outcomes (41). Another PDP, Medicines for Malaria Venture, is also actively working to enhance the accessibility of malaria prevention and treatment medications for pregnant women through its Malaria in Mothers and Babies (MiMBa) strategy, which aims to ensure drug availability for children and pregnant women (42).

Alongside these policies, by actively considering the gender dimension during the R&D process, PDPs can work to identify and address biases that might be present in their products and services, hopefully leading to the creation of products that better address the unique requirements of women. For instance, The Foundation for Innovative New Diagnostics incorporates gender dynamics from the outset of diagnostic research and ensures the appropriate utilisation of diagnostics within gender-specific contexts, addressing how people initially seek care (40, 43).

Finally, PDPs can create avenues for scientists and healthcare professionals from underrepresented groups to actively participate in and contribute to scientific progress, promoting female representation in R&D (40) to help counteract the underrepresentation of women in science and technology. DNDi, for instance, promotes the participation and empowerment of women and young women in science throughout their partnerships and collaborations (44). EDCTP has also been very keen on increasing female participation in its funding programs. More specifically, 37% of EDCTP-supported projects are led by women, and 49% of the 692 African academic trainees (Bachelors, Masters and PhD students) supported by EDCTP are female. In addition, 39% of EDCTP technical reviewers are female (45).
Neglected disease R&D: strategic implications for the funding landscape

Every dollar invested in neglected disease R&D between 1994 and 2040 returns an average of $405 to society, mostly in the form of improved health outcomes in low- and middle-income countries. This provides an unequivocal answer to our initial question, “What is the impact of investing in global health R&D?”

This provides a compelling argument for continued and increased investment and changes the paradigm of how the returns for these investments can be assessed.

The economist’s rule of thumb is that where your return on investment is very high, you are not investing enough. If harvesting the lowest-hanging research opportunities yields a 405:1 return, it will be worth your while to keep climbing higher. If funding the best ideas you can identify pays for itself hundreds of times over, the next best opportunities are also clearly deserving of funding. Which projects went unfunded because neglected diseases received perhaps 10 cents out of every hundred dollars spent on R&D? How many more lives could have been saved if developers had been able to say ‘yes’ to twice as many ideas? Or ten times as many?

Invest now and sustain investment efforts at the portfolio level into the future

The benefits don’t peak, even in discounted terms, until 2036. If this benefit is to be realised, there needs to be sufficient ongoing investment in R&D to deliver the products that have not yet been approved but are expected based on the current state of the pipeline, and to continue scaling existing products.

Over 70% of the benefit from the past 20 years of investment will occur between now and 2040.

But how much should we be spending on R&D for neglected diseases? While our modelling clearly tells us what direction funding should be moving in, it doesn’t tell us where to stop. What we can determine from the impacts shown in our calculations, though, is that further investment should be made immediately.

Part of the reason R&D is such a valuable investment, and part of the reason why it can be difficult to make the case for increased funding, is that it delivers its benefits over a long period of time: years or even decades after the initial funding was provided.

Figure 13.
R&D funding ($m, left axis) vs DALYs averted (right axis), 1994-2022

Key
- Funding ($m)
- DALYs
It is critical that further investment occur as soon as possible so that existing products can be completed on the timeline we have projected, and new ones can begin their journey along the winding path between scientific discovery and large-scale delivery. Below is a concrete, illustrative example of the serious implications of a significant lag between regulatory approval and product scale-up; an issue faced by countless global health products.

Efficiency as a key enabler for health and economic impact: an example from malaria

The first-ever vaccine against malaria, RTS,S/AS01, was recommended for widespread use in regions with moderate to high malaria transmission by the WHO in October 2021. Just two years later, a second malaria vaccine, R21/Matrix-M, received the same recommendation. However, while these vaccines ultimately received WHO endorsement for widespread use in relatively close succession, they progressed from Phase III clinical trials at markedly different speeds. For RTS,S, more than a decade elapsed between the primary completion of its Phase III trial in early 2011 and broad WHO endorsement in late 2021. Despite receiving regulatory approval from the European Medicines Agency in July 2015 (around 18 months after its Phase III trial formally concluded), it took an additional four years before RTS,S was piloted in three countries – Ghana, Malawi and Kenya – through the malaria vaccine implementation programme. It was nearly five more years before its first formal introduction into national immunisation programmes. In contrast, R21 was recommended for widespread use by WHO just over six months after the primary completion of its Phase III trial. Now, RTS,S and R21 are being introduced into national immunisation programmes within a year of each other.

As a next-generation iteration of the RTS,S approach, R21 undoubtedly benefited from the groundwork laid by RTS,S, and it is highly unlikely that the timeline to introduction for R21 would have been quite so rapid had RTS,S not preceded it. However, this can’t entirely explain the stark difference in the approval timeline for these vaccines. Imagining a world where RTS,S was able to duplicate R21’s path to approval can help provide an upper bound estimate of the impact that can be realised from shortening the timeframe from late-stage clinical trials to widespread product introduction.

If RTS,S had progressed as quickly as R21 from the primary completion of its Phase III clinical trial to WHO recommendation for widespread use, then its widespread introduction into country immunisation programmes would have been fast-forwarded by a decade. Had this happened, an estimated 590,000 deaths and 52.4m DALYs would have already been averted by the beginning of 2024. Instead, RTS,S is only now beginning wider introduction. Looking ahead to 2033, bringing forward the introduction of RTS,S by a decade would have saved an additional 2m lives and averted 181m DALYs since 2014, equating to an estimated economic benefit of $3.4tn.  

[Figure 14. Comparative timeline of RTS,S and R21]

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5 The $19,985 VSL used relies on the overall impact across the countries analysed in this report and has not been adjusted for the specific distribution of malaria (see Appendix I for more detail on the methodology).
What this model flags for funders and decision makers

Continuing to invest in global health R&D will deliver high impact in health and economic outcomes for the most affected countries and populations. The sheer size of the ROI we’ve estimated means that this key policy recommendation is a robust one. We may be somewhat wrong about how new products will alter the spread of old diseases, or about exactly how much it will cost to deploy a new vaccine in 2030, or about the value citizens of LMICs place on reducing the risk of death, or about how sharply we should discount lives saved in the future. Perhaps, with a crystal ball and an army of health economists, our 405:1 estimated ROI should actually be 212:1; or 508:1. But there is no plausible set of assumptions under which it should be less than ten, or even less than 50.

The other immutable takeaway from our model is that investors should hurry. R&D takes a long time to pay off, and funders need to adopt a long-horizon and commit to every stage of the product development process to realise those 405:1 returns.

Alongside faster investment comes the imperative to minimise the delay between R&D being completed and new products reaching populations at risk. Today, delays in gaining access in target markets and funding for large-scale rollout are further adding to the long gap between dollars invested and DALYs delivered. Funders and national governments must work together to make post-approval scale-up quicker and more predictable, so that the benefits we project for future product launches can be delivered on time.

What our model can’t tell decision makers though, is the exact products they should be investing in

We’ve been careful to include the full costs of R&D: the underlying basic research, the failed products, and those that targeted a problem too small or too complicated to be properly captured in our epidemiological models. Our modelling does not, for example, capture the benefits of having a reliable point-of-care diagnostic that can be used in low resource settings despite our knowledge that...
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accurate diagnosis is of great importance to patients and practitioners alike.

The predictive power of our results also drops sharply as we zoom in on individual products. Product-level health and economic impact, cost efficacy, cost effectiveness and ROI require a level of specificity, data and resources that were never intended to be captured in this project. Therefore, these results should not be used for decision making at the individual product level. One can’t simply cherry-pick the products our model suggests had the greatest impact and hope to replicate that impact in the future, both because our data lacks the resolution to support those sorts of projections and because the needs of the future may not match those of the past.

Public and philanthropic investment has been driving investment in global health R&D

According to the G-FINDER survey, the following stakeholders make up the top 10 funders of R&D for neglected diseases between 2007 and 2022, representing 88% ($56bn) of total funding:

1. US National Institutes of Health (43%, $27.5bn)
2. Bill & Melinda Gates Foundation (17%, $10.7bn)
3. Industry (13%, $8.2bn)
4. European Commission (3.3%, $2.1bn)
5. US Department of Defense (3.0%, $1.9bn)
6. Wellcome (2.6%, $1.6bn)
7. United States Agency for International Development (USAID) (2.5%, $1.6bn)
8. UK Foreign, Commonwealth and Development Office (1.9%, $1.2bn)
9. UK Medical Research Council (1.1%, $717m) and
10. Indian Council of Medical Research (ICMR) (1.0%, $642m).

66% of all R&D funding for neglected diseases has come from the public sector ($42bn), followed by 21% from philanthropic ($13bn) and 13% from private ($8.2bn). Since 2007, private sector funding has grown an average of 8% per year with a peak in 2018 associated with several pivotal clinical trials that have helped progress products through the pipeline.

The US government makes up 74% of all public funding ($31bn), nearly all of which comes from the US NIH. While the UK government is the second largest all-time contributor of public funding (5.2%, $2.2bn), its investment in recent years has significantly dropped off and is now below that of third-largest contributor, the EC (4.9%, $2.1bn). The next largest contributions come from France (2.6%, $1.1bn), India (2.1%, $871m) and Germany (1.4%, $791m). India is the only LMIC government to feature in not only the top governments, but also in the top 10 organisations.

Similarly, the philanthropic landscape is dominated by one funder, the Bill & Melinda Gates Foundation, making up 82% ($11bn) of total funding from the sector. With a similar level of consistency at a lower scale, Wellcome has been the second largest funder each year, and has contributed 13% of all funding ($1.6bn). Other philanthropic funders like Médecins Sans Frontières (1.1%, $141m) and Gavi (0.9%, $117m) have featured in the top funders across the last 16 years. Most recently, Open Philanthropy, which started reporting funding in 2018, has entered the top funders and is the fourth largest overall funder (0.6%, $82m).

This underscores the critical role of government and philanthropic organisations in driving the development of health innovations for neglected diseases. It also highlights the need for collaboration between governments, philanthropic organisations, academia and industry to foster innovation and ensure that research efforts are aligned with the needs of affected communities. Ultimately, funders in this space cannot abandon the equity-driven underpinnings of how this ecosystem works and need to align investments and R&D priorities to accelerate progress and deliver lifesaving health innovations needed in LMICs.
Looking ahead: shaping the future of investing in global health R&D

With these data, insights and tools in hand, we have an opportunity to collectively shape the future of investing in global health R&D, so the world can benefit from the existing and future products that will continue to change the landscape of neglected diseases and the communities they impact. It is imperative that we:

1. **Pursue collaborative mechanisms for financing global health R&D.** Funders, product developers and researchers must collaborate to explore new mechanisms for investing in R&D. This entails fostering more equitable power-sharing and resource allocation while leveraging policy to shape investment opportunities and regulatory strategies. Additionally, innovative financing models should be explored to ensure sustainable support for R&D initiatives.

2. **Focus on portfolio investment for greatest returns.** Attributing success in global health R&D can be challenging. However, continuing to coordinate priorities for the global health R&D agenda and promoting strategic diversification across various technologies, product types and research avenues can mitigate risks and maximise impact.

3. **Optimise regulatory and access pathways to reduce time from product approval to scale-up.** Use data and evidence to implement more streamlined clinical trial and regulatory approaches, enhance capacity in LMICs, ensure efficient product approval timelines, and plan access strategies at the earliest stages of product development. All of these require deeper collaborations across the entire R&D ecosystem to safely traverse the intricate investment-impact relationship, especially in areas prone to market failures.

4. **Recognise the strategic value in investing in impact assessment.** With a cohesive understanding of the nexus between funding, products and impact, all stakeholders in the R&D ecosystem will be better placed to develop impact-driven agendas and policies. Focusing attention on better demonstrating the impact of key challenging product types such as diagnostics and vector control products could accelerate investment and product development in these areas.

5. **Strengthen collaboration between R&D and access.** Ensure that the continuum of product development is aligned with efforts to improve access to healthcare, fostering synergies between research, development and implementation strategies. This entails integrating considerations for affordability, availability and accessibility throughout the R&D process, ultimately optimising the impact of innovations on global health outcomes.

We believe we have been restrained about what to include in our models and realistic about the accuracy one can hope to provide for the complex question we sought to answer. **The headline conclusion is so robust that there is no room for doubt: funding for neglected disease R&D is an incredibly powerful tool to deliver improved health and spur economic growth. Now is the time to continue to invest.**
Appendix I.
ROI - sensitivity analysis

The single most consequential choice we made in our model was to treat the value of averting a DALY as a function of the average income in the country where the DALY was averted. This means that life years, and therefore lives, are treated as being less valuable in low-income countries.

This sounds like a terrible idea; many experts believe it to be a terrible idea. However, the reason it remains much more popular than the alternatives is that people rationally and systematically make different choices about their health and the risks they accept depending on their income. A risk-reducing innovation that is expected to save a single life at a cost of $12.3m just about breaks even in the United States but would represent a massive waste of resources based on the actual preferences of people living in a low-income country. With some hesitation, we chose to respect those different preferences by assigning a different value to risk, and therefore health, and therefore life.

Below, we set out the ROI calculated using different approaches to valuing life or different discount rates. The overall policy advice remains unequivocal: investing in R&D for neglected diseases delivers very high societal returns.

High societal returns remain even for different approaches to valuing life

If, instead of varying the value of life based on average national income, we had assumed that the $12.3m value applies universally, our ROI would be much, much higher—over 9,000, in fact. This seems potentially unrealistic and harmful to the project’s credibility.

More promisingly, Open Philanthropy—a funder of R&D and one of the funders of this project—uses a universal DALY valuation of $100k, which it has calculated based on the approximate trade-offs between life, money, and the pursuit of happiness. Using this figure instead of our $19,985 figure takes the ROI on R&D funding from 405:1 to 2,016:1.

A third alternative might be to continue treating the value of a life as a function of income but to calculate a universal value based on average global income, rather than the weighted average income of the nations where new products have the most impact. This is roughly equivalent to measuring the value of health based on the preferences of the average human rather than the average beneficiary. This yields a value of a statistical life of $3.48m (up from $0.55m when using beneficiaries’ income) and an ROI of 2,563:1.

At the other extreme, some economists might want to measure the value of saving a life based on how much extra productivity that person can have: the ‘human capital’ model. If we assign a value to each life year based on average national wages, employment rate and typical ages of labour force participation, then the total value of DALYs averted drops from around $49tn to around $7.5tn, lowering our ROI to 65:1 but still delivering very high returns on the investment in global health R&D.

High societal returns remain even for different discount rates

The other big, plausible change we could make to our model is to change the discount rate we apply when comparing future gains to past costs. The substantial time lag between funding R&D and saving lives means that this measure of society’s patience greatly influences our results.

We ultimately decided on a discount rate of 2%, in line with the recently announced US government policy but lower than the values commonly used in similar studies. If we instead applied the commonly used alternative of 3%, our ROI falls a little to 351:1. Were society even more impatient, treating each additional year as 5% less valuable than the last, our ROI would drop by almost half, to 266:1—remaining still at very high levels of return. A higher 5% discount rate is used exclusively for calculating the rate at which new scientific knowledge becomes less valuable over time, on the assumption that it is more likely to be superseded or to have been independently replicated in the interim.

Many experts believe, though, that a life saved in 2040 is just as valuable as one saved today. Most would accept some small discount rate based on the possibility that the long-delayed benefits become irrelevant or would eventually have been achieved by other means. Were we to accept that claim and adopt a zero discount rate—for lives saved and money spent—the ultimate returns from R&D look even more impressive, delivering an ROI of 542:1.
Figure I.
Return on investment for different values of life and discount rate

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Return on Investment</th>
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<tbody>
<tr>
<td>Central estimate - By country, elasticity 1.2; discount rate 2%</td>
<td>405</td>
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<tr>
<td>By country, elasticity 1.2; discount rate 3%</td>
<td>351</td>
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<tr>
<td>By country, elasticity 1.2; discount rate 0%</td>
<td>542</td>
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<tr>
<td>By country, elasticity 1.2; discount rate 5%</td>
<td>266</td>
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<td>By country, human capital; discount rate 2%</td>
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<tr>
<td>By country, elasticity 1.1; discount rate 2%</td>
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<tr>
<td>By country, elasticity 1.5; discount rate 2%</td>
<td>187</td>
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<tr>
<td>Universal, $100k/year; discount rate 2%</td>
<td>2,016</td>
</tr>
<tr>
<td>Universal, by global average; discount rate 2%</td>
<td>2,563</td>
</tr>
<tr>
<td>US value everywhere; discount rate 2%</td>
<td>9,050</td>
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## Appendix II.
### Expert advisory group

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Organisation</th>
<th>Country</th>
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<tbody>
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<td>Name</td>
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References


32. Unitaid. FIND and Unitaid, through the ACT-Accelerator, seek organizations to advocate and raise awareness on COVID-19 testing and treatment solutions. 2022.


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