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LANDSCAPE OF EMERGING INFECTIOUS DISEASE RESEARCH AND DEVELOPMENT: PREVENTING THE NEXT PANDEMIC

EXECUTIVE SUMMARY

Background and scope of the G-FINDER EID survey

Each year since 2007, the G-FINDER project has provided policy-makers, donors, researchers and industry with a comprehensive analysis of global investment into research and development (R&D) of new products to prevent, diagnose, control or cure neglected diseases in developing countries.

In response to the 2014 West African Ebola epidemic, Policy Cures Research began tracking funding for R&D targeting Ebola and related multi-filoviral research using the G-FINDER survey. This tracking effort was expanded in 2015 to include other viral haemorrhagic fevers and Zika, and then again in 2016 to align with the priority diseases identified in the 2018 World Health Organization's newly-developed *R&D Blueprint for Action to Prevent Epidemics* ('the R&D Blueprint'). The R&D Blueprint list of priority diseases – including 'Disease X', which it defines as *'the knowledge that a serious international epidemic could be caused by a pathogen currently unknown to cause human disease'* – have formed the foundation of the G-FINDER emerging infectious disease (EID) survey ever since.

Policy Cures Research is pleased to present the first ever *Landscape of Emerging Infectious Disease R&D* report, presenting for the first time all of the emerging infectious disease investment data collected since 2015.

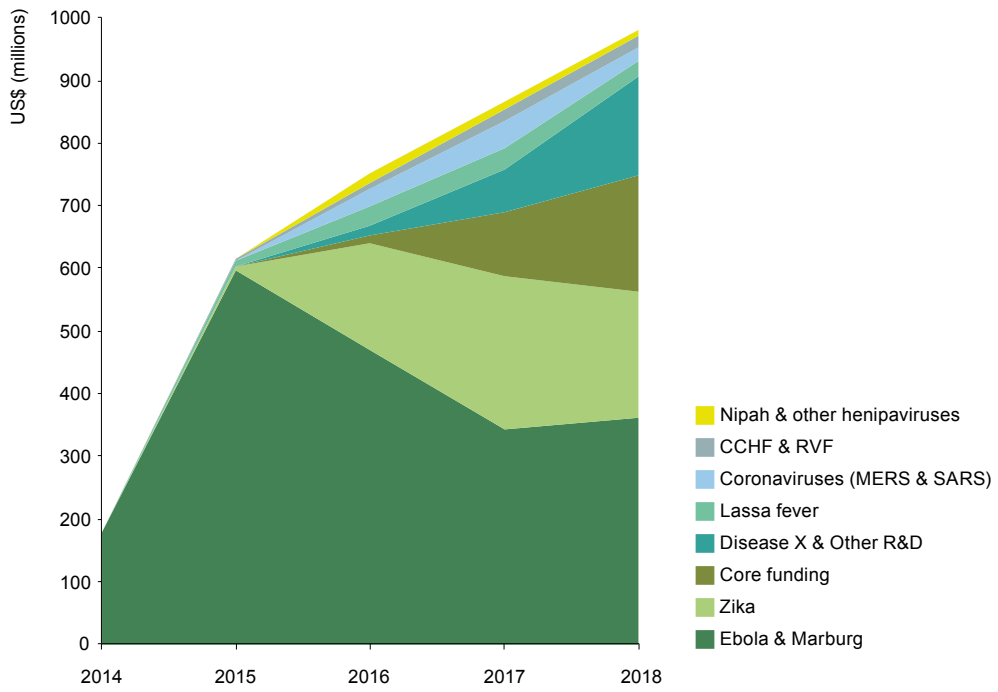
Overview of EID R&D funding

Funding for emerging infectious disease basic research and product development reached $886m in 2018, comfortably the highest total in the five years covered by this report and a 14% increase over 2017's previous record high.[1] In fact, measured funding to EID product developers has grown every year since we began collecting data on it in 2014, when we found just $178m in total funding – a fifth of the 2018 total.

Some of this growth stems from our improving understanding of which emerging infectious diseases should be included in our survey and the expansion of our survey scope to align with the WHO R&D Blueprint. Figure 1 – which also includes additional core funding to intermediaries on top of the $886m total – provides a sense of how overall funding has grown, and the areas where most of this growth has come from.

1 All figures mentioned are in 2018 US dollars converted at average 2018 exchange rates.

Figure 1. Total funding for emerging infectious diseases 2014-2018



The key factors driving higher EID R&D spending since 2014 were the Ebola and Zika epidemics, the establishment of the Coalition for Epidemic Preparedness Innovations (CEPI), and growing investment in 'Disease X' as an R&D priority. Funding for Ebola & Marburg more than tripled between 2014 and 2015 in response to the West African Ebola pandemic, making it responsible for basically all of the 2015 growth in funding. As the pandemic waned in 2016 and late-stage clinical trials for Ebola products became impossible, Ebola funding dropped too, falling by around $125m in both 2016 and 2017. The growth in overall funding in the face of such steep drops for Ebola was due to the emerging Zika epidemic, which began in Brazil in 2015 and was declared a Public Health Emergency of International Concern in February 2016. The global response to Zika pushed its funding from just $6m in 2015 to $170m in 2016, and higher still – $243m – in 2017. With clinical trials and funding both tailing off in 2018, a fresh outbreak of Ebola in the Democratic Republic of Congo brought an end to the decline in Ebola funding, and mostly offset the falls in funding for Zika.

The establishment of CEPI in 2017 is another big part of the story. It received $84m in 2017 and $134m in 2018, accounting for most of the net funding gains in each of those years. The other major area of recent funding growth relates to future, rather than current, epidemics: Disease X. 'Disease X' is the label given by the WHO to 'as-yet-unknown' pathogens with epidemic potential, and our R&D efforts to prepare for them. Since its inclusion in our survey in 2016, funding under our broad heading of 'Disease X & Other R&D' has grown rapidly – from $14m in 2016, to $73m in 2017, to $171m in 2018. Some of this growth reflects the difficulty in defining the borders of research into the unknown: our categorisation includes a range of genuinely pathogen-agnostic R&D, like platform technologies, broad-spectrum antivirals and fundamental research, but it also acts as a catch-all for 'Other R&D', which includes projects targeting multiple disease families where a breakdown of funding is unavailable. However much of this growth was driven by truly pathogen-agnostic R&D, with sharp increases in funding for platform technologies in both 2017 and 2018, headlined by a tenfold increase for general diagnostic platforms. Fundamental research spending has also more than doubled since we first included it in the survey in 2016.

FUNDING BY DISEASE

Funding for the other priority disease families covered in our survey – Lassa fever, coronaviruses, Crimean-Congo haemorrhagic fever, Rift Valley fever and Nipah – has tended to play second-fiddle to outbreak response, with each of these disease families receiving 5% or less of global funding. This picture should improve as CEPI's investments continue to ramp up; Lassa fever, for example, saw its funding jump in 2018 once it became the prime beneficiary of CEPI's first round of disbursements. Annual R&D investments by disease family between 2014-2018 are shown below in Table 2. Much more disease-specific analysis is included in the full report, including detailed breakdowns of funding by disease and product type.

Table 2. R&D funding by disease 2014-2018

Disease or R&D area / US$ (millions)	2014	2015	2016	2017	2018	Cumulative total	2018 % of total
Ebola & Marburg^	178	595	470	343	362	1948	41
Zika		6.1	170	243	202	621	23
Lassa fever		9.6	32	34	45	121	5.1
Coronaviruses (MERS & SARS)			25	44	41	110	4.6
CCHF & RVF		2.0	9.7	18	19	49	2.1
Nipah & other henipaviruses			14	13	11	37	1.3
Core funding of a multi-disease R&D organisation			11	13	34	58	3.9
Disease X & Other R&D			14	73	171	259	19
Other R&D			0.5	20	78	99	8.9
Multi-disease vector control products				26	36	62	4.1
Platform technologies			4.7	15	39	59	4.4
Fundamental research			6.3	8.7	16	31	1.8
Broad-spectrum antivirals			2.6	2.9	2.0	7.4	0.2
Total EID R&D funding	178	612	745	781	886	3203	100

Category not included in G-FINDER

^ Ebola was the only disease included in the 2014 survey. Value for Ebola in 2014 may include combined filoviral R&D.

* Due to significant changes in the survey scope, totals for 2014 and 2015 cannot be directly compared to totals in later years, or to each other.

FUNDING BY PRODUCT

Overall EID funding was focused on vaccine R&D, which received just over half of all funding between 2014 and 2018. Basic research received the next largest share – 17% – just ahead of the combined total for biologics (9.4%) and drugs (6.7%). Diagnostic products received only 3.6% of total funding, while vector-control products (VCPs) received just 2.4%, but a considerably larger share starting in 2017, when we began to include the full value of multi-disease VCPs as part of EID funding. The remaining funding was split between various multi-disease and non-disease-specific products, most notably core funding and funding which did not specify a product.

The dominance of vaccine funding peaked in 2015, at the height of the West African Ebola epidemic, at nearly 70% of the global total. Nearly three-quarters of the disease-specific vaccine funding over the period went to Ebola & Marburg with most of the remainder, a further 22%, going to Zika. The share of funding going to vaccines has declined every year since, falling below 40% in 2018. Funding in recent years has shown an increased focus on basic research, as well as big rises in core and multi-disease funding. The shares going to drugs, biologics and diagnostics have remained relatively consistent over the last few years.

Funding for basic research was split much more evenly across the priority pathogens than vaccine development, but still saw 70% of its overall funding go to either Ebola & Marburg or Zika. The other significant recipients of basic research funding were coronaviruses and Lassa fever, with 8 and 9% of total funding respectively. The US National Institutes of Health (US NIH) was by far the largest funder of basic research overall, contributing over three-quarters of all funding ($425m, 76%), nearly twenty times the contribution of the European Commission (EC), the next biggest funder.

FUNDING TO INTERMEDIARIES

Intermediary organisations can take many forms, from product development partnerships (PDPs) to initiatives such as CEPI and the European and Developing Countries Clinical Trials Partnership (EDCTP), but fundamentally they all provide a coordinating mechanism which pools funding from different organisations to advance a portfolio of candidates or projects.

Intermediary organisations have long played a significant role in the landscape of R&D for neglected diseases such as malaria and tuberculosis, and – especially in the case of CEPI – have been a central feature of the response to COVID-19, helping to form the pillars of the Access to COVID-19 Tools (ACT) Accelerator. But until relatively recently this wasn't true for EIDs; there was no funding to intermediaries reported in 2014, and only limited funding in 2015 and 2016, reflecting the absence of intermediary organisations focused on EID R&D prior to the West African Ebola outbreak.

The picture changed following the 2017 establishment of CEPI, and the subsequent uptick in funding from governments and philanthropic organisations. Funding for intermediaries increased nearly tenfold between 2016 and 2017, surpassing $100m, and increased again in 2018 to reach an all-time high of $155m. CEPI was by far the largest recipient of funding to intermediaries both in 2018 and overall, receiving 80% ($219m) of all funding to intermediaries during the period from 2014-2018, despite only being active for two of these five years.

After CEPI, the intermediary to receive the most funding was the EDCTP, though none of its inward funding was earmarked specifically for EIDs; the funding included has instead been calculated based on the proportion of EDCTP's onward funding that targeted priority EIDs. The rising share of EDCTP onward funding going to EIDs reflects the expansion of its scope from neglected diseases alone to also cover emerging infectious diseases like Ebola and wider pandemic preparedness.

The German BMBF was the largest funder of intermediaries in 2018 and overall, providing just under $47m to CEPI since its inception, while also directing $13m in funding to the German DZIF – the German public body devoted to coordinating its domestic infectious disease research.

FUNDERS

The funder landscape for emerging infectious disease R&D has been characterised by an overwhelming dominance of public sector funding, despite a significant – and in comparison to neglected diseases, unprecedented – level of industry investment in the wake of the 2014-16 West African Ebola epidemic. Philanthropic funding for EIDs has remained relatively limited.

At its peak, in 2015, industry collectively provided 40% of global EID R&D funding, making it by far the biggest contributor in that year. Industry funding declined rapidly after the conclusion of the West African Ebola epidemic in mid-2016, which limited opportunities for further clinical trials. Though industry was still, as a collective, the third-largest funder in 2018, the two-thirds fall in its spending since 2015 has left EID funding increasingly dominated by the high-income country public sector, particularly the big US funders, who together accounted for more than two-thirds of all public funding in 2018.

The US government provided 61% of global funding to product developers between 2014 and 2018. Combined with investment made by US-based pharmaceutical companies, almost three-quarters of global funding for EID R&D during this five year period came solely from the United States. The US NIH consistently dominated global EID funding, providing more funding than any other entity for every single priority pathogen family, and giving the US government an 80% share of global basic research funding. Its role is complemented by that of the US Biomedical Advanced Research and Development Authority (BARDA), by far the largest funder of clinical development. Along with self-funded research by the pharmaceutical industry, which has seen its role decline steeply from a peak driven by Ebola clinical trials in 2015, the US NIH and BARDA together accounted for nearly 70% of all global funding, with a further 5% coming from the US Department of Defense.

This US-centric picture began to change a little in 2017 and 2018. The US share of public funding for EID R&D sank to a low of 68% in 2018, down from a high of 84% in 2014. The governments of the United Kingdom, France and Germany all increased their share of global funding in both 2017 and 2018, while the creation of CEPI provided a vehicle for new streams of funding from national governments – like those of Japan and CEPI's host nation, Norway – and the major philanthropic funders of neglected disease R&D: the Gates Foundation and the Wellcome Trust. These new funding streams, accompanied by the consistent efforts of the EC, the fourth-largest funder overall, have gone some way towards rebalancing the funding of EID R&D.

DISCUSSION

Funding for emerging infectious disease R&D rises rapidly following a major outbreak

The world responded to large-scale outbreaks of Ebola across Africa and Zika in South America with rapid increases in both basic research and clinical development funding. After the conclusion of the West African outbreak in 2016, funding for Ebola began to tail off, only to rebound slightly in 2018 as a new outbreak took hold in the DRC. Funding for Zika followed a similar pattern, peaking a year after the outbreak began, before falling by nearly a fifth in 2018 after the virus was brought under control.

These post-outbreak reductions in spending are mostly due to the practical difficulties in conducting late-stage clinical trials in the absence of new infections, underlining the importance of taking maximum advantage of the (hopefully brief) window available for conducting clinical trials in high-prevalence populations. It is important to provide R&D funding early in a pandemic and to conduct the underlying basic research before time begins to run out.

Disease X and preparing for the unknown

If funders are currently too reactive in their responses to pandemic risk, how should they deal with the unavoidable uncertainty about which pandemics represent the greatest future threat?

One strategy is to focus funding on cross-cutting R&D applicable to a range of existing EIDs, or to build the foundation for responding to as-yet-unidentified pathogens. This is the kind of funding recognised by the WHO Blueprint under the title of 'Disease X'. Disease X R&D which focuses on currently unknown pathogens must be genuinely agnostic as to the diseases it targets – a category which includes fundamental research, platform technologies and broad spectrum antivirals. The second definition of Disease X funding – cross-cutting R&D – potentially includes any funding which is not earmarked for a single specific priority pathogen.

Our vision of preparing for 'Disease X' could even be extended to include the provision of core funding for multi-disease organisations, representing funders' choice to support cross-cutting R&D rather than targeting specific diseases. Supporting these organisations allows funders to delegate, and defer, decisions about where their funding should be directed, and recipient organisations to redirect funding in response to crises. So, the rapid growth in core funding, driven by the creation of CEPI, represents a valuable counterweight to the kind of purely reactive post-outbreak funding that dominated the landscape between 2014 and 2016.

How the creation of CEPI changed the funding landscape

With the establishment of CEPI in 2017, its public and philanthropic funders committed themselves to a cross-cutting approach to vaccine R&D. CEPI provides a new financing model, uniting funders to help meet the high costs of late-stage vaccine trials across a range of pathogens. But it also gives funders a means to pre-commit resources to combating as-yet-unknown diseases, positioning CEPI as the key custodian of the world's preparations for Disease X. With the right support, we hope to see CEPI become both a stable, ongoing source of funds for proactive, forward-looking research, and a global 'emergency preparedness fund', with committed funding held in reserve to respond to the emergence of an unknown pathogen. CEPI's reach is undermined, though, by its exclusive focus on vaccines. The world needs to maintain funding for a broad range of R&D, including basic research, drugs, and diagnostics.

Did the world do enough to prepare for COVID-19?

The COVID-19 pandemic has given us a clearer picture of the kind of crisis the world ought to have been planning for. The purely economic costs of the pandemic have been estimated at $375 billion per month. These losses dwarf our collective historical global spending on EID R&D and suggest that EID R&D funding should have considered the worst-case scenarios alongside what we thought we knew about pandemic potential. By concentrating basic research funding on the cause of the last major outbreak, the world remained overconfident in our ability to predict the direction of the next threat.

With the sudden arrival of exactly the kind of crisis EID research was supposed to prevent, or at least contain, it seems clear that more could and should have been done to prepare for the potential emergence of something like COVID-19. One key lesson is that future R&D funding needs to be much more diversified: less focused on basic research for the one or two pathogens most recently in the news, less focused on vaccines to the exclusion of other vital tools, and supported by a wider range of funders – in contrast to our current near-complete reliance on the United States government.

The United States dominates global funding for EID R&D

Global funding for EID R&D is very narrowly focused on recent large-scale outbreaks, but it is also supported by only a few key funders.

The US government provides more than 80% of basic research funding and nearly 96% of public sector funding for drug R&D, making it the dominant player in both product-specific and early-stage research. The funding provided by the US government via the NIH is distributed across a wide range of priority pathogens. While a little more than half of NIH funding between 2014 and 2018 was for Ebola, making it the top funder of Ebola R&D, it is also the overall top funder of every other Blueprint priority disease group, including Disease X.

A truly global commitment to pandemic preparedness needs to be bigger, more proactive, and less reliant on the foresight and goodwill of a single government. The evolving global response to the COVID-19 pandemic suggests that this lesson is hopefully being learned.