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Special Series on Trade and Health

Financing Research and Development for New Vaccines in Asia-Pacific Developing Countries



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ASIA-PACIFIC RESEARCH AND TRAINING NETWORK ON TRADE

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ASIA-PACIFIC RESEARCH AND TRAINING NETWORK ON TRADE

WORKING PAPER

Financing Research and Development for New Vaccines in Asia-Pacific Developing Countries

Gavin Yamey, Kaci Kennedy McDade, Wenhui Mao, Ekene Osakwe¹

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Abstract

There have been many important innovations in the landscape of vaccine development for neglected and emerging infectious diseases, such as the launch of public-private product development partnerships (PDPs). However, there is still a gap in funding the development of such vaccines, especially when it comes to financing late-stage trials. There is a financial risk in investing in late-stage trials, and there is no guarantee of a commercial market, particularly for the most neglected diseases of poverty. One result of the funding gap is that there are many infectious diseases with a high burden in the Asia-Pacific region for which there are no licensed, highly effective vaccines, including HIV/AIDS, tuberculosis, soil-transmitted helminths and schistosomiasis. There are also neglected infectious diseases that affect populations in the region where the existing vaccines have limitations, such as malaria, dengue, and Japanese encephalitis.

Understanding how much additional financing is needed for vaccine research and development (R&D) for neglected and emerging infections is a crucial first step in closing the financing gap. Annual spending on vaccine R&D for neglected diseases was approximately \$1 billion in 2020. Our previous modelling research, using a financial tool called the Portfolio to Impact model, estimated that \$3 billion is needed annually, suggesting there is an annual financing gap of \$2 billion. For vaccine R&D for emerging diseases, annual spending on the Blueprint diseases was \$350 million in 2018, but the annual financing need is approximately \$400 million to \$520 million, suggesting an annual funding gap of \$50 million to \$170 million.

How much is the Asia-Pacific region investing in vaccine R&D through the public, private, and philanthropic sectors and via PDPs? Using data from the G-FINDER database, we estimate that from 2018–2020, there was only \$35 million annually being invested in the region in neglected disease vaccine R&D and \$3.8 million annually being invested in emerging infectious disease vaccine R&D. These are very low levels of financing compared with the need. Despite such low levels of financing, our report finds that there is significant vaccine trials and manufacturing capacity in many developing countries of the region.

Closing the vaccine R&D funding gap in the Asia-Pacific region would have enormous health and economic returns. The various policy approaches to closing this gap can be organized into (1) resource mobilization (e.g. government contributions, airline ticket levies), (2) pooling of resources (e.g. a regional pooled R&D fund), and (3) strategic purchasing (see figure).

Keywords: COVID-19, Vaccines, R&D, R&D financing, Asia-Pacific

JEL Codes: F21, O32

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Abbreviations and acronyms

ADB	Asian Development Bank
AMR	antimicrobial resistance
APVAX	Asia Pacific Vaccine Access Facility
CCHF	Crimean Congo haemorrhagic fever
CEPI	Coalition for Epidemic Preparedness Innovations
COVID-19	coronavirus disease
DALYs	Disability-adjusted life years
GDP	gross domestic product
GHIT	Global Health Innovative Technology Fund
GloPID-R	Global Research Collaboration for Infectious Disease Preparedness
GPGs	global public goods
HICs	high-income countries
HPV	human papillomavirus
IAVI	International AIDS Vaccine Initiative
IVI	International Vaccine Institute
JE	Japanese encephalitis
LICs	low-income countries
LMICs	lower-middle-income countries
MERS	Middle East respiratory syndrome coronavirus
MICs	middle-income countries

MVAC	market-driven, value-based advanced commitment
OECD	Organisation for Economic Co-operation and Development
P2I	Portfolio to Impact tool
PDPs	product development public-private partnerships
R&D	research and development
RIGHT	Research Investment for Global Health Technology
SARS	severe acute respiratory syndrome
TB	tuberculosis
UNICEF	United Nations Children's Fund
WHO	World Health Organization

1. Introduction

There have been many important shifts and innovations in the landscape of vaccine development for neglected and emerging infectious diseases in recent years. These have included the launch of new public-private product development partnerships, the mobilization of funding for vaccine research and development (R&D) from bilateral development agencies and philanthropies, and the emergence of new networks and partnerships devoted to such R&D. In addition, the development of vaccines against the coronavirus disease (COVID-19) in under one year—the fastest vaccine development in history—has injected optimism that a new vaccine revolution could be under way, using next generation vaccine platforms such as viral vectors and mRNA. As we have previously argued: the success of the COVID-19 vaccine enterprise may be transferable to emerging infections and some neglected diseases such as tuberculosis (TB) if the protective antigens are known (Yamey, 2021).

Despite these positive trends, there still remain major gaps in funding the development of vaccines for neglected and emerging infections, especially when it comes to financing late-stage development. The improvements in the landscape mentioned above have mostly targeted early-stage development. Rappuoli and colleagues (2019) recently concluded that “these improvements in the early development process have revealed a new, and possibly more perilous, Valley of Death in the late vaccine development phase.” There are many reasons to explain this funding gap, but three of the most important are:

- Late-stage trials are costly, there is a financial risk in investing in them, and there is no guarantee of a commercial market, particularly for the most neglected diseases of poverty (patients themselves and Governments of low-income countries (LICs) may be unable to pay for vaccines);
- There is no overarching prioritization, coordination or governance mechanism for vaccine R&D—the result is that the vaccine R&D landscape remains highly fragmented with multiple overlapping and duplicative efforts;
- There has been too little inclusion of voices from LICs and middle-income countries (MICs) when it comes to decision-making around vaccine R&D, even though these countries suffer a disproportionate burden of vaccine-preventable illness (Yamey and others, 2020).

These ongoing funding gaps mean that there are many emerging and infectious diseases that lack safe, high efficacy vaccines. There are many diseases that have a high burden in the Asia-Pacific region for which there are not yet any licensed, highly effective vaccines. Four examples include:

- **HIV/AIDS:** The region has more people living with HIV/AIDS (5.8 million in 2020) than any other region except sub-Saharan Africa (UNAIDS, 2022). There are no licensed HIV vaccines.

- **TB:** This disease is the leading cause of infectious disease deaths in the Asia-Pacific region. More than 40 per cent of new annual cases and almost half of all annual TB deaths are in India, Indonesia and Pakistan alone (OECD and WHO, 2020). The only licensed vaccine is the Bacillus Calmette–Guérin (BCG) vaccine, introduced in 1921. While it provides moderate protection against severe forms of TB in infants and young children, it is ineffective in preventing TB disease in adults, either before or after exposure to TB infection (WHO 2021).
- **Hookworm and other soil-transmitted helminths:** More than half of the world’s population live in places where soil-transmitted helminths are endemic (Hotez and others, 2014), and soil-transmitted helminths are highly prevalent in the Asia-Pacific region. For example, hookworm prevalence in Lao People’s Democratic Republic, Viet Nam and Cambodia is 30 per cent, 29 per cent and 28 per cent, respectively, while roundworm prevalence in the Philippines, Malaysia and Myanmar is 76 per cent, 72 per cent and 53 per cent, respectively (Silver and others, 2018). Vaccines are needed because the only current way to achieve parasite control is through repeated bouts of mass drug administration. As Roy Anderson (2011) says, “The neverending requirement for mass drug administration in the absence of transmission interruption makes clear the urgent need for other interventions.”
- **Schistosomiasis:** Three species of *Schistosoma* are endemic and cause disease in many Asia-Pacific countries—the most prevalent is *S. japonicum*, followed by *S. mekongi* and *S. malayensis* (Gordon and others, 2019). The disease is endemic in six countries in the region – China, Cambodia, Indonesia, the Lao People’s Democratic Republic, Malaysia and the Philippines – and is emerging in a seventh: Myanmar (Soe and others, 2017). A safe, effective vaccine will be needed to achieve sustained control and eventual elimination (Molehin, 2020).

In addition, there are neglected infectious diseases that affect populations in the region where the existing vaccines have limitations. For example:

- **Malaria:** More than 2 billion people are at high risk of malaria in Asia and the Pacific, and the disease is endemic in 17 nations in the region (Bangladesh, Cambodia, China, Democratic People’s Republic of Korea, India, Indonesia, the Lao People’s Democratic Republic, Malaysia, Myanmar, Nepal, Pakistan, Papua New Guinea, the Philippines, the Republic of Korea Solomon Islands, Thailand and Viet Nam) (OECD and WHO, 2020). There is only one licensed malaria vaccine (RTS,S) and its efficacy against clinical malaria is low: 35.9 per cent efficacy in the first year after vaccination, falling to 2.5 per cent in the fourth year (Olotu and others, 2016).
- **Dengue:** Approximately 3.9 billion people worldwide are at risk of dengue—of whom 70 per cent live in the Asia-Pacific region—and there are an estimated 390 million dengue virus infections per year, of which 96 million present clinically (WHO, 2022). Only one vaccine, CYD-TDV (Dengvaxia; Sanofi Pasteur), has been licensed in selected countries but often with major restrictions. In their review

of dengue vaccine development, Wen-Hung Wang and colleagues (2021) note that the vaccine has “demonstrated low efficacy in children and dengue-naïve individuals and also increases the risk of severe dengue in young vaccinated recipients.”

- **Japanese encephalitis:** *Japanese encephalitis* (JE) virus is the most important vaccine-preventable cause of encephalitis in the Asia-Pacific region (Heffelfinger and others, 2017). Although JE vaccines have been available for decades, Kirsten Vannice and colleagues (2021) note that “the high cost and multiple-dose regimen of the older, inactivated mouse brain-derived vaccine limited JE vaccine introduction.”

The Asia-Pacific region has also been at the epicentre of several emerging infectious diseases, including severe acute respiratory syndrome (SARS), avian influenza and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and developing and stockpiling vaccines against emerging threats is a critical foundation in the World Health Organization (WHO) *Asia Pacific Strategy for Emerging Diseases*.

Given this critical need to develop new vaccines for a range of infectious diseases, a new urgency is also needed to mobilize additional financing for vaccine R&D in the Asia-Pacific region. In this paper, we begin by laying out the estimated financing gap for developing vaccines for neglected and emerging infections and exploring the reasons why this gap persists. We then examine the current landscape of financing for vaccine R&D in Asia and the Pacific, focusing on both the strengths and weaknesses. In this landscaping, we describe the main funders and funding recipients, the recent initiatives aimed at raising financing (e.g. public-private partnerships), and the levels of funding that have been mobilized. Next, we look at the value proposition for increased investments in vaccine R&D in the region. Finally, we propose policy options to close the financing gap for vaccine R&D in Asia and the Pacific. This analysis was based on a rapid review of the peer-reviewed and grey literature and key informant interviews with relevant experts in the region. The study was screened and approved for exemption by the institutional review board at Duke University.

2. Vaccines for neglected and emerging infections: the financing gap

Understanding how much additional financing is needed for vaccine R&D for neglected and emerging infections is a crucial first step in closing the financing gap. Unfortunately, for several reasons discussed below, there have been very few estimates of this gap, and all available estimates are subject to many limitations.

2.1 Current spending on research and development for neglected diseases

The best available evidence on current public, private and philanthropic spending on vaccine R&D for neglected and emerging infections comes from the annual G-FINDER survey conducted by Policy Cures Research, a global health think tank. The survey has been published annually since 2008. The most recent report, published in 2021, provides estimates of funding in the year 2020 for R&D for basic research, drugs, vaccines, biologics, diagnostics, microbicides, vector control products and “unspecified funding” across 45 disease categories, as well as funding for platform technologies, multi-disease vector control products, core funding for multi-disease R&D organizations and funding for “unspecified diseases” (**Error! Reference source not found.**).

Table 1: G-FINDER 2021 survey: Neglected diseases, products and technologies

Disease	Basic research	Drugs	Vaccines	Biologics	Diagnostics	Microbicides	Vector control products
HIV/AIDS	Restricted	Restricted	✓	Restricted	✓	✓	-
Tuberculosis	✓	✓	✓	✓	✓	-	-
Malaria							
	✓	✓	✓	✓	✓	-	✓
	✓	✓	✓	✓	✓	-	✓
	✓	✓	✓	✓	✓	-	✓
Diarrhoeal diseases							
	✓	Restricted	✓	Restricted	✓	-	-
	✓	Restricted	✓	Restricted	✓	-	-
	Restricted	-	Restricted	-	-	-	-
	✓	Restricted	✓	Restricted	✓	-	-
	Restricted	-	✓	-	✓	-	-
	-	-	✓	-	✓	-	-
	-	-	-	-	✓	-	-
	✓	Restricted	✓	Restricted	✓	-	-
Kinetoplastid diseases							
	✓	✓	✓	✓	✓	-	-
	✓	✓	✓	✓	✓	-	✓
	✓	✓	✓	✓	✓	-	✓
	✓	✓	✓	✓	✓	-	✓
Helminth infections (worms & flukes)							
	✓	✓	✓	✓	✓	-	✓
	✓	✓	✓	-	✓	-	✓
	✓	✓	-	-	✓	-	✓
	✓	✓	-	-	✓	-	✓
	✓	✓	✓	-	-	-	-
	✓	✓	✓	-	-	-	-
	✓	✓	✓	-	-	-	-
	✓	✓	✓	-	✓	-	-
	✓	✓	✓	-	-	-	-
	✓	✓	✓	-	✓	-	✓
Salmonella infections							
	✓	✓	✓	✓	✓	-	-
	✓	✓	✓	✓	✓	-	-
	✓	✓	✓	✓	✓	-	-
Dengue	✓	✓	-	✓	✓	-	✓
Bacterial pneumonia & meningitis							
	Restricted	-	Restricted	-	✓	-	-
	Restricted	-	Restricted	-	✓	-	-
	Restricted	-	-	-	✓	-	-
Hepatitis B	Restricted	Restricted	-	Restricted	✓	-	-
Hepatitis C	-	Restricted	✓	-	✓	-	-
Rheumatic fever	-	-	✓	-	-	-	-
Snakebite envenoming	Restricted	Restricted	-	Restricted	Restricted	-	-
Leprosy	✓	✓	✓	✓	✓	-	-
Cryptococcal meningitis	-	✓	-	✓	-	-	-
Histoplasmosis	✓	✓	-	-	✓	-	-
Buruli ulcer	✓	✓	✓	-	✓	-	-
Trachoma	-	-	✓	-	✓	-	-
Leptospirosis	-	-	-	-	Restricted	-	-
Scabies	Restricted	✓	-	-	✓	-	-
Mycetoma	✓	✓	-	-	✓	-	-

Investment applicable to more than one neglected disease, or to more than one global health area*					
Platform technologies					
General diagnostic platforms	Adjuvants & immunomodulators	Drug delivery technologies & devices	Vaccine delivery technologies & devices	Multi-disease vector control	Core funding of a multi-disease R&D organisation
Restricted	Restricted	Restricted	Restricted	✓	✓

✓ denotes a category where a disease or product is included in the survey

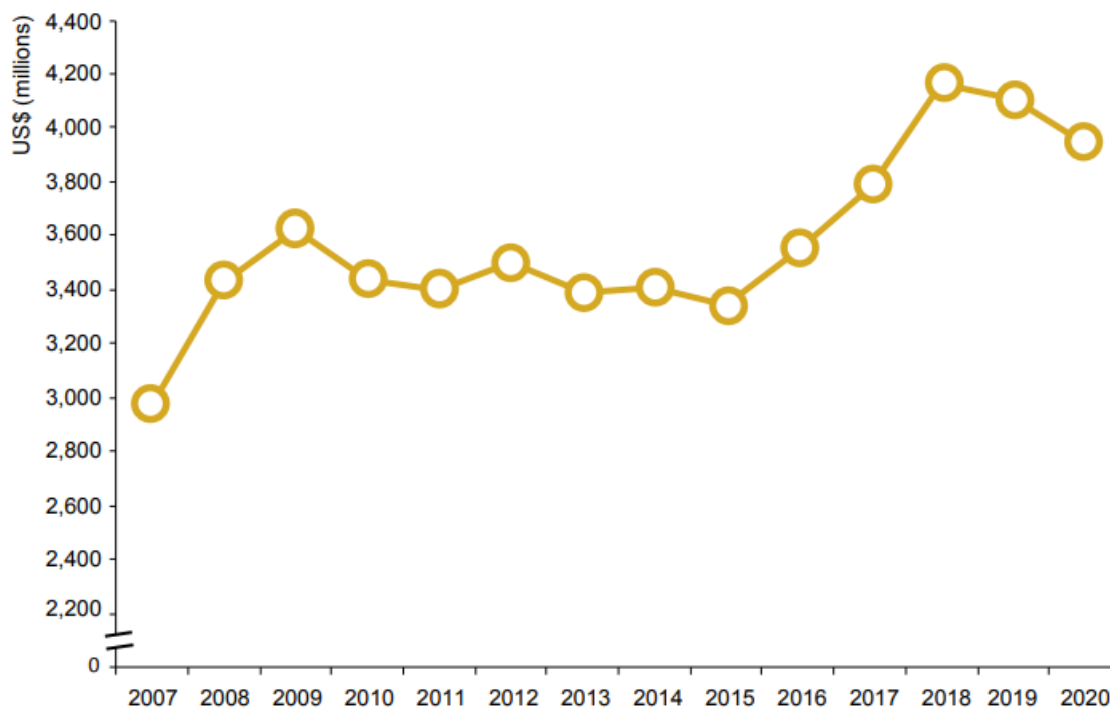
Restricted denotes a category where only some investments are eligible, as defined in the G-FINDER neglected disease R&D scope document

* The G-FINDER project covers three global health areas: neglected diseases, emerging infectious diseases, and sexual & reproductive health issues

Source: Policy Cures Research, 2021, *Neglected Disease Research and Development: New Perspectives*. Available at <https://policy-cures-website-assets.s3.ap-southeast-2.amazonaws.com/wp-content/uploads/2022/01/02212458/2021-G-FINDER-Neglected-Disease.pdf>.

In 2020, total funding was approximately \$4 billion (\$3,937 million), a small decrease from the near-record high in 2019 (**Error! Reference source not found.**). In 2020, approximately one quarter of this total—\$1.1 billion—was for vaccine R&D against specific disease categories, \$47 million was for vaccine delivery technologies and devices, and \$24 million was for adjuvants and immunomodulators. **Error! Reference source not found.** shows the breakdown of vaccine R&D funding in 2020 by broad disease category. In Section 3, we disaggregate vaccine R&D funding for neglected diseases to show recipients of funding in the region and who is funding these recipients.

Figure 1: Annual funding for research and development for neglected diseases, 2007–2020

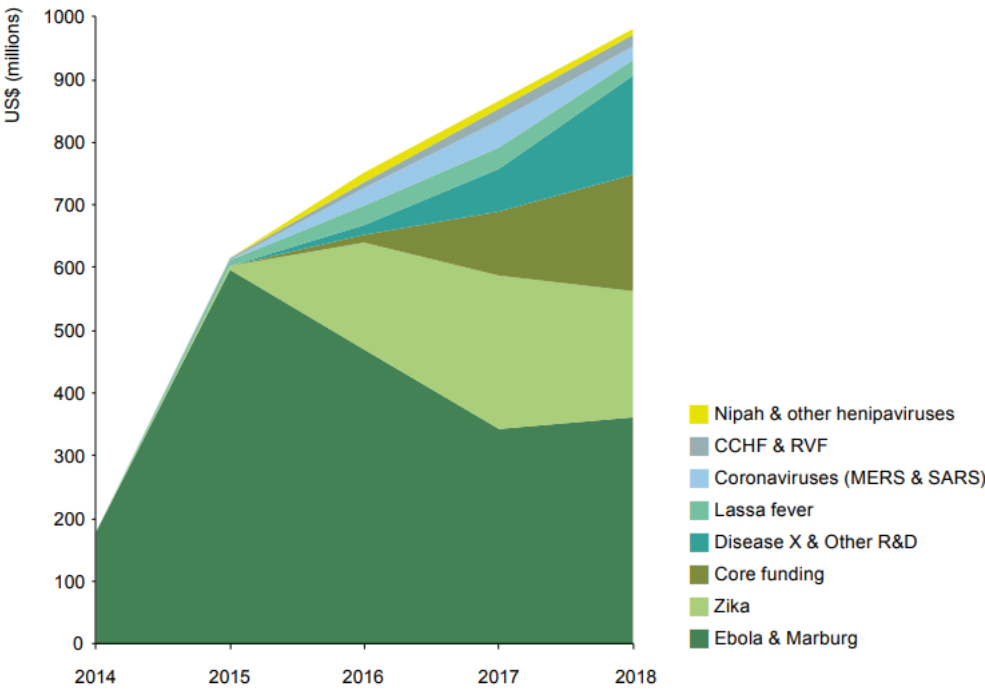


Source: Policy Cures Research, 2021, *Neglected Disease Research and Development: New Perspectives*. Available at <https://policy-cures-website-assets.s3.ap-southeast-2.amazonaws.com/wp-content/uploads/2022/01/02212458/2021-G-FINDER-Neglected-Disease.pdf>.

Table 2: Vaccine research and development funding for neglected diseases in 2020 by broad disease category	
Broad disease category	2020 funding (Millions of United States dollars)
HIV/AIDS	710.31
TB	72.94
Malaria	117.58
Diarrhoeal diseases	75.54
Kinetidoplastid diseases	4.66
Helminth infections (worms and flukes)	5.52
Salmonella infections	32.91
Bacterial pneumonia and meningitis	61.06
Hepatitis C	2.46
Rheumatic fever	15.59
Leprosy	0.43
Buruli ulcer	0.02
Trachoma	1.91
Total	1 100.93
<i>Source:</i> See table 1.	

When the Ebola virus disease epidemic began in 2014 in West Africa, Policy Cures Research started tracking funding for R&D for the Ebola vaccine and related multi-filoviral research. 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’)”(Policy Cures Research, 2020). Policy Cures Research recently published their estimates of annual funding for such emerging infectious diseases from 2014 to 2018, which showed that funding reached a record high of \$886 million in 2018 (**Error! Reference source not found.**). The sharp rise in annual funding for R&D for such diseases was driven by the Ebola and Zika epidemics, the launch of the Coalition for Epidemic Preparedness Innovations (CEPI) and the rising interest in funding R&D for what the R&D Blueprint calls “Disease X” (i.e. an epidemic or pandemic caused by a pathogen currently unknown to cause human disease).

Figure 2: Funding for emerging infectious disease research and development, 2014–2018



Source: Policy Cures Research, 2020, Landscape of Emerging Infectious Disease Research and Development: Preventing the next pandemic. Available at https://s3-ap-southeast-2.amazonaws.com/policy-cures-website-assets/app/uploads/2020/09/16021630/GFINDER_LEIDR_EXEC_SUMMARY.pdf.
 Abbreviations: CCHF, Crimean-Congo haemorrhagic fever; MERS, Middle East respiratory syndrome; RVF, Rift Valley fever; SARS, severe acute respiratory syndrome.

Out of the \$886 million spent in 2018, about 40 per cent (\$350 million) was invested in vaccines for specific emerging infectious diseases. The breakdown of vaccine R&D financing into broad disease categories is shown in **Error! Reference source not found.** In addition, for Disease X and other R&D, \$10.09 million was spent on adjuvants and immunomodulators, \$2.57 million was spent on vaccine delivery technologies and devices, and \$7.78 million was spent on vaccine platforms and multi-family vaccines. In Section 3, we disaggregate this vaccine R&D funding for emerging infections by funder type.

Table 3: Vaccine research and development funding for emerging infectious diseases in 2018 by broad disease category	
Broad disease category	2018 funding (Millions of United States dollars)
Filoviruses - Ebola and Marburg	187.63
Zika	102.59
Arenaviruses - Lassa fever	25.16
Coronaviruses - MERS and SARS	22.14
Bunyaviruses - CCHF and RVF	10.40
Henipaviruses – Nipah virus and other henipaviruses	2.39
Total	350.31

Source: Policy Cures Research, 2020, Landscape of Emerging Infectious Disease Research and Development: Preventing the next pandemic. Available at https://s3-ap-southeast-2.amazonaws.com/policy-cures-website-assets/app/uploads/2020/09/16021630/GFINDER_LEIDR_EXEC_SUMMARY.pdf.

Abbreviations: CCHF, Crimean-Congo haemorrhagic fever; MERS, Middle East respiratory syndrome; RVF, Rift Valley fever; SARS, severe acute respiratory syndrome

2.2 Estimates of research and development funding needs

In Section 2.1., we summarized estimates of the current levels of financing of vaccine R&D for neglected and emerging infections. How do these levels compare with estimates of funding needs—in other words, what is the likely financing gap?

There is no straightforward answer to this question, given the challenges in estimating the costs to develop vaccines for neglected and emerging infections. Proprietary concerns, for example, have meant that vaccine companies have been reluctant to share information on the cost, success rate and cycle time per phase for vaccine development. The different cost structures for developing vaccines for different infections are poorly understood, as are the differences between costs for simple versus complex vaccines.

Despite these limitations, there several recent efforts have attempted to estimate vaccine R&D costs for neglected and emerging infections, which provide a helpful starting point in understanding the likely size of the financing gap. We acknowledge that these are necessarily crude numbers, but no accurate figures on the gap are available.

2.2.1 The cost to develop vaccines for neglected diseases

In 2018, in the first study of its kind, Ruth Young and colleagues (2020) conducted a product pipeline portfolio review for 35 neglected diseases and then used a new financial modelling tool, the Portfolio to Impact (P2I) tool, to estimate the costs to move these existing product candidates through the pipeline over the next decade and the likely launches. Given that the existing pipeline was unlikely to yield several highly needed technologies, the authors also estimated the costs to develop a set of 18 priority “missing”

products. These priority products were highly effective vaccines for HIV, TB, malaria, hepatitis C, diarrhoea (a combined vaccine against rotavirus, enterotoxigenic *E. coli*, typhoid and shigella), a new TB drug co-formulation, and a new drug for each of 12 different neglected tropical diseases. The study included costs for advanced preclinical to phase 3 trials (i.e. it did not estimate earlier basic research or any costs after phase 3, so it underestimated total costs).

Their key findings were:

- As of 31 August 2017, they found 538 product candidates in the pipeline.
- They estimated that about \$16.3 billion would be needed to move these candidates through the pipeline, with three quarters of the costs incurred in the first five years, resulting in about 128 expected product launches. Based on the existing pipeline, they found that “there would be few launches of complex new chemical entities; launches of highly efficacious HIV, TB, or malaria vaccines would be unlikely.”
- Launching one of each of 18 key missing products would cost an additional \$13.6 billion assuming lowest product complexity or \$21.8 billion assuming highest complexity.
- Over the next five years, total estimated costs to move existing candidates through the pipeline and develop these 18 missing products would be \$4.5 billion (low complexity missing products) or \$5.8 billion per year (high complexity missing products).
- Since annual global spending on neglected disease R&D was estimated at \$3 billion from 2008 to 2017, the study suggested that the annual funding gap over the next five years was at least \$1.5 billion to \$2.8 billion.
- Focusing on vaccine development alone, they estimated that \$9 billion would be needed to move vaccine candidates through the pipeline (again, three-quarters of the costs would be incurred in the first five years). Launching “missing” vaccines for HIV, TB, malaria, hepatitis C, and diarrhoea would cost an additional \$12.5 billion to \$13.2 billion (depending on vaccine complexity). Thus, over the next five years, total estimated costs to move existing vaccine candidates through the pipeline and develop these five missing vaccines would be \$16.1 billion to \$16.7 billion, or \$3.2 billion to \$3.3 billion annually.

As shown in **Error! Reference source not found.**, annual spending on vaccine R&D for HIV, TB, malaria, hepatitis C, and diarrheal diseases was approximately \$1 billion (\$978 million) in 2020. Thus, we estimate that the funding gap for these five neglected diseases alone is \$2 billion annually.

2.2.2 The cost to develop vaccines for emerging infectious diseases

In 2010, Dimitrios Gouglas and colleagues (2018) conducted a pipeline portfolio review of vaccine candidates for 11 diseases with epidemic potential and used a stochastic optimization model to estimate the minimum costs to progress at least one vaccine for each disease through to the end of phase 2a. The study included the 11 diseases

included in R&D Blueprint at the time: Crimean Congo haemorrhagic fever (CCHF), chikungunya, Ebola, Lassa, Marburg, Middle East respiratory syndrome coronavirus (MERS), Nipah virus, Rift Valley fever, SARS, severe fever with thrombocytopenia syndrome (SFTS) and Zika.

Given the likely success rates at each phase of development, Gouglas and colleagues estimate that the average cost of advancing at least one vaccine from preclinical through to the end of phase 2a ranges from \$319 million to \$469 million, which includes the cumulative cost of failed vaccine candidates through the R&D process. They conclude that “assuming these candidates and funding were made available, progressing at least one vaccine through to the end of phase 2a for each of the 11 epidemic infectious diseases would cost a minimum of \$2.8 billion to \$3.7 billion.”

The authors estimate that the average timeline bringing emerging infectious disease vaccine development projects from preclinical through end of phase II is 6–7 years. Thus, the annualized financing need is \$400 million to \$520 million. As shown in **Error! Reference source not found.**, annual spending on the R&D Blueprint diseases was \$350 million in 2018, suggesting an annual funding gap of **\$50 million to \$170 million**.

3. Barriers to funding vaccine research and development

In Section 2, we showed that the estimated annual financing gap for vaccine R&D for neglected diseases is \$2 billion and the gap for vaccine R&D for emerging infectious diseases is \$50 million to \$170 million. Why does such a gap persist? In other words, what have been the barriers to research funders mobilizing additional financing? As figures 1 and 2 show, there certainly has been increased attention from funders towards R&D for neglected and emerging infectious diseases, but the underlying reasons for the ongoing gap have not been addressed in a fundamental, “game-changing” way. In this section, we briefly describe five of the most important barriers to mobilizing finance.

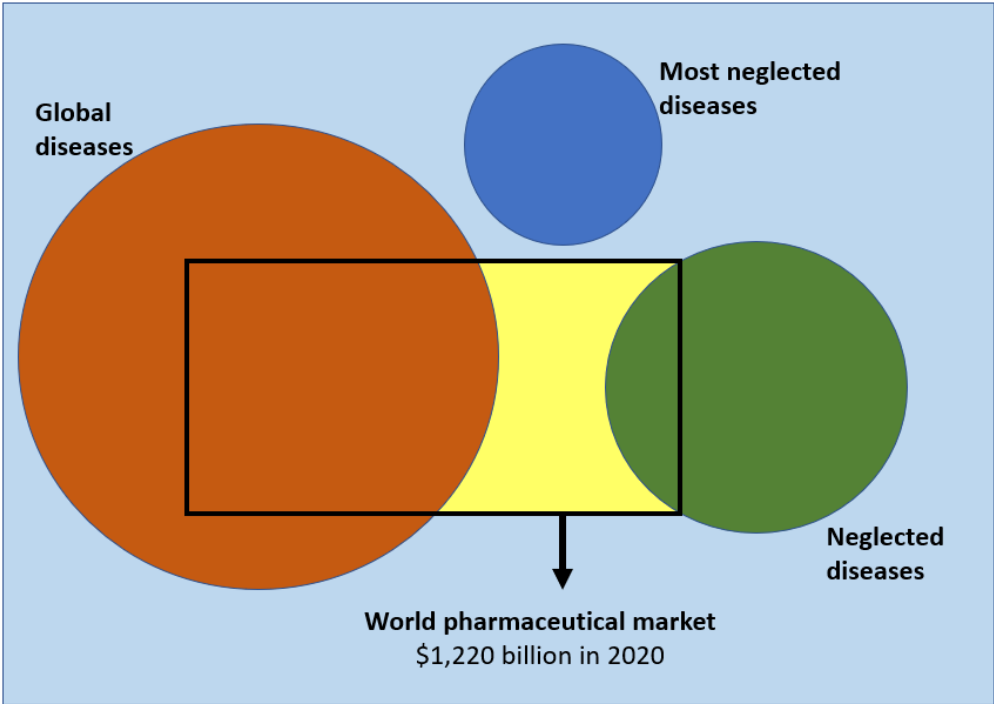
3.1 Market failure

Market failure continues to impede vaccine R&D financing, especially for the “most neglected” diseases (those that currently attract the lowest amounts of funding). The patients in countries most affected by these diseases, including those in Asia-Pacific countries — as well as the Governments of these countries—do not have much purchasing power. Such purchasing power is particularly limited in low-income countries (LICs) and lower-middle-income countries (LMICs), such as Cambodia, the Democratic People’s Republic of Korea, Solomon Islands, Timor-Leste and Viet Nam. Pharmaceutical companies see little financial incentive in making vaccines for diseases that disproportionately affect LICs and LMICs—they do not have enough of a market for such vaccines in high-income countries (HICs).

One way to attract industry to develop vaccines for neglected and emerging infectious diseases is through product development public-private partnerships (PDPs), which we

describe in section 4. However, it has been hard to persuade industry to enter into PDPs for the most neglected diseases (Yamey, 2002). As we have previously argued, when industry sees at least some market (e.g. HIV affects people in rich nations), then the public sector can use bargaining power (i.e. push and pull mechanisms), to persuade industry to enter into PDPs (as it did with the International AIDS Vaccine Initiative (IAVI)). Such mechanisms include reducing the costs of research R&D through grants, tax credits, or public support for clinical trials or creating an advanced purchase commitment that guarantees purchase of vaccines that come to market. However, when it comes to the world's most neglected diseases, “these present absolutely no market opportunities. Without such opportunities, there is no incentive for the pharmaceutical industry to invest in drug R&D. The patients have no purchasing power, no vocal advocacy group is pleading for their needs, and no strategic interests—military or security—are driving concern about these conditions. This is why no public-private partnerships exist specifically for the most neglected diseases” (Yamey, 2002). **Error! Reference source not found.** shows how the most neglected diseases fall fully outside the global pharmaceutical market.

Figure 3: Relationship between the most neglected diseases and the world pharmaceutical market

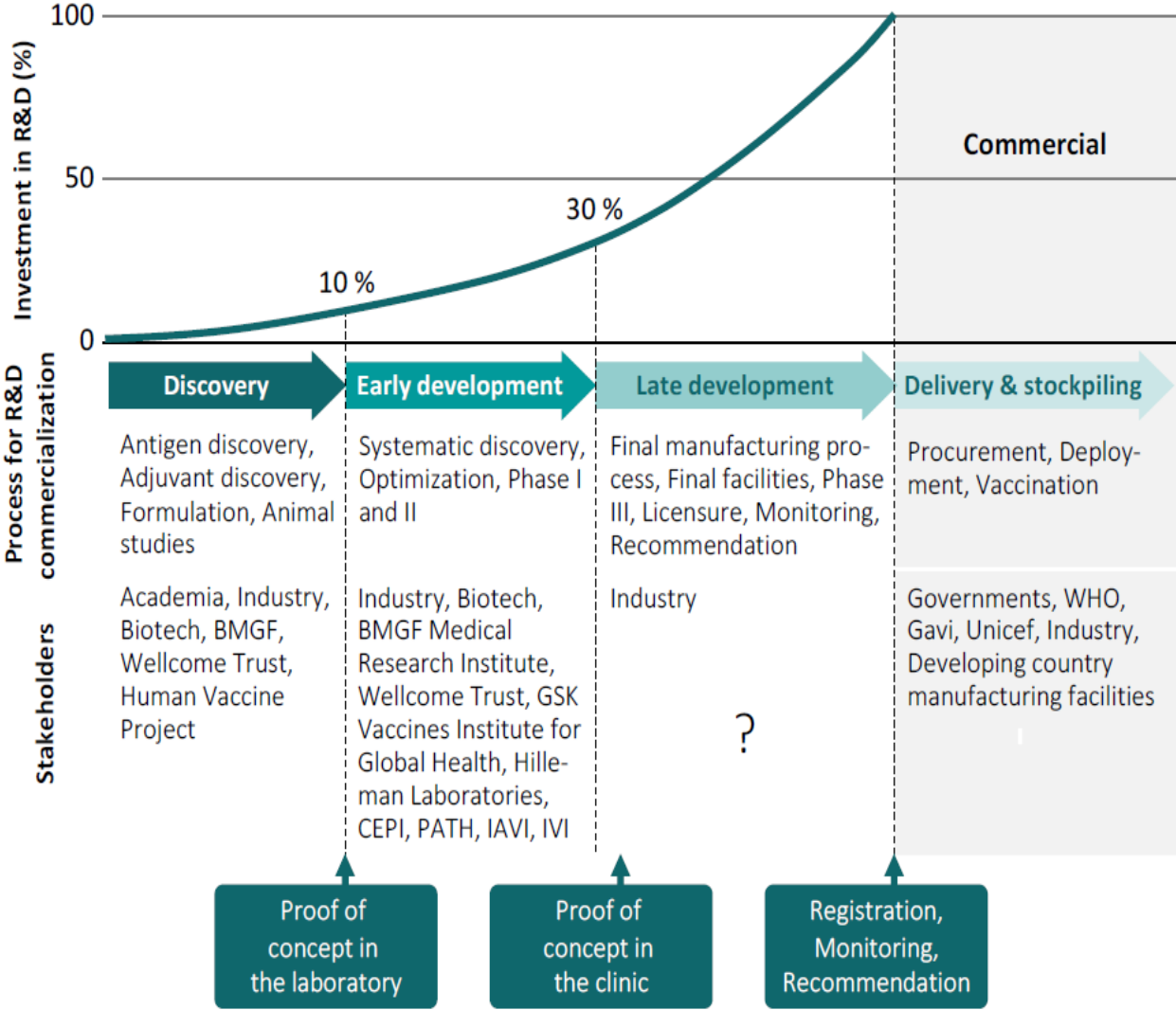


Source: G. Yamey, 2002, The world’s most neglected diseases. *BMJ* (325):176–177.

Without a market, vaccine companies are particularly reluctant to invest in late-stage vaccine trials, as these are the costliest aspect of development. Rappuoli and colleagues (2019) estimate that late-stage trials are responsible for about 70 per cent of all neglected disease vaccine development costs (**Error! Reference source not found.**). The high costs of late-stage development are due to the costs to conduct phase 3 trials themselves, to produce vaccine candidates according to good manufacturing practice

standards in purpose-built production facilities, conduct post-marketing surveillance and submit data to regulators.

Figure 4: Proportion of vaccine research and development costs across different stages of development and delivery



Source: G. Yamey and others (2020). Developing an aggregator mechanism for late-stage clinical trials of neglected disease product candidates. The Center for Policy Impact in Global Health. Duke Global Working Paper Series, No. 23, October.

Note: The figure shows that discovery is 10 per cent of the R&D budget, early development is 20 per cent of the budget and late development is 70 per cent of the budget. Under the graph are the funders and stakeholders involved in each of these stages. There is a large gap in the vaccine R&D financing architecture for late development (denoted by “?”).

3.2 The free-rider problem

A second barrier to closing the vaccine R&D finance gap is the so-called “free-rider” problem. As Suerie Moon and colleagues (2012) say, “If one country can benefit from the investment of another, there is a powerful temptation to “free-ride” on the other’s

efforts; the end result may be aggregate global underinvestment in R&D". The free-rider problem means some nations may stay on the sidelines when it comes to funding R&D—they can “reap the benefits without taking any risks” (Rappuoli, Black and Bloom, 2019).

When it comes to vaccine development for neglected and emerging diseases, the free-rider problem has been well described. For example, Michael Kremer and Christopher Snyder (2020) estimated the magnitude of the free-rider problem as it relates to developing vaccines for endemic neglected diseases such as HIV or malaria. More specifically, they estimated the size of the per-vaccine government subsidy that would be needed to overcome the free-rider problem. For their analysis, they assume a basic reproductive number (R_0) of 4. They find that: “The free-rider problem exacerbates monopoly incentives to distort quantity downward to keep prices high. We find that to counteract the severe distortions and achieve the first best when $R_0 = 4$ would require a per-dose subsidy for the vaccine that would be roughly three times estimates of the monetary value that those afflicted with the disease would be prepared to pay to recover. A more practical government policy would therefore involve negotiating a bulk purchase for the population.”

3.3 Poor coordination of global vaccine research and development for neglected and emerging infectious diseases

The past two decades have seen the emergence of new mechanisms and initiatives aimed at mobilizing financing for neglected and emerging infectious disease vaccine R&D, including in the Asia-Pacific region. Examples include IAVI, CEPI, Biomedical Advanced Research and Development Authority, the Meningitis Vaccine Project, and the Japan-based Global Health Innovative Technology Fund (GHIT). However, one major governance problem is that there is no clear, consistent global mechanism for R&D prioritization and coordination. There are several overlapping initiatives. The landscape of vaccine R&D financing suffers from duplication, fragmentation and inefficiencies, all of which can lead to resources being wasted and delays being incurred in vaccine development.

This problem is longstanding. For example:

- A 2010 report from the WHO expert working group on research and development financing argued that global health R&D is “highly fragmented, most organizations working either in isolation or as part of small groups or networks of limited subsets of entities with shared goals. Thus, partial efforts are made to coordinate selected aspects of the overall system, often involving only a section of the innovation pipeline” (WHO, 2010).
- In 2012, the WHO Consultative Expert Working Group on Research and Development: Coordination and Financing concluded that the absence of action to close the global health R&D financing gap “is itself a reflection of the difficulty of improving coordination precisely because the field is so fragmented and the interests of funders and researchers are so diverse” (WHO, 2012).

- In 2017, in an analysis called “In search of global governance for research in epidemics,” David Peters and colleagues argued that Ebola vaccine development during the 2014–2016 Ebola virus disease epidemic in West Africa was hindered by poor overarching vaccine R&D governance.

While WHO has recognized this problem and has begun to address it—such as through the launch of its Global Observatory on Health R&D and its target product profile directory—these efforts remain at a nascent stage.

3.4 Exclusion of policymakers from low- and lower-middle-income countries funding decisions

A fourth barrier to raising additional financing for vaccine R&D for neglected and emerging infectious diseases is that key decision-making processes and forums have done poorly at including decision-makers from countries that are the most affected by these diseases. Decision-making on funding for such vaccines, especially at PDPs, has tended to be top down rather than bottom up—in other words, policymakers from LICs and LMICs, who are tackling the highest burden of these diseases, are often not at the decision-making table. The result is that they are left out “when it comes to deciding on what gets funded, where research is conducted, who gets access to intellectual property, and where and how the technologies end up being manufactured” (Yamey and others, 2020).

3.5 Limited vaccine manufacturing capacity in high burden countries

Finally, when it comes to what Rappuoli and colleagues (2019) call the “Valley of Death in the late vaccine development phase”—the lack of financing for phase 3 trials—many LICs and LMICs are stuck in a catch 22 situation. Because they may lack clinical trial capacity and expertise—for example, they may have weak regulatory processes for clinical trials of vaccines, too few facilities to conduct trials, and a lack of trained personnel—funders may be reluctant to invest in R&D in these settings. Improving capacity and expertise would help to create a virtuous cycle that could attract new financing.

While there is some vaccine manufacturing capacity in LICs and MICs in Asia and the Pacific (described in Section 4), it is mostly traditional (e.g. manufacturing cell culture-based inactivated vaccines) and small scale. The innovative next generation vaccine R&D platforms that were validated during the COVID-19 pandemic—mRNA and viral vectors (Yamey, 2021)—have not yet been adopted at scale by vaccine manufacturers in the region.

4. The landscape of vaccine research and development financing in the Asia-Pacific region

Earlier in this report, we showed that \$1.1 billion is invested annually in developing vaccines for neglected diseases and \$350 million is invested annually in developing vaccines for the R&D Blueprint diseases. We estimated that the annual financing gap for vaccine R&D for neglected diseases is \$2 billion and the gap for vaccine R&D for emerging infectious diseases is \$50 million to \$170 million. We examined the reasons why this financing gap persists, including market failure, the free-rider problem, poor governance and coordination of the global vaccine R&D enterprise, exclusion of decision-makers from LICs and LMICs in decisions about vaccine R&D and limited vaccine manufacturing capacity in many of these countries. We now focus on the vaccine R&D financing landscape in the Asia-Pacific region itself, in order to identify weaknesses and opportunities for future resource mobilization.

4.1 Levels of financing for vaccine research and development

We conducted a rapid search of the G-FINDER database to estimate how much funding there is for developing vaccines in the Asia-Pacific region. Below we summarize our initial findings on total funding for financial years 2018, 2019 and 2020 and we also give an annualized estimate across this three-year period. The G-FINDER database does not capture all vaccine R&D funders (e.g. it does not capture smaller funders in Thailand), so our numbers are likely to be an underestimate of total funding. Our analysis includes 58 eligible member countries of the Economic and Social Commission for Asia and the Pacific (ESCAP). We do not include vaccine delivery and technologies from the G-FINDER database, as it is quite small and limited to only a few funders.

4.1.1 Funding for vaccine research and development for neglected diseases

We estimate that \$106.6 million was invested in vaccine R&D for neglected diseases in the Asia-Pacific region from 2018 to 2020, or an average of \$35.5 million annually. **Error! Reference source not found.** shows the breakdown of this total by source and recipient type (academic, national government, PDP, or other). The largest amount of funding over this three-year period was from the United States (\$49.6 million), followed by Australia (\$26.3 million) and then industry (\$14.7 million). Approximately two thirds of all funding went to academic/research institutions and one quarter went to PDPs.

Out of the total funding of \$106.6 million from 2018 to 2020, only \$40.1 million came from within the Asia-Pacific region, which is further disaggregated in Table 5. The largest financing sources from within the region over this three-year period were from Australia, in particular the Medical Research Future Fund (\$17.6 million) and National Health and Medical Research Council (\$8.2 million), and from India through the Indian Council on Medical Research (\$5.2 million). Table 6 shows the breakdown of the total \$106.6 million by disease area—the largest amount of funding is for bacterial pneumonia

and meningitis (\$33 million), followed by rheumatic fever (\$25.3 million), salmonella infections (\$22 million) and diarrhoeal diseases (\$13 million).

Thus, the overall level of funding—\$35.5 million per year—is tiny compared with the estimated funding gap of around \$2 billion per year, and there are very low levels of funding for diseases that have a high burden in the region.

Source	Country income status	Funding to academic and research institutions	Funding to national government agencies	Funding to product development partnerships	Funding to other recipients	Total
United States of America	High	21 654 873	4 447 139	23 523 015	n/a	49 625 027
Australia	High	26 254 622	n/a	n/a	n/a	26 254 622
Industry	N/A	14 620 304	n/a	109 765	n/a	14 730 069
India	Lower-middle	3 407 105	6 049 071	n/a	132 980	9 589 156
Switzerland	High	2 259 909	n/a	n/a	n/a	2 259 909
United Kingdom	High	144 557	460 262	1 078 761	n/a	1 683 581
European Union	High	643 759	n/a	472 648	n/a	1 116 226
South Korea	High	n/a	n/a	649 651	n/a	649 651
New Zealand	High	469 466	n/a	n/a	n/a	469 466
Japan	High	170 430	91 343	n/a	n/a	261 772
Total	n/a	68 094 392	11 047 815	25 833 840	132 980	106 639 479

Note: Figures are in United States dollars.

Abbreviations: HIC, high-income country; LMIC, lower-middle-income country.

Source	Country income status	Amount
Australia	HIC	26 254 622
Medical Research Future Fund		17 646 874
National Health and Medical Research Council		8 210 864
Australian Centre for HIV and Hepatitis Virology		305 047
Melbourne Children's		48 407
CASS Foundation		39 960
Far North Queensland Hospital Foundation		3 470
India		LMIC
Indian Council of Medical Research	5 249 732	
Undisclosed	4 750 466	

Indian DBT		1 695 969
Buimerc Core Investments		154 114
Republic of Korea	HIC	749 651
Korean Ministry of Food and Drug Safety (KMFDS)		647 844
Korean HIDI		100 000
Kim & Chang		1 807
New Zealand	HIC	469 466
Health Research Council of New Zealand (HRC)		469 466
China	UMIC	401 705
Lanzhou Institute of Biological Products (LIBP)		401 705
Japan	HIC	261 772
Japan Society for the Promotion of Science (JSPS)		261 772
Malaysia	UMIC	140 054
University of Malaya		140 054
Total		40 127 551

Note: Figures are in United States dollars.

Abbreviations: HIC, high-income country; LMIC, lower-middle-income country; UMIC, upper-middle-income country.

Table 6: Funding for neglected disease vaccine research and development in the Asia-Pacific region, 2018–2020	
Disease	Amount
Bacterial pneumonia and meningitis	32 262 112
Rheumatic fever	25 326 794
Salmonella infections	22 050 095
Diarrhoeal diseases	13 046 040
Tuberculosis	5 594 660
Malaria	2 250 078
HIV/AIDS	2 212 473
Kinetoplastid diseases	1 096 246
Helminth infections (worms and flukes)	880 399
Hepatitis C	859 938
Leprosy	37 478
Buruli ulcer	23 165
Total	106 639 479

Note: Figures are in United States dollars.

4.1.2 Funding for vaccine research and development for emerging infectious diseases

We estimate that \$11.4 million was invested in vaccine R&D for emerging infectious diseases in the region from 2018 to 2020, or an average of \$3.8 million annually (a low level of funding compared with the \$50 million to \$170 million annual funding gap for these diseases). Table 7 shows the breakdown of this total by source and recipient type (academic, national government, PDP). The Republic of Korea is by far the largest funder (\$7.8 million over the three-year period) and all of its funding is to PDPs. Table 8 shows the breakdown of funding by disease; almost two thirds of all funding was for coronaviral diseases (including MERS, SARS and COVID-19).

Table 7: Sources of funding for emerging infectious disease vaccine research and development in the Asia-Pacific region, 2018–2020					
Source	Country income status	Funding to academic and research institutions	Funding to national government agencies	Funding to product development partnerships	Total
Republic of Korea	HIC	n/a	n/a	7 793 253	7 793 253
Australia	HIC	1 665 900	n/a	n/a	1 665 900
India	LMIC	722 131	795 921	n/a	1 518 052
European Union	N/A	203 598	n/a	n/a	203 598
Industry	N/A	138 365	n/a	n/a	138 365
Japan	HIC	56 046	41 376	n/a	97 422
Total	n/a	2 582 442	837 279	7 793 253	11 416 589

Note: Figures are in United States dollars.

Abbreviations: HIC; high-income country, LMIC; lower-middle-income country.

Table 8: Funding for emerging infectious disease vaccine research and development in the Asia-Pacific region by disease, 2018–2020	
Disease	Amount
Coronaviral diseases (including MERS, SARS, COVID-19)	7 283 572
Zika	1 606 167
Chikungunya	1 368 780
Bunyaviral diseases (including CCHF, RVF, SFTS)	621 673
Filoviral diseases (including Ebola, Marburg)	536 397
Total	11 416 589

Note: Figures are in United States dollars.

Abbreviations. CCHF, Crimean-Congo haemorrhagic fever; COVID-19, coronavirus disease; MERS, *Middle East respiratory syndrome*; RVF, Rift Valley fever; SARS, *severe acute respiratory syndrome*; SFTS, *Severe fever with thrombocytopenia syndrome*.

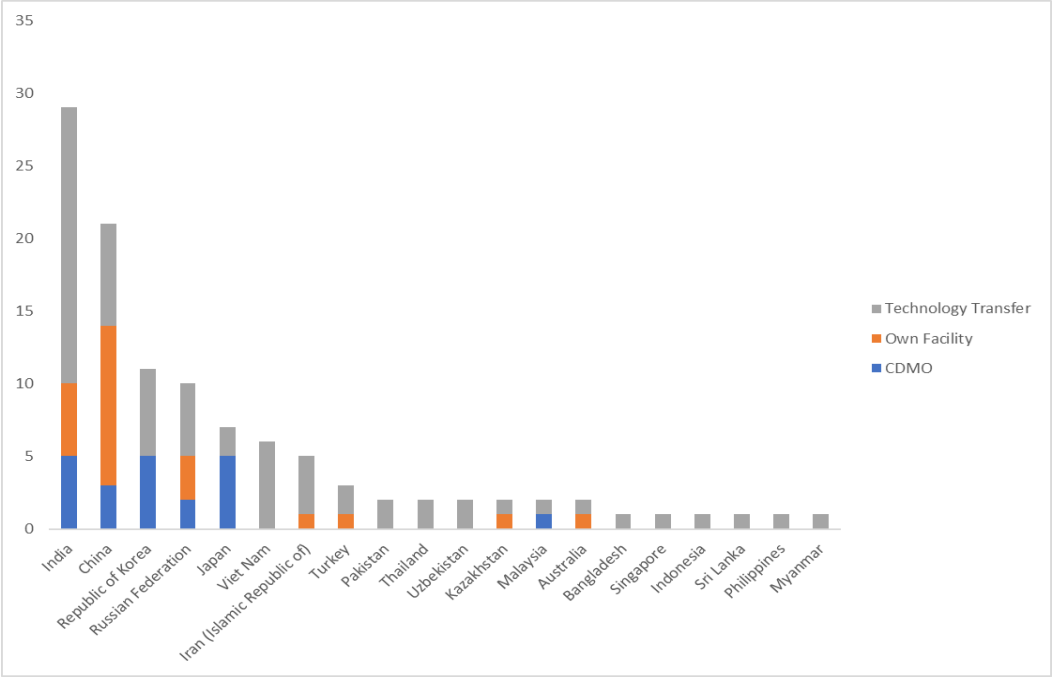
4.2 Vaccine clinical trials in the Asia-Pacific region

The Asia-Pacific region has substantial clinical trial capacity, though it is highly concentrated in a small number of countries. An analysis of the ClinicalTrials.gov database by Antonio Postigo (2022) found that a quarter (24.1 per cent) of all vaccine trials worldwide as of November 2021 were conducted in the region, or 2,629 trials out of 10,873 trials. Of the 2,629 trials conducted in the region, around 60 per cent were conducted in just six countries. One fifth (21.7 per cent) of the trials were conducted in China, 9.9 per cent in Australia, 8.5 per cent in the Republic of Korea, 7.6 per cent each in Japan and Thailand, and 5.9 per cent in India.

4.3 Vaccine manufacturers in the Asia-Pacific region

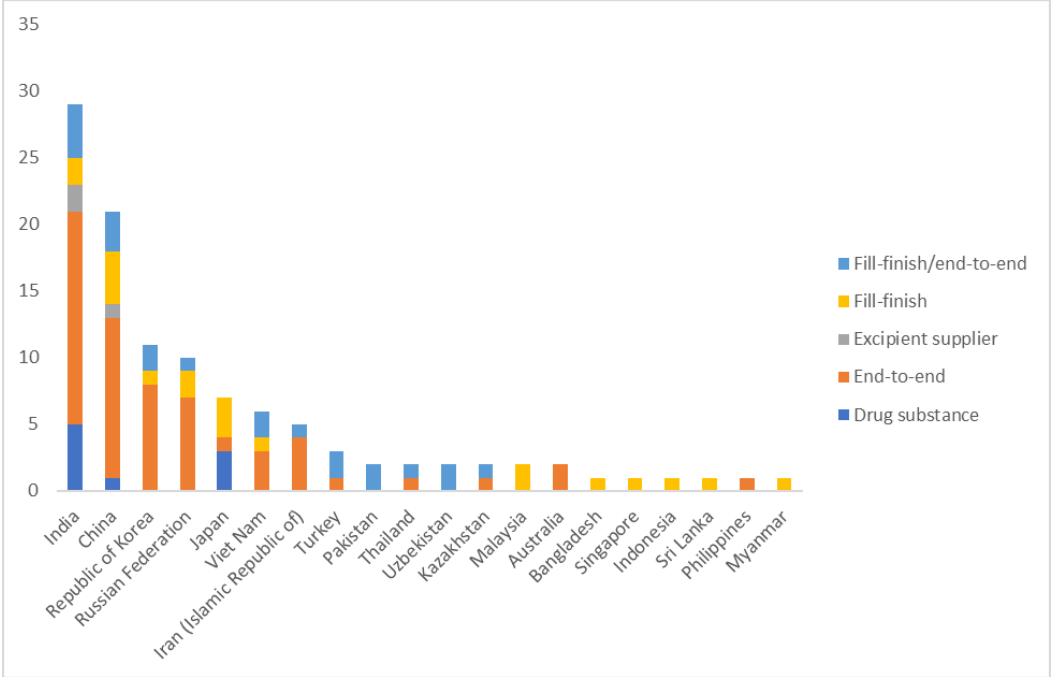
In this section, we briefly summarize the landscape of vaccine manufacturing in the region. The United Nations Children’s Fund (UNICEF) maintains a COVID-19 Vaccine Market Dashboard that captures information about vaccine makers worldwide. The information on the dashboard can be used as a proxy for where vaccine manufacturing for other diseases is taking place in the region. We identified 110 vaccine makers in Asia and the Pacific listed on the dashboard. Figure 5 shows the countries where the vaccine makers are based and the manufacture type (technology transfer, own facility, or contract development and manufacturing organization), and Figure 6 shows the breakdown by production type (fill-finish/end-to-end, fill-finish, excipient supplier, end-to-end, drug substance). Figures 5 and 6 show that vaccine manufacturing in the region is dominated by India, an LMIC (29 vaccine makers, mostly technology transfer), and China, an upper-middle-income country (21, mostly own facilities), followed by the Republic of Korea (11), the Russian Federation (10) and Japan (7).

Figure 5: Number of vaccine manufacturers in Asia-Pacific countries by manufacturer type



Source: UNICEF COVID-19 Vaccine Market Dashboard.
 Abbreviation: CDMO, contract development and manufacturing organization.

Figure 6: Number of vaccine manufacturers in the Asia-Pacific countries by production type



Source: UNICEF COVID-19 Vaccine Market Dashboard.

An additional resource for understanding where there is vaccine manufacturing capacity in the Asia-Pacific region is the Developing Countries Vaccine Manufacturers Network, an alliance of vaccine manufacturers from developing countries that aims to make a consistent supply of high quality vaccines that are accessible to protect people against known and emerging infectious diseases globally. Figure 7 shows the global distribution of the 41 manufacturers in the network, including those that have manufactured WHO prequalified vaccines; 34 are in Asia and the Pacific.

Figure 7: Global distribution of vaccine manufacturers in the Developing Countries Vaccine Manufacturers Network



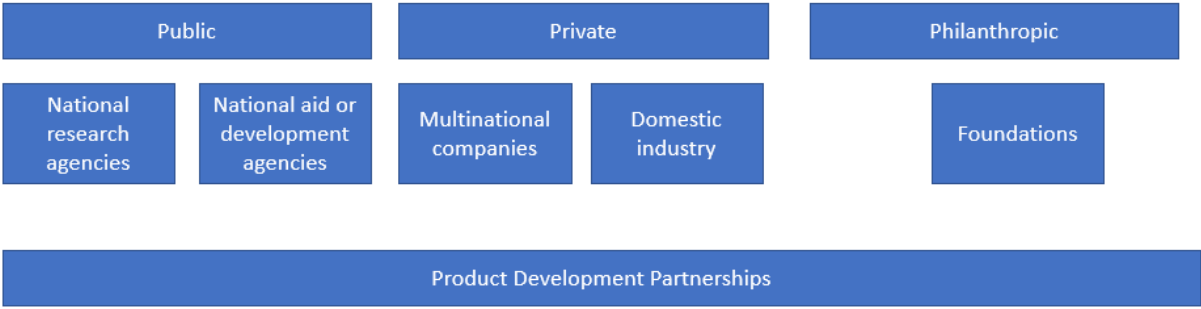
Note: In 2019 there were 41 manufacturers from 14 countries and territories.

Comparing figures 5–7 (which show where there is manufacturing capacity) with tables 5 and 7 (which show Asia-Pacific countries that are funding R&D) shows that there are many countries—including developing countries—that have vaccine manufacturing capacity but are not significant funders of vaccine R&D. Similarly, several developing countries are conducting significant numbers of vaccine trials (e.g. Thailand had conducted 200 vaccine trials by November 2021) that are not significant funders of vaccine R&D. This mismatch suggests there is untapped potential in vaccine manufacturing nations (e.g. Malaysia, Thailand, Viet Nam) and nations that have clinical trial sites (e.g. Thailand) to step up their R&D financing.

4.4 Current sources of financing for vaccine research and development in the Asia-Pacific region

The three key sources of financing for vaccine R&D in Asia and the Pacific are public, private and philanthropic (**Error! Reference source not found.**).

Figure 8: Sources of financing for vaccine research and development in the Asia-Pacific region



4.4.1 Public funding for vaccine research and development

Public funding is chiefly from national research agencies and national aid or development agencies—both within and outside the Asia-Pacific region (see tables 4, 5 and 7). Many national Governments in the region fund universities and research institutes to conduct vaccine R&D. These efforts are mostly very small scale, with some exceptions, including the Medical Research Future Fund and National Health and Medical Research Council in Australia and the Indian Council of Medical Research (tables 5 and 7).

There is little public information on the funding of vaccine R&D from the Government of China, but its investments in COVID-19 vaccine development, including launching the world’s first COVID-19 vaccine trial in Wuhan (Zhu, 2020), have helped to shine a light on its R&D for other vaccines. Yinglian Hu and Simiao Chen (2021) note that COVID-19 vaccine R&D in China represents the success of state-driven collaborative research, but such an approach has not been strategically applied to other vaccines. They say that “compared with developed countries such as the United States and the United Kingdom, China generally lags behind in non-COVID-19 vaccine R&D, production and regulatory capacity.”

Key informants interviewed for this analysis argued that government-funded academic research on vaccines in the Asia-Pacific region is not yet at a level that is ready for industry translation. There has been little in the way of adopting and adapting newer vaccine technologies and platforms or improving vaccine R&D infrastructure, and R&D has been traditional (e.g. developing inactivated vaccines via cell culture), as mentioned earlier. Few countries in the region have made any public commitments to stepping up funding for vaccine R&D to develop vaccines that the region needs (e.g. vaccines for dengue, JE and malaria). There are two exceptions. The first is the Republic of Korea—the Government announced in January 2021 that it would spend 41.9 billion won (\$37

million) to develop treatments and vaccines against new infections as part of a 5.8 trillion won (\$5.2 billion) budget for science and information and communications technology for the year – a 12 per cent rise on 2020 with a focus on basic research, as well as new technologies such as artificial intelligence to drive its innovation-led economy (Sharma, 2021). The second is Japan, where the Government launched the Strategic Center of Biomedical Advanced Vaccine Research and Development for Preparedness and Response (SCARDA) in March 2022, housed within the Japan Agency for Medical Research and Development. The Center aims to promptly deliver safe and effective vaccines against infectious diseases on the Government’s priority list. The Government of Japan plans to spend “51.5 billion yen (\$420 million) to prepare major development sites and allocate 150.4 billion yen for R&D for vaccines against communicable diseases found on its priority list, along with new technologies associated with them” (Tominga, 2022).

4.4.2 Private funding for vaccine research and development

Private financing is from domestic industry, multinational companies and foreign direct investment. However, the amount of funding is small. From 2018 to 2020, the Policy Cures Research database captures only \$14.7 million in industry funding for neglected disease vaccine R&D, though it is possible that proprietary concerns impede reporting.

4.4.3 Philanthropic funding for vaccine research and development

There has been some philanthropic support for vaccine R&D in Asia and the Pacific — for example, the Bill and Melinda Gates Foundation has funded human papillomavirus (HPV) vaccine R&D at the Serum Institute of India and measles and rubella vaccine development at PT Bio Farma (Persero) in Indonesia. Key informants noted that two Asian philanthropies—the Tahir Foundation and the Li Ka Shing Foundation—have funded research initiatives in the region (e.g. dengue control and laboratory upgrades) and so could be a source of future funding for vaccine R&D. There are also several initiatives, described further below, that aggregate private funding with public and philanthropic funding through PDPs.

4.5 Innovations in financing vaccine research and development: product development partnerships and regional approaches

In addition to direct government, private and philanthropic funding of vaccine R&D, there have been innovations in the governance of vaccine R&D financing that have led to additional resource mobilization. These innovations have included PDPs and regional approaches to financing.

4.5.1 Product development partnerships

PDPs have become an important vehicle for vaccine R&D financing. From 2018 to 2020, PDPs were responsible for a quarter of the neglected disease vaccine R&D financing in Asia and the Pacific (Table 5) and 70 per cent of the emerging infectious disease vaccine R&D financing in the region. Below we give five examples:

- PATH supported a Japanese encephalitis vaccine developed by the Chengdu Institute in China, a vaccine that has been prequalified by WHO (PATH, 2013).
- A partnership between PATH, WHO, the Governments of the United States and Viet Nam, and the Institute of Vaccines and Medical Biologicals in Viet Nam led to the development and licensure of a Viet Nam-produced seasonal influenza vaccine (PATH, 2019).
- The International Vaccine Institute (IVI) of the Republic of Korea is a non-profit PDP that develops vaccines for global health. It has 160 partners from government (with core funding from the Government of the Republic of Korea as well as the Governments of India, Finland and Sweden), industry, philanthropy (e.g. grants from the Gates Foundation, the Wellcome Trust, and the Samsung Life Public Welfare Foundation), academia and multilateral and international organizations (e.g. Gavi, UNICEF, CEPI, WHO). IVI supports technology transfer and provides technical and financial support for process development and scale-up to clinical development, registration and WHO pre-qualification. Its portfolio includes cholera, typhoid, dengue, MERS, schistosomiasis, chikungunya, COVID-19, HPV, TB and antimicrobial resistance.
- GHIT is a PDP that has invested \$276 million to date for drug, diagnostic and vaccine R&D in Japan for malaria, TB and neglected tropical diseases. Approximately one quarter (24 per cent) of investments have been for vaccine R&D. Most of the total funding (57 per cent) has been for preclinical research, with 26 per cent for clinical research and 17 per cent for discovery.
- The Research Investment for Global Health Technology (RIGHT) Fund, launched in July 2018, is a partnership between the Government of the Republic of Korea, Korean life science companies and international funders such as the Gates Foundation. The fund finances the development of drugs, diagnostics and vaccines for a range of neglected diseases, including soil-transmitted helminth infections, malaria and TB. By September 2020, it had mobilized more than 50 billion won (\$44 million), half from the Government, and one quarter each from Korean companies and the Gates Foundation (Hotez, 2020). The RIGHT Fund has invested in the development of two vaccines—one for cholera and a hexavalent vaccine (diphtheria whole-cell pertussis-tetanus toxoid vaccine, inactivated polio vaccine, recombinant hepatitis B vaccine and *Haemophilus influenzae* type b (Hib) vaccine).

4.5.2 Regional approaches

Regional approaches to fostering vaccine R&D in Asia and the Pacific have mostly focused on enhancing research collaboration, such as through the Association of Academies and Societies of Sciences in Asia. A more recent regional initiative, the Asia Pacific Vaccine Access Facility (APVAX), has focused on COVID-19 vaccine procurement. APVAX has a \$9 billion budget from the Asian Development Bank (ADB), which it has used for both grants and loans (ADB, 2020). While APVAX is not directly financing vaccine R&D, the pooled purchasing efforts by large-scale regional

procurement mechanisms such as APVAX and the African Union's Vaccine Acquisition Trust (AVAT) help provide a guaranteed market for new vaccines, thus supporting R&D.

5. Mobilizing additional vaccine research and development financing: the value proposition

We have argued that there is currently underinvestment in vaccine R&D financing in the Asia-Pacific region. Why should investment be increased? In this section, we briefly lay out the value proposition for increasing the levels of investment in vaccine R&D in the region. We focus on the costs of inaction and the large economic returns to such investments.

5.1 The high costs of inaction

Developing new, effective vaccines could avert a huge amount of suffering, disability and death—as well as economic harm—from neglected and emerging infectious diseases. COVID-19 has shown the scale of health, social and economic devastation that an emerging infection can cause. For example, the International Monetary Fund estimates that the economic losses caused by COVID-19 will be \$13.8 trillion from 2020 to 2024 (Gopinath, 2022). Estimated annual losses from influenza pandemic risk are \$500 billion or 0.6 per cent of global income per year (Fan, Jamison and Summers, 2018). Developing new vaccines is also an important strategy for preventing antimicrobial resistance (AMR), which in 40 years could lead to an annual gross domestic product (GDP) loss of \$454 billion per year if current rates of AMR persist (Naylor and others, 2018). The levels of funding needed to develop vaccines for neglected and emerging infections are tiny compared to the scale of the economic losses caused by these diseases.

5.2 The enormous health and economic returns of investment

In addition to averting a huge number of deaths and disability-adjusted life years (DALYs), investing in vaccines can reap large economic returns, especially through regional investment hubs. For example, in the first study of its kind, Marco Schäferhoff and colleagues (2022) applied investment case modelling and assessed how many cases, deaths and DALYs could be averted from the development and manufacturing of new technologies (therapeutics and vaccines) in three MICs: India, Kenya and South Africa. They then estimated the economic benefits that might accrue from making these investments and developed benefit-cost ratios for each country. The study modelled development of new therapeutics and vaccines for five infectious diseases: HIV, TB, malaria, pneumonia and diarrhoeal diseases. The authors found that scaling up such investments in India from 2021 to 2036, provided that the technologies were for a regional market (all South-East Asian nations), could avert almost 9.8 million deaths and 374.4 million DALYs in South-East Asia. The regional economic returns would outweigh investments by a factor of 68 (i.e. a benefit-cost ratio of 68:1).

Previous vaccine development has also had large economic returns. The polio vaccine was developed through a \$26 million investment by the March of Dimes. In the United States alone, since routine vaccination was introduced, more than 160,000 polio deaths and approximately 1.1 million cases of paralytic polio have been prevented. Treatment cost savings have generated a net benefit of approximately \$180 billion (Thompson and Tebbens, 2006).

6. Policy options to increase vaccine research and development financing in the Asia-Pacific region

In Section 2, we showed that the annual financing gap for vaccine R&D for neglected diseases is \$2 billion and the gap for vaccine R&D for emerging infectious diseases is \$50 million to \$170 million. In Section 3 we examined the reasons for this ongoing financing gap. In Section 4 we estimated that from 2018 to 2020 in the Asia-Pacific region only \$35 million was invested annually in neglected disease vaccine R&D and \$3.8 million annually was invested in emerging infectious disease vaccine R&D—very low levels of financing compared with the need. Despite such low levels of financing, there is significant vaccine trial and manufacturing capacity in many developing countries of the region. In Section 4, we shone a light on public, private and philanthropic sources of vaccine R&D financing in the region, on PDPs and on recent innovations in the financing space. In Section 5, we made the case for increased investment in vaccine R&D in the region, based on the high cost of inaction and the enormous health and economic benefits of scaling up such financing.

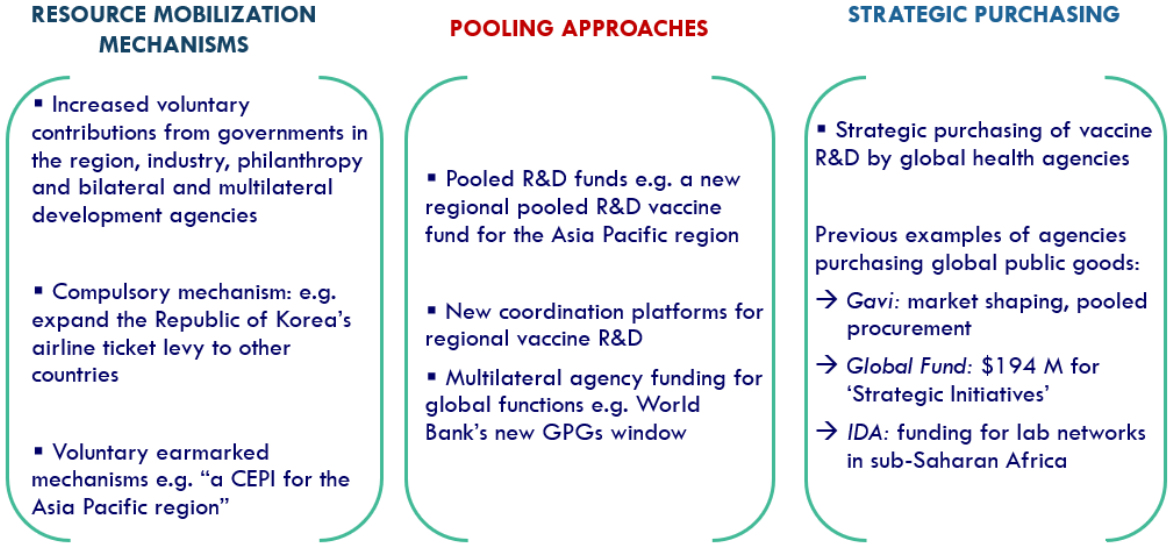
As described earlier in this report (see Section 1), there are many reasons why vaccine R&D is underfunded; the financing gap is particularly acute for late-stage trials. Given that late-stage trials are particularly costly and incur a financial risk (there is no guarantee of a launch or of a commercial market, especially for neglected diseases), approaches to close the financing gap need to overcome these root causes. Such approaches have been broadly categorized as push and pull mechanisms:

- Push mechanisms recognize that vaccine R&D is expensive and so they involve subsidizing the costs. These mechanisms include directly funding the research, tax credits on R&D and research grants.
- Pull mechanisms incentivize funders to take a risk on funding research by rewarding successful R&D. They include advanced purchase agreements (e.g. a funder such as Gavi may commit to purchasing millions of doses of a successful, highly needed vaccine) or prizes for innovation.

What are the options for scaled-up financing of vaccine R&D in the region using such mechanism? Below, we lay out several mechanisms through which vaccine R&D in the region could be better financed. We organize these into **resource mobilization, pooling**

of resources and **strategic purchasing** (Figure 9). Most of these are push mechanisms (i.e. they involve mobilizing additional finance to subsidize R&D costs), though there are also examples of pull mechanisms (e.g. the market-driven, value-based advance commitment (MVAC) and the Life Prize).

Figure 9: Mechanisms to close the finance gap for vaccine research and development in the Asia-Pacific region



Abbreviations: CEPI, Coalition for Epidemic Preparedness Innovations; GPGs, global public goods; IDA, International Development Association; R&D, research and development.

6.1 Resource mobilization

Governments of Asia-Pacific countries could increase their investments, either into their own domestic R&D enterprise if it is mature enough—several countries have significant trial and manufacturing capacity but are spending very little on vaccine R&D—or into new regional mechanisms (see below). Increased domestic financing on developing vaccines for neglected and emerging infectious diseases would reap major public health gains while generating large economic returns. The global movement towards universal health coverage has included a call for greater investment in health research—this movement provides a window of opportunity for governments in the region to commit a percentage of their domestic health budgets to R&D, including vaccine R&D.

One mechanism that has previously been proposed for mobilizing additional government funding is an **R&D tax** (Røttingen and Chamas, 2012), such as allocating 0.01 per cent of GDP towards product development for neglected diseases, which could be explored for the region. There is precedent for using taxes to raise funds for global health: UNITAID mobilized more than \$2 billion from 2006 to 2011 for HIV, TB, and malaria control through an **airline ticket levy** (a “solidarity tax”) (KFF, 2011). In the countries that joined the scheme, including the Republic of Korea, a small levy was added to the price of airline tickets.

The Republic of Korea is using a similar airline solidarity levy to support the Global Disease Eradication Fund. An analysis by Jisun Song and Lynn Pyun (2022) of the country's airline ticket solidarity levy suggests that it could be extended to support vaccine R&D and could be adopted by other Asia-Pacific countries to create "sustainable finance schemes." A region-wide airline tax could help support regional vaccine R&D. Other types of taxes have been proposed for mobilizing R&D finance in the region, such as a tax on financial transactions, foreign exchange transactions, or the sale of shares, bonds and derivatives.

An alternative to an R&D tax would be some kind of voluntary regional earmarked mechanism for vaccine R&D. An example of a such a voluntary vaccine R&D mechanism is CEPI, which has shown proof of principle as a global mechanism. There would be value in exploring the feasibility of and appetite for a "CEPI for the Asia Pacific Region." Such a voluntary earmarked mechanism might also attract additional funding from donor agencies. If donors worked more closely with experts in disease-endemic low- and middle-income countries in the region to identify vaccine R&D priorities, this could help to address the documented mismatch between global and national research priorities (Viergever, 2013). Another way for donors to help to support Governments of Asia-Pacific countries to invest more in vaccine R&D would be through a matching fund—in other words, donors could agree to match Government investments.

Multilateral funders have shown increased interest in recent years in funding global public goods (GPGs) for health, including global health R&D. Our own recent policy analysis, which examined the role of intensified multilateral cooperation on GPGs for health argued that "in the current climate of growing worldwide nationalism and populism, the multilateral institutions now find themselves well positioned to become a countervailing force in taking international collective action and supporting GPGs for health" (Center for Policy Impact in Global Health, 2018).

As shown in tables 4 and 6, there has been minimal investment by **industry** into vaccine R&D in the region — just \$14.7 million into neglected disease vaccine R&D and \$0.14 million into emerging infectious disease vaccine R&D from 2018 to 2020. This amount represents a tiny fraction of total private sector investment into neglected disease product development. The 2021 G-FINDER report found that in 2020, the private sector invested \$491 million in neglected disease basic research and product development (or 12 per cent of global funding). Multinational pharmaceutical companies were responsible for 90 per cent of the private funding and small pharmaceutical and biotechnology firms contributing the other 10 per cent.

Private funders could be incentivized to fund vaccine R&D through the launch of new PDPs, in which the financial risk is shared by bringing public, private and philanthropic investors together. Such partnerships, which take a needs-based approach, have shown proof of concept for launching new global health technologies and should be explored for the region. In a recent analysis of PDPs, Bulc and Ramchandani (2021) argue that the same five assumptions that led to the PDP model still hold true to today: they help to

address market failure, they use a portfolio approach to R&D, they aim to maximize cost-effectiveness, they build R&D capacity and they catalyse access for health impact. Nevertheless, the authors argue that PDPs need to do better at coordinating their disparate activities and at priority setting—both of which could be achieved through new pooled approaches (see 6.2 below).

Philanthropic investors have not yet made large-scale, sustained investments into vaccine R&D in the region. Several philanthropies have made small contributions to R&D more broadly (not specifically vaccine R&D), suggesting that it may be possible to attract philanthropic support for vaccine development. Key informants argued that a pool of sustained philanthropic funding could create a legacy in the region, supporting innovative platforms and serving regional needs.

As we have previously argued, “the public and philanthropic sectors should continue to expand successful incentive mechanisms and test new ones to attract industry to participate in product development for neglected diseases” (Yamey and others 2018). Beyond traditional push and pull incentives (e.g. public investments into translational research, advanced purchase agreements), newer approaches should also be tested. One example is the Life Prize, “which combines upfront grants with pooling of intellectual property into a patent pool” (Center for Policy Impact in Global Health, 2018).

6.2 Pooling of resources

There is growing interest among funders in developing innovative approaches to global health R&D, including new pooled financing mechanisms. For example, we conducted a study to assess the appetite among funders for a global funding platform—an aggregator for funding late-stage clinical trials (Yamey and others, 2020). We interviewed 192 relevant stakeholders worldwide and found very widespread buy-in for the idea of a new pooled fund. Key informants argued that they would be more likely to participate in a pooled fund if it:

- Provided financial support for clinical trial capacity in LICs and MICs;
- Brought domestic commercial benefits to these countries through local manufacturing; ownership of intellectual property, and free licensing;
- Led to wide availability of low-cost products in these countries;
- Facilitated global knowledge sharing;
- Promoted “an equal partnership between Northern and Southern countries across all dimensions, e.g. participation in global governance structures, data ownership, and trial leadership (making sure, for example, that trials have principal investigators from the Global South)” (Yamey and others, 2020).

Another example of a pooled R&D fund is the proposal developed by the Center for Global Development to use pooled financing to incentivize the development of urgently-needed new TB tests, drugs and vaccines (Silverman, 2019). The proposed pool, called the market-driven, value-based advance commitment (MVAC), would be financed by

MICs, especially those with a high burden of TB. The idea is that MICs would commit to purchase new TB technologies by supporting an up-front pool of funding, thus “providing guarantees of a market to pharmaceutical companies for newly developed products” (Yamey and others, 2019).

This type of pooling could be established at a regional level—it would be valuable to explore the appetite for and feasibility of a new pooled R&D vaccine fund for the region. Such a pooled approach would be especially valuable if it also served as a coordination platform. Such platforms could not only help to mobilize funding, but also support priority-setting processes and transparency about investment decisions. A coordination platform for vaccine R&D in the Asia-Pacific region could serve as a kind of “one stop shop,” informing existing and new public, private and philanthropic investors about “R&D needs, candidate products in the pipeline, estimated development costs and financing gaps, likely markets, and expected health and economic benefits” (Center for Policy Impact in Global Health, 2018).

In a policy analysis by Naomi Beyeler and colleagues (2019), called “Improving resource mobilization for global health R&D: a role for coordination platforms?,” the authors argued that R&D coordination platforms should have four key functions: “building consensus on R&D priorities; facilitating information sharing about past and future investments; building in accountability mechanisms to track R&D spending against investment targets and curating a portfolio of prioritised projects alongside mechanisms to link funders to these projects.” Their analysis also suggested that several design features would maximize success, such as making sure there is a strategy for sustainably funding the platform’s secretariat, separating out the coordination from the financing functions, and including multiple diseases. CEPI and GloPID-R (the Global Research Collaboration for Infectious Disease Preparedness) have shown the value of establishing research priorities across multiple diseases. The risks of launching a coordination platform for just a single disease, argue Beyeler and colleagues, include creating “a fragmented funding environment where platforms compete for limited funds” and missed opportunities for basic science investments with benefits across multiple diseases.

6.3 Strategic purchasing

Finally, we have previously noted that “several global health agencies have progressively developed a ‘strategic purchasing’ function through the development of prioritization models to allocate their funding” (Yamey and others 2018). Examples include:

- Gavi, the Vaccine Alliance allocates approximately 20 per cent of its funding to support GPGs for health, such as market shaping and pooled procurement (Jamison and others, 2013).
- The Global Fund’s 2017–2022 strategy included \$194 million for strategic initiatives, many of which were GPGs for health, such as pilot studies of malaria vaccine introduction.
- The International Development Association (IDA) funds regional public goods, such as the East Africa Public Health Laboratory Network (World Bank, 2019).

This trend suggests that there may be a role for ADB to support regional GPGs for health, including vaccine R&D, building on its support for APVAX.

Annex: Policy checklist on mechanisms to close the vaccine research and development finance gap in the Asia-Pacific region

Policy area 1: Resource mobilization mechanisms

Issue of consideration 1: Government investment in vaccine R&D

Guiding Questions

- ◆ How much are governments in the region investing in vaccine R&D?
- ◆ Given anticipated trends (economic stagnation, contraction, or growth), how much *could* governments increase their domestic spending on such R&D?
- ◆ Would region-wide approaches (e.g. regional earmarked mechanisms or taxes) be a politically feasible approach to mobilize additional government spending?

Potential Challenges

- ❖ Data on national public spending on vaccine R&D are incomplete, and better data collection and transparency are needed.
- ❖ The COVID-19 pandemic has been a global economic challenge, and in many countries it is a drag on economic growth—this in turn could make it hard for some nations to commit to higher spending on vaccine R&D.

Recommended Actions (national)

- ❖ Governments in the region should publish data on levels of public spending on vaccine R&D, disaggregated by disease, funding recipient and type of research (preclinical, phase 1-3 trials, platform technologies, etc.).
- ❖ Governments should set out explicit spending targets for vaccine R&D and report annually on their progress towards reaching these targets.

Recommended Actions (regional)

- ❖ Explore the political feasibility of and support for region-wide approaches:
 - A region-wide R&D tax, for example, allocation of 0.01 per cent of GDP towards vaccine R&D;

- A region-wide airline tax to support regional vaccine R&D (modeled upon the Republic of Korea’s airline solidarity levy that supports the Global Disease Eradication Fund);
- A voluntary regional earmarked mechanism for vaccine R&D (a “CEPI for the Asia-Pacific region”); such a mechanism could also potentially attract donor agency funding.

Issue of consideration 2: Investment by the private sector, including through public-private product development partnerships (PDPs)

Guiding Questions

- ◆ Which private actors are currently investing in vaccine R&D in the region?
- ◆ Are they large multinational pharmaceutical companies, small pharmaceutical firms, or small biotechnology firms?
- ◆ What are the incentives for the private sector to invest in vaccine R&D in the region and how could these incentives be strengthened further?
- ◆ Have push mechanisms (e.g. R&D tax breaks) or pull mechanisms (e.g. R&D prizes) been tried as a way to attract industry? If they have, were they successful?
- ◆ Given the success of PDPs in launching new health technologies for neglected and emerging infectious diseases, are there opportunities to launch new PDPs for vaccine R&D in the Asia-Pacific region?
- ◆ Would the launch of new PDPs aimed at funding vaccine R&D in the region help to address market failure, prioritize R&D needs (see below), and build R&D capacity?

Potential Challenges

- ❖ Proprietary concerns can be a barrier to companies sharing information about their R&D investments and their future investment strategy—this is one challenge in trying to understand pharmaceutical industry investments in neglected and emerging disease R&D.
- ❖ There may not be good data on the impact of incentives in attracting industry funding in the Asia-Pacific region.

Recommended Actions

- ❖ It would be valuable to conduct a detailed landscaping analysis of (a) the private sector's role in funding vaccine R&D in the Asia-Pacific region, (b) the existing PDPs that support vaccine R&D in the region (e.g. in the Republic of Korea, the International Vaccine Institute and its Research Investment for Global Health Technology (RIGHT) Fund; in Japan, the Global Health Innovative Technology Fund (GHIT), etc.) to learn lessons for attracting additional industry funding.

Issue of consideration 3: Investment by philanthropy

Guiding Questions

- ◆ Are there untapped opportunities for philanthropic investors to make large-scale, sustained investments into vaccine R&D in the region?
- ◆ Given that philanthropies have made small contributions to R&D (though not specifically vaccine R&D), do these small investments signal a potential willingness for scaled up support?

Potential Challenges

- ❖ There is little publicly available information on the landscape of philanthropic support for vaccine R&D in the region.

Recommended Actions

- ❖ It would be valuable to conduct a detailed analysis of the landscape of potential philanthropic investors and the potential for them to invest in vaccine R&D in the region.

Policy area 2: Polling and prioritization approaches

Issue of consideration 1: Establishing pooled funding approaches for vaccine R&D in the region

Guiding Questions

- ◆ Is there regional policy appetite for launching a new pooled R&D vaccine fund?
- ◆ If there is policy interest in such a fund, what are the key considerations for its design and its governance?

- ◆ If a pooled fund were to be launched, what is the business case for launching a narrow fund (focusing on a narrow set of diseases) versus a broad fund (focusing on a wide range of diseases)?
- ◆ What would be the modeled health and economic benefits of such a pooled fund? Could the return on investment be estimated?
- ◆ Could a new pooled R&D fund for vaccine R&D in the region (i) mobilize additional funding, (ii) help to establish regional consensus on R&D priorities, (iii) bring country partners to the table (including in conducting trials and manufacturing products), (iv) facilitate information sharing across investors and research institutions, and (v) curate a portfolio of prioritized R&D investment opportunities?
- ◆ Which countries in the region have the political will to explore such a fund, or even to take a leadership role in such an enterprise?
- ◆ Does the current policy interest in launching regional vaccine manufacturing hubs (e.g. see the launch of the mRNA vaccine hub in South Africa) open a window of opportunity to link a vaccine manufacturing hub in the Asia-Pacific region with a new pooled R&D fund?

Potential Challenges

- ❖ Existing pooled R&D mechanisms have not done well at mobilizing financing for late-stage trials and there has been little coordination between them; adding a new mechanism could contribute to the fragmentation of the landscape.
- ❖ The global economic downturn caused by the COVID-19 pandemic could make it challenging for countries to support a new financing mechanism.
- ❖ Policymakers may be concerned that a new mechanism could divert funds from other priorities.

Recommended Actions

- ❖ It would be valuable to conduct an analysis of the case for launching a new pooled R&D fund for vaccines—assessing the demand for and potential design of such a fund and estimating the health and economic returns.
- ❖ Such a study could examine previous pooled R&D mechanisms to learn potential lessons for the Asia-Pacific region, interview stakeholders in the region, and model the health and economic benefits of different types of pooled mechanisms.

Issue of consideration 2: Prioritization of vaccine R&D needs in the Asia-Pacific region

Guiding Questions

- ◆ How is vaccine R&D currently prioritized in the region? What are the pros and cons of current prioritization approaches?
- ◆ What are the options for improving the prioritization of vaccine R&D in the region?
- ◆ Could a new pooled mechanism play a role in guiding such prioritization?

Potential Challenges

- ❖ Different stakeholders in the R&D process may have their own key priorities, and different nations in the region may also have their own national priorities, both of which could be a challenge for regional prioritization.

Recommended Actions

- ❖ Examine current regional approaches to prioritization and explore opportunities for harmonized regional approaches.

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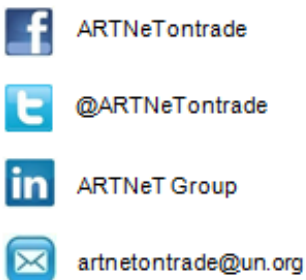
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