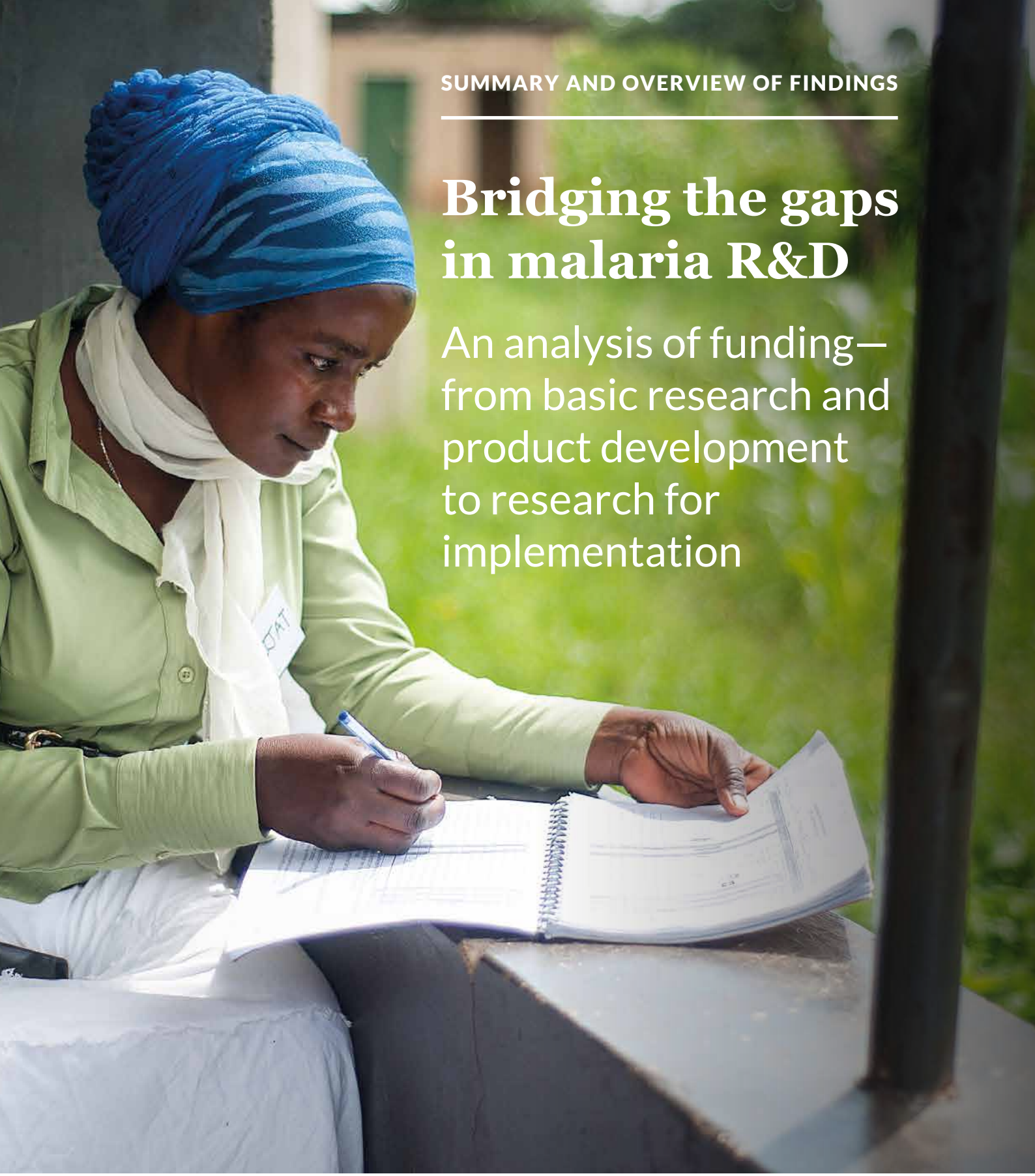

SUMMARY AND OVERVIEW OF FINDINGS

Bridging the gaps in malaria R&D

An analysis of funding—from basic research and product development to research for implementation

PATH

World Health Organization

TDR For research on diseases of poverty
UNICEF • UNDP • World Bank • WHO

malaria NO MORE united kingdom

MMV Medicines for Malaria Venture

FIND Because diagnosis matters

IVCC Building Partnerships Creating Solutions Saving Lives

POLICY CURES RESEARCH.

Acknowledgments

This is a summary of the full report, *Bridging the Gaps in Malaria R&D: An Analysis of Funding—From Basic Research and Product Development to Research for Implementation.* The development was led by a core group of representatives from PATH, the Special Programme for Research and Training in Tropical Diseases (TDR), and Malaria No More UK. The following have provided input: Medicines for Malaria Venture (MMV), the Innovative Vector Control Consortium (IVCC), the Foundation for Innovative New Diagnostics (FIND), and the World Health Organization's Global Malaria Programme.

The data were collected by Policy Cures Research, which also provided input into the overall text.

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Foreword

Progress against malaria has recently flatlined, and in some areas, malaria cases are on the rise. This is a threat to more than a decade of progress and investments in the global fight against malaria—and to the lives and livelihoods of millions of people. Valuable tools have been developed, and more are on the way, but lagging behind are the systems, finances, and political will to ensure that they are implemented, used appropriately, and easily accessible to everyone in need.

Consequently, there is an increasing demand for research that can support broader and better implementation and thus greater impact. However, significant challenges exist to measuring the current effort—let alone accurately assessing the need.

Understanding the volume and uses of funds across malaria research and development—from basic research through implementation—is one way to identify potential gaps in the field. Past reports on funding patterns have shown their usefulness in prompting more attention and marshalling more resources.

In the study summarized here, we expand that effort to include data from a pilot survey on funding for research for implementation and the challenges to tracking the resources that support those efforts.

By integrating data on funding for basic research and product development with similar data on research for implementation, this report builds on previous work and provides a broader view of funding patterns. Although focused on malaria, it offers insights that are applicable across other disease areas.

This research is intended to inform ongoing discussions—among funders, policymakers, product developers, and program implementers—on how best to approach the challenge of improving specific health outcomes in a health system context, the role of resource tracking in meeting this challenge, and ways to fill critical data gaps. It provides recommendations on funding for malaria research and development, and a call to action: to ensure that tools to fight malaria are developed and deployed efficiently, effectively, for optimal impact.

In the end, it is about staying on course—ensuring that the many countries faced with high burdens of malaria have the right tools and strategies and use them—so that this scourge can be eliminated once and for all.

David C. Kaslow, MD, Larry Slutsker, MD | PATH

John Reeder, PhD | Special Programme on Research and Training in Tropical Diseases (TDR)

James Whiting | Malaria No More UK

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Introduction

After more than a decade of progress in reducing the burden of malaria disease and death, the total number of estimated malaria cases rose in 2016 by more than 5 million over the previous year.[1] Increases in malaria burden were reported from countries in all regions of the World Health Organization (WHO) between 2014 and 2016.

As new tools have become available, there are growing challenges to the health care systems to ensure that the drugs, diagnostics, vaccines, and vector control products are designed for the conditions in which they are used; reach the right place, at the right time, in the right quantities; and are delivered appropriately.

In the past, there was more funding in basic research and insufficient investment into product development. Publicly reported funding data helped to illuminate the gaps and to raise commitments toward addressing what was called the valley of death.

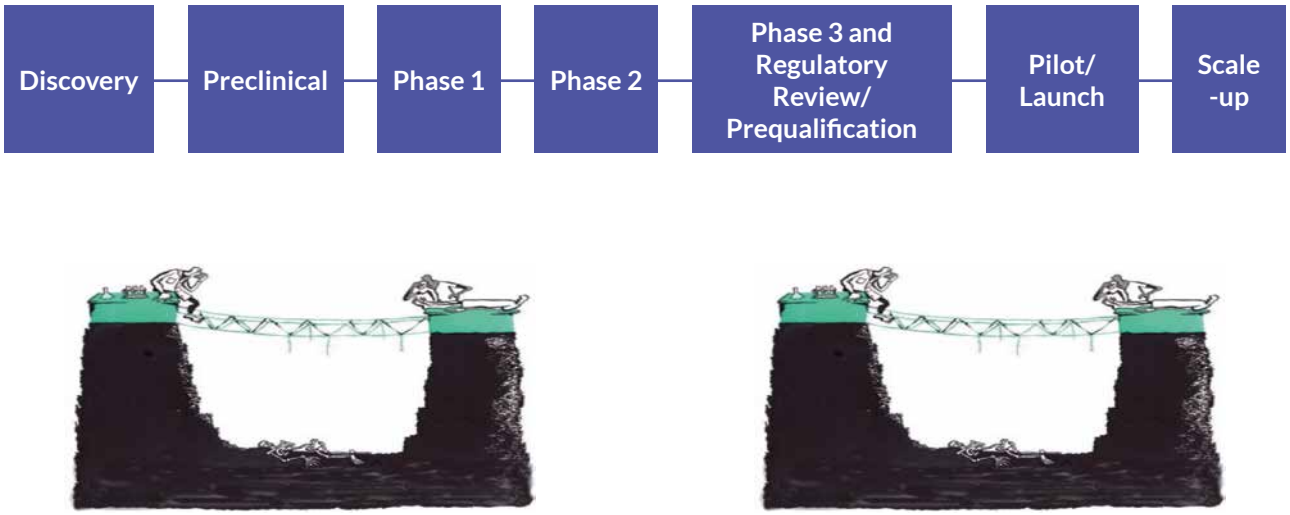
Today, the questions are whether there is enough funding into research for implementation that would improve access to the health products and services now available, and how well what is funded is aligned to the product pipeline and health system needs.

A SECOND VALLEY OF DEATH?

There is growing recognition of a possible second valley of death. The first valley of death addressed the gap of translation from basic research into product development.[2] Funding data helped to illuminate the gaps and to raise commitments toward addressing that valley. Today, there appear to be challenges in translating the fruits of product development into access and health impact consistently across the countries burdened with high malaria rates.[3]

Research for implementation is perceived as a bridge over this valley, helping to ensure that tools reach the intended population and actually work in real-life settings with challenges such as harsh weather, remote conditions and limited training. This research can also ensure that the investments already made are not lost, but rather are built upon, thereby improving control and supporting disease elimination. Like any bridge, however, it has to be built and maintained—and this requires money.

Figure 1. **A second valley of death?**



The first valley of death: from basic research to product development[2]

The second valley of death: from licensure to routine use and scale-up[3]

The report, *Bridging the gaps in malaria R&D*, covers findings from a pilot study on funding for malaria research for implementation funding, which includes implementation research, operational research, and health systems research. For the first time, these data are combined with those from the broader malaria basic research and product development pipeline funding already tracked annually by Policy Cures Research for the G-FINDER (Global Funding of Innovation for Neglected Diseases) surveys.[4]

In early 2018, Policy Cures Research conducted a survey asking for data or access to publicly available databases on disbursements on research for implementation for the years 2014–2016. Questions also examined perceptions of, and commitments to, this field. An explanation of the survey methodology and the organizations included is available in the full report. Of the 26 organizations polled, 77% provided funding data and 69% responded to the qualitative questions.

The results provide a first picture of how funds are being spent across the different research for implementation fields. They also highlight opportunities for improved monitoring and analysis of funding flows. There are significant challenges to getting complete data that cover research for implementation, including a lack of consensus around categories and definitions, and insufficient application of these categories and location of research within funding databases.

The report on the findings of this pilot survey is intended to inform ongoing discussions—among funders, policymakers, product developers, and program implementers—on how best to approach the challenge of improving specific health outcomes in a health system context, the role of resource tracking in meeting this challenge, and ways to fill critical data gaps. It provides recommendations on funding for malaria R&D, and a call to action: to ensure that tools to fight malaria are developed and deployed efficiently, effectively, and for optimal impact.

Key findings

Table 1 summarizes funding trends between 2007 and 2016 for basic research and product development, based on data from the 2016 G-FINDER survey of 187 organizations. Research for implementation funding is tracked only between 2014 and 2016 among a subset of 26 organizations thought to either be funding or conducting this type of research.

Funding is highly concentrated, with the top 12 funders in 2016 accounting for 93% of total malaria R&D funding, and the top 3 funders (the Bill & Melinda Gates Foundation, US NIH, and industry) collectively contributing 71% of total investment.

Total funding for malaria basic research and product development peaked at $656 million in 2009. It has remained at a steady level since then—between $540 million to $600 million per year, as shown in Table 1.

Funding of research for implementation increased from $99 million in 2014 to $123 million in 2016, bringing total malaria R&D funding (including basic research, product development, and research for implementation) to $689 million in 2016.

Table 1. **Leading funders of malaria research and development funders, by volume** (in million US dollars, adjusted to 2016 dollars to account for inflation).

Funder	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Gates Foundation	146.0	206.0	215.0	103.0	170.0	137.0	127.0	178.0	155.0	176.0
US NIH*	99.0	123.0	136.0	156.0	144.0	177.0	144.0	161.0	168.0	174.0
Aggregate industry	83.0	85.0	96.0	115.0	93.0	106.0	76.0	118.0	142.0	137.0
Unitaid*	-	-	-	-	-	-	5.9	28.0	22.0	37.0
US DOD	39.0	36.0	44.0	27.0	21.0	11.0	23.0	19	30	31.0
UK DFID	5.3	4.2	6.6	25.0	19.0	6.0	27.0	20	21	17.0
Wellcome Trust	24.0	23.0	24.0	29.0	27.0	27.0	24.0	22	17	14.0
USAID*	11.0	10.0	9.6	10.0	9.1	12.0	6.6	11	14	12.0
UK MRC	16.0	17.0	18.0	20.0	17.0	16.0	16.0	14	9.2	11.0
EC*	34.0	32.0	28.0	23.0	25.0	19.0	26.0	26	31	9.4
ICMR		10.0	7.0	5.0	5.1	6.7	7.5	7.0	7.8	9.0
US CDC	2.6	3.1	1.7	4.2	3.0	1.7	4.2	10	2.9	8.2
Subtotal of basic research and product development funding	518.0	606.0	656.0	581.0	600.0	587.0	544.0	562.0	567.0	566.0
Total funding	518.0	606.0	656.0	581.0	600.0	587.0	544.0	662.0	667.0	689.0

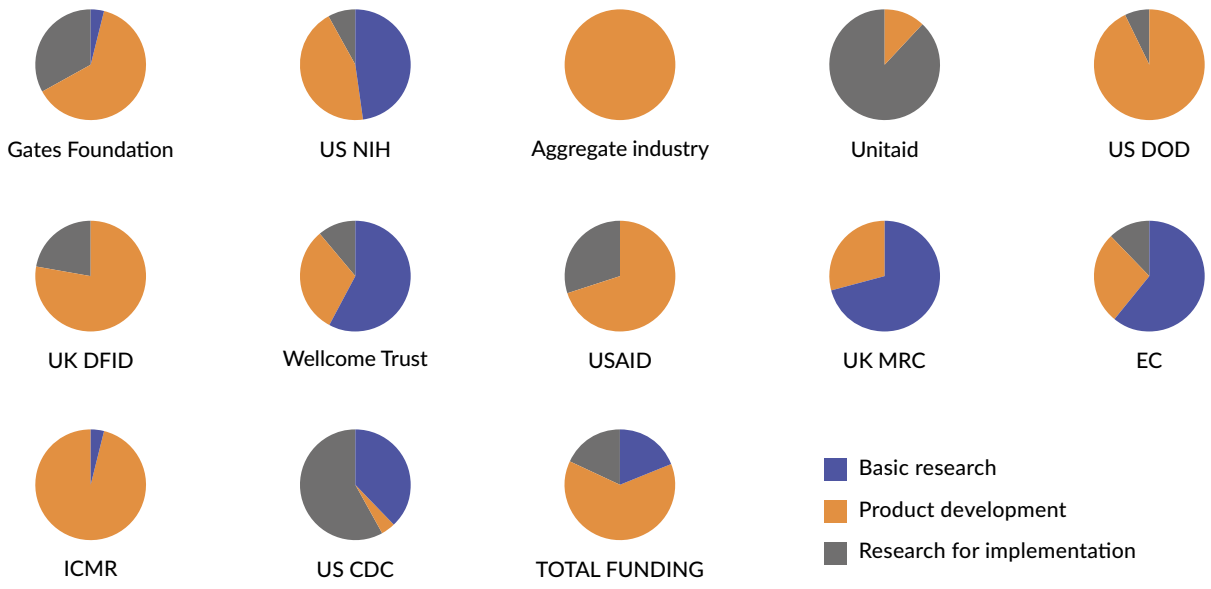
*Research for implementation data were extracted from publicly available databases and were not verified by the organization.

Funding organization did not participate in the G-FINDER survey for this year.

Funding totals include data from the pilot survey on research for implementation during 2014 to 2016 only.

Note: Funder acronyms listed at bottom of page.

Figure 2. **Relative allocations of funding, by funder, by category of malaria basic research and product development (2016).**



Abbreviations: BMBF = Federal Ministry of Education and Research; CDC = Centers for Disease Control and Prevention; DFID = Department for International Development; DOD = Department of Defense; EC = European Commission; Gates Foundation = Bill & Melinda Fates Foundation; ICMR = Indian Council of Medical Research; MRC = Medical Research Council; NIH = National Institutes of Health; UK = United Kingdom; US = United States; USAID = US Agency for International Development.

Table 2. **Leading recipients of external malaria research and development funding, by volume of funding received.**

Recipient	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Medicines for Malaria Venture	85.0	50.0	45.0	73.0	76.0	52.0	65.0	74.0	77.0	60.0
Innovative Vector Control Consortium	-	11.0	16.0	16.0	<0.1	5.5	14.0	6.4.0	18.0	32.0
Malaria Consortium	-	-	-	0.9	0.6	0.8	-	13.0	12.0	28.0
PATH	13.0	84.0	90.0	4.4	44.0	26.0	22.0	71.0	28.0	26.0
Aggregate industry	9.9	21.0	29.0	24.0	17.0	41	30.0	29.0	20.0	22.0
University of Oxford	13.0	12.0	17.0	13.0	10.0	8.0	16.0	26.0	17.0	20.0
University of California San Francisco	-	1.7	1.6.0	3.2	6.7	4.9	7.5	12.0	13.0	17.0
Imperial College London	1.4	2.0	2.2	2.3	3.0	1.9	3.5	4.2	1.9	16.0
Clinton Health Access Initiative	-	-	-	-	-	-	-	6.4	5.4	14.0
Liverpool School of Tropical Medicine	45.0	17.0	18.0	9.8	11.0	10.0	9.0	8.8	2.9	10.0
University of Maryland, Baltimore	-	3.0	1.4	2.6	2.2	5.6	5.4	5.0	8.4	9.6
Foundation for Innovative New Diagnostics	0.2	3.3	3.1	3.4	2.8	4.0	5.9	4.2	4.1	6.6
Subtotal of basic research and product development external funding	355.0	432.0	461.0	382.0	431.0	424.0	400.0	380.0	342.0	347.0
External R&D funding received	355.0	432.0	461.0	382.0	431.0	424.0	400.0	478.0	441.0	466.0

Funding totals include data from the pilot survey on research for implementation.

Note: G-FINDER is primarily a survey of funders. Therefore, recipient totals may underestimate the funds received by research organizations, particularly those that did not participate in G-FINDER surveys. Abbreviations: R&D = research and development.

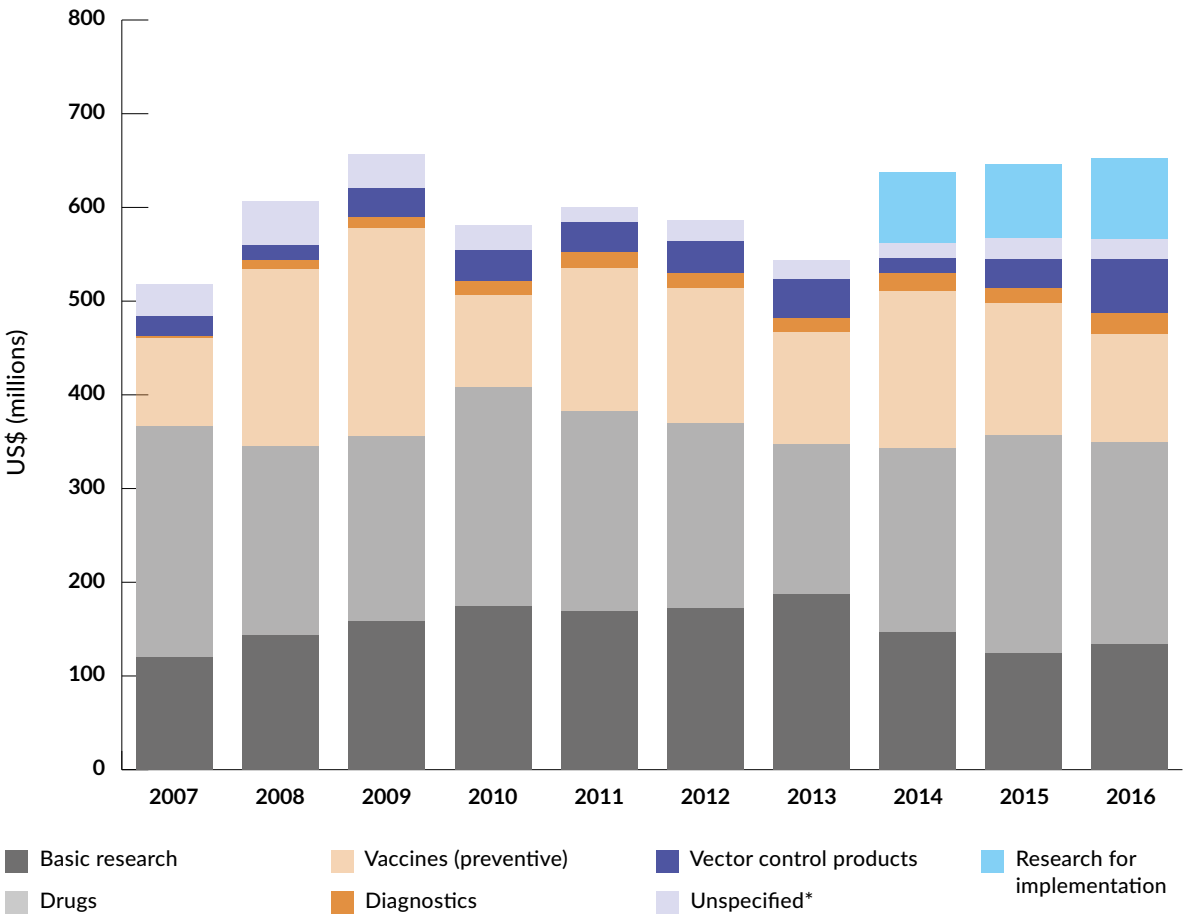
Just under a third of all funding for malaria R&D in 2016 ($223 million, 32%) was invested by funders in their own internal R&D activities. The remaining 68% was either given directly to researchers and product developers, or channeled via product development partnerships and other intermediaries, with three organizations (MMV, IVCC, and PATH) receiving 93% of this total.

The Malaria Consortium, Clinton Health Access Initiative, and University of California San Francisco were among the top 12 recipients, largely because of their work in research for implementation.

In addition to the funds that they invest in their own internal R&D programs, industry also receives funding from external sources to support these activities. Collectively, aggregate industry received an average of $24 million of external funding each year between 2014 and 2016, mainly from a small group of funders including the US NIH, Gates Foundation, Wellcome Trust, US Department of Defense, and European Commission.

Summary of funding by type of research

Figure 3. **Malaria research and development funding by product/area.**



** Unspecified funding refers to basic research and product development investments that could not be allocated to a specific product or research area.*

Note: Investments in research for implementation were not captured before 2014. What is illustrated here only represents funding reported by 20 organizations. The G-FINDER survey of basic research and product development funding was more extensive, with 187 participants in 2016.

Basic research and product development funding and achievements

Basic research received one-quarter ($1.5 billion, 25%) of all global malaria R&D funding from 2007 to 2016, with the public sector providing the vast majority ($1.3 billion, 85%). As Figure 3 illustrates, funding for basic research peaked in 2013 and has trended downward over the last few years. This raises the question of whether current funding levels remain sufficient for the need.

This funding has provided greater understanding of both parasite and mosquito biology, as well as the interactions between the two; development of mouse models that facilitate understanding of the biology of the liver-stage parasite, in both *P. falciparum* and *P. vivax* parasite species; and the ability to culture *P. vivax* hypnozoites in culture.

In addition, a key tool for evaluation of drugs and vaccines—the controlled human malaria infection (CHMI) or "challenge" model used to evaluate liver-stage interventions targeting the sporozoite—has been complemented by development of a blood-stage CHMI model and, more recently, by progress toward a model for evaluating transmission-blocking approaches. A second area of progress with implications for drug and vaccine development, as well as vector control, are the various genome-editing systems, including CRISPR-Cas9.

Diagnostic investments grew between 2007 and 2016, from $2.1 million to $26 million—a more than tenfold increase—although this still represented only a small percentage (3.8%) of all malaria R&D funding in 2016.

The Foundation for Innovative New Diagnostics (FIND), PATH, and their partners have made significant advances in developing innovative, ultra-sensitive diagnostics to support the elimination of malaria. The first product from this portfolio was launched in 2017 (the Alere™ Malaria Ag P.f test), with progress underway on the others. These tests have the potential to significantly impact transmission of malaria, with point-of-care detection of low-density malaria infections.

Similarly, temperature-stable loop-mediated isothermal amplification (LAMP) kits and assays specifically for *P. vivax* detection that work in field conditions have already made it possible to effectively identify these infections, which may be low-density and asymptomatic. Both diagnostic tools—the ultrasensitive rapid diagnostic test and the LAMP—may be useful adjuncts to malaria elimination efforts.

Drug research and development experienced peaks in funding in 2007, 2010, and 2015 to 2016, with the last peak reflecting an increased focus on clinical development as product candidates advanced through clinical trials.

Funding has allowed Medicines for Malaria Venture (MMV) to co-develop with R&D partners 7 medicines that have saved at least 1.5 million lives, as well as to take stewardship for 2 products developed and launched by the Drugs for Neglected Diseases initiative (DNDi). For uncomplicated malaria, this includes 2 formulations specifically for children: Coartem® Dispersible, and Pyramax® granules. Severe malaria treatments include Guilin's artesunate injection Artesun® and Cipla and Strides Shasun's rectal artesunate (Artecap™) suppository products. In addition, to protect children, MMV supported Guilin to obtain WHO prequalification for SPAQ-CO™ for seasonal malaria chemoprevention.

In 2014, a ten-year effort to establish and validate a manufacturing process to produce semisynthetic artemisinin (ssART) at industrial scale resulted in the first delivery of antimalarial treatments manufactured with a ssART derivative. The project, led by PATH's Drug Development program, brought together partners from academia, industry, and the public sector—including Sanofi—to address the historically volatile botanical supply chain and thus help to ensure that the global demand for ACTs can be met.

Vaccine R&D funding shows the impact of late-stage vaccine development over the period from 2007 to 2016. This includes a large funding peak in 2008-2009, related primarily to large up-front disbursements to cover the cost of late-stage clinical trials for the RTS,S malaria vaccine.

Investments in malaria vaccine development have resulted in one vaccine, RTS,S, that is advancing toward introduction. Developed through a collaboration between GlaxoSmithKline (GSK) and PATH, the vaccine, which targets the *P. falciparum* parasite, is intended to prevent disease in young African children. In a large-scale phase 3 trial, the vaccine prevented 4 in 10 (39%) cases of clinical malaria and 3 in 10 (29%) cases of severe malaria, in young children who received four doses of RTS,S, over 4 years of follow-up. RTS,S has been positively reviewed by the European Medicines Agency and recommended by WHO for pilot implementation, which is expected to begin in selected areas of Ghana, Kenya, and Malawi in late 2018. The Malaria Vaccine Implementation Programme is a country-led, WHO-coordinated initiative to assess—in the context of routine use—the feasibility of delivering the required four doses of RTS,S and its safety, as well as the vaccine's potential role in reducing childhood deaths.

At any one time, there are roughly 2 dozen vaccine candidates undergoing testing in human volunteers, and others following behind in the pipeline, as illustrated by the so-called "Rainbow Tables" maintained by the WHO's Department for Immunization, Vaccines and Biologicals.[5]

Vector control product research and development investment nearly tripled over the period from 2007 to 2016 (from $21 million to $58 million), almost entirely due to increased funding from the Gates Foundation.

Investments have allowed the Innovative Vector Control Consortium (IVCC) and its industry partners to develop three indoor residual sprays (K-Othrine® Polyzone, Actellic® 300CS, SumiShield™ 50WG) and a dual active-ingredient insecticide bednet (Interceptor® G2). These products are aimed at preventing the build-up of insecticide resistance in mosquitoes.

Basic research and product development challenges

The key challenges for these areas include:

- **Continued underinvestment in *P. vivax*,** a parasite species that is growing as a proportion of the total malaria burden. This is seen in low investments in basic research, in limited numbers of diagnostics and drugs for this species, and in vaccine development.
- **Unpredictable or unknown regulatory and/or policy pathways,** noted for vector control products, but also affecting other areas.
- **Resistance on the part of the parasite and vector** to drugs and insecticides, respectively.

As the product portfolio has matured, all areas are finding issues around access to new or improved products. The challenges to testing a product in field conditions, and moving it through weak health systems, has led to new emphasis on research for implementation to better understand the obstacles and identify solutions. This is the key driver behind the study to begin to collect funding data in this area.

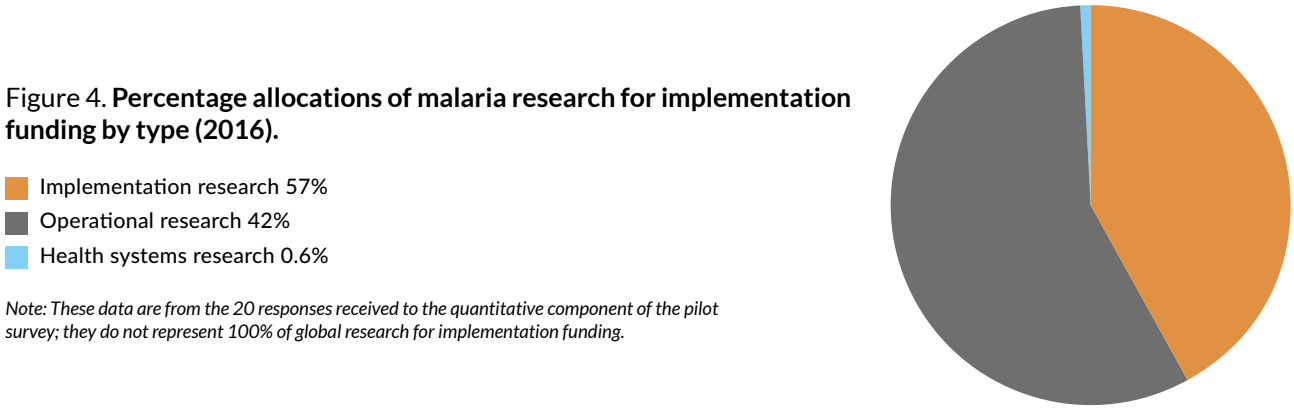
Research for implementation funding

Investments of $99 million in research for implementation were documented in 2014, amounting to 15% of total malaria funding. Investments increased slightly to 18% of the total amount in 2016. This is based on the 2018 survey sent to 26 organizations that provide or receive funds for research for implementation.

Just over half ($71 million, 57%) of all reported funding for research for implementation in 2016 was for implementation research, up from $61 million in 2014 (see Figure 4).

The share of research for implementation funding invested in operational research rose to 42% ($52 million) in 2016, an increase from 38% ($38 million) in 2014. Health systems research made up a tiny proportion (0.4%), reinforcing earlier reports like malERA 2017,[6] that complained that "too little investment and progress have been seen in this area" and called for a new tool to "identify bottlenecks (and) test different approaches to overcome them."

Figure 4. **Percentage allocations of malaria research for implementation funding by type (2016).**



Note: These data are from the 20 responses received to the quantitative component of the pilot survey; they do not represent 100% of global research for implementation funding.

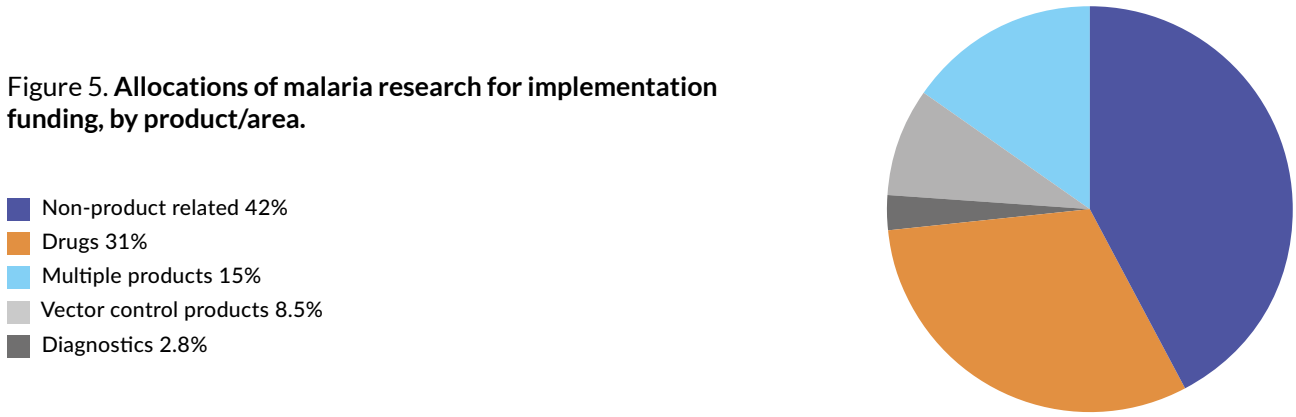
Where is research for implementation focused?

A large portion of research for implementation funding was invested in research that was not related to specific products ($52 million, 42%) (see Figure 5).

Almost a third of research for implementation funding ($38 million, 31%) was for drugs, whereas $10 million was invested in research for implementation for vector control products. Diagnostics received less attention ($3.4 million, 2.8%).

Very little funding of vaccine-related research for implementation was reported ($0.2 million), as research related to the pilot implementation of RTS,S, the malaria vaccine most advanced in development globally, had not yet started in 2016 and key organizations involved in funding vaccine R&D (i.e., industry) were not included in the pilot survey. The $240,000 reported for 2015 to 2016 by PATH was for preparatory work related to the health care utilization study profiled in Case study 4 (in the full report).

Figure 5. **Allocations of malaria research for implementation funding, by product/area.**



Challenges in research for implementation

As new tools have become available, there are growing challenges to the health care systems to ensure that the drugs, diagnostics, vaccines, and vector control products are designed for the conditions in which they are used; reach the right place, at the right time, in the right quantities; and are delivered appropriately.

ACCESS TO DIAGNOSTICS

Diagnostics are hardly covered by research for implementation. Is the low level of funding reported an accurate representation of a lack of research, a reflection of the limited data, or an indication that research in this area is less expensive? Given the critical role of diagnostics in preventing the use of the wrong treatment—and thus delayed treatment, unneeded costs, and increased parasite resistance—it is important to get an accurate picture of how much research for implementation is being used and what it costs.

ACCESS TO DRUGS

The *World Malaria Report 2017* found that almost one-third of patients who sought malaria treatment at a public health facility did not receive artemisinin-combination treatments (ACTs), the most effective antimalarial drug that is the result of years of R&D investment. The numbers receiving this treatment were even lower in the private sector. And at the antenatal clinics, 25% of pregnant women in sub-Saharan Africa still do not get even a single dose of IPTp, the intermittent preventive treatment.[1]

ACCESS TO VECTOR CONTROL

Investments in vector control R&D are now offering the possibility of new insecticides, which are urgently needed, given increasing resistance to current insecticides.

A comprehensive toolbox to prevent malaria is becoming available, but knowing how and when to best use these tools in many different settings is essential. Overall, training and documentation are required. As stated in the *IVCC Annual Report 2016–17*: "For products to be accepted by countries and implementation partners, evidence on their cost effectiveness and impact is imperative."[7]

ACCESS TO VACCINES

As the first malaria vaccine moves toward implementation, key issues to be addressed include how to ensure that children receive all 4 recommended doses and that use of other malaria interventions—and other vaccines—is maintained. The evaluation components of the pilot implementation program, including the health care utilization study described in Case study 4 (in the full report), are critical to answering these and other questions.

CHALLENGES FOR MALARIA PROGRAMS

African leaders have doubts that the 2030 targets for malaria elimination will be achieved without big changes in funding and delivery. The *Malaria Futures for Africa*[8] report states that "new discoveries are adopted slowly, or not at all, because countries lack the operational research infrastructure to test different deployment methods and to assess the impact that each has." The report called for "more high-quality data on how to use the tools they already have as effectively as possible." These leaders also expressed concern about the impact of increased trade and travel in speeding up resistance to the ACTs, and about how to track substandard and counterfeit medicines.

A review of the literature on malaria control and elimination between 2008 and 2013 (15,886 articles) revealed that less than 4% met the definition of operational research.[9] A commentary in the *Malaria Journal* asked, "Why is so little operational research done when much of it would be straightforward and inexpensive and could be done within the context of routine malaria programme activities?"[10]

This is not unique to malaria. A report of a 2010 meeting of the Global Fund to Fight AIDS, Tuberculosis and Malaria noted that operational research was often absent or inadequately elaborated in proposals that clearly described bottlenecks to progress, and recommended that "Technical Partners work with applicants to help translate programmatic constraints and identified bottlenecks into relevant operational research to support implementation research and to formulate programmatic changes based on research results".[11]

This study raises questions as to whether there is enough funding going into research for implementation that would improve access to the health products and services now available, and how well what is funded is aligned to the product pipeline and health system needs.

Recommendations

Average annual funding for basic research and product development (as distinct from research for implementation) falls short of the need. The WHO's Global Technical Strategy for Malaria estimated average annual investment needs at close to $700 million over the period 2016 to 2030.[12] Annual funding over the period 2014 to 2016 has averaged about $100 million less than that figure, and it remains to be seen if these funds will be made available.

This analysis shows that malaria R&D does not need an endless blank check, but rather, requires targeted funding to develop customizable toolboxes designed to meet the unique needs of each country and region. This includes, in particular, a toolkit to tackle *P. vivax* malaria.

The findings for malaria research for implementation and its funding have implications for not only this disease, but across other diseases affecting low- and middle-income countries. The R&D pipeline is dominated by three diseases—malaria, HIV/AIDS and tuberculosis—which comprised more than half of all product candidates and received 70% of all R&D funding for neglected diseases, or more than $2.2 billion of the more than $3.2 billion invested in 2016.[4] Consequently, any evolutions in collection of funding data and balancing of portfolios within malaria could be applied to other diseases.

The stalled progress against malaria (and in some areas rises in the number of cases) reminds the world of the need to stay on course. Thus for funders, policymakers, product developers, and other malaria stakeholders, four overarching recommendations emerge from the research behind this report:

1. IMPROVED COORDINATION ACROSS INTERVENTION AREAS (FROM BASIC THROUGH IMPLEMENTATION RESEARCH).

Product developers must work together to ensure that next-generation interventions will fit together seamlessly. Although this is already happening periodically, a sustained and ongoing effort is needed to ensure that scarce resources have maximum impact.

2. MORE INNOVATIVE FUNDING APPROACHES.

There is little or no high-income market for the malaria interventions needed in endemic regions and the regions most affected are struggling with the systems required to implement, let alone monitor, them. While the maturity of the current product pipeline is an emerging success story, that success could be limited by the absence of sufficient resources to optimize the impact of new tools. New types and approaches of funding mechanisms and incentives are clearly needed.

3. CONTINUE EXISTING TRACKING OF FUNDING FLOWS AND STRENGTHEN SYSTEMS TO ADDRESS DATA GAPS.

Tracking efforts must be sustained for basic research and product development, and data gaps addressed—particularly for research for implementation. The findings in this pilot survey provide only a partial picture and do not address the evolving nature of malaria and tools required. Key stakeholders, including those who have experience tracking resource flows and conducting research, should work together—and in particular—on research for implementation.

Key discussion topics include:

AGREE TO DEFINITIONS AND A CORE DATA SET TO TRACK RESEARCH FOR IMPLEMENTATION.

The use of a range of definitions complicates and, in some cases, prevents tracking and analysis into funding flows. Few funders are doing this, and many who would like to do this do not have the systems or personnel to do it.

DETERMINE HOW TO COLLECT DATA ON RESEARCH FOR IMPLEMENTATION FUNDING AT THE INSTITUTIONAL, NATIONAL, AND SUBNATIONAL LEVELS.

This survey has been limited to a subset of organizations. However, there is a deep well of research to be mined at the local level that is necessary to complete the full picture. The *Malaria Futures for Africa* report of views from 68 key stakeholders in 14 sub-Saharan countries stated that, "Much more emphasis should be placed on operational research, which most respondents considered underfunded. They felt there should be much more emphasis on how interventions are best delivered through health systems."[8] Is it possible to track funding flows to this, ensuring investments are not double counted? If not, could projects themselves be better tracked, using case studies to explore the funding requirements for implementing certain types of products or services, and how this differs by country or region?

INVESTIGATE THE VALUE OF TRACKING FUNDING FOR TRAINING AND CAPACITY BUILDING FOR RESEARCH FOR IMPLEMENTATION.

Several organizations provided funding for building this capacity, yet this report (and others) have identified gaps in research capacity. Can the tracking of funding for training be useful for funders and program planners? A baseline is needed for further analysis on the gaps which could also be applied to other diseases.

REVIEW DIAGONAL VERSUS HORIZONTAL RESEARCH FOR IMPLEMENTATION.

How can the outcomes of research for implementation be shared across health systems so that the learnings do not remain siloed within a particular disease area or type of intervention? Those working in other disease areas are thinking about this issue, and there is the general belief that working across diseases can increase the value of the research. Can this be monitored and evaluated through funding data?

CONSIDER A FUNDING TARGET FOR RESEARCH FOR IMPLEMENTATION AS PART OF ANY ELIMINATION OR CONTROL PROGRAM.

Review other disease elimination programs and how research for implementation was funded, such as with the Onchocerciasis Elimination Program for the Americas[13] and the Polio Eradication Initiative.[14] Is it possible to identify appropriate levels of investment in this area, and/or to prioritize topics or areas for research for implementation, or to establish targets for percentages of the total research funding that should be devoted to research for implementation? The goal would be to increase funding to the areas with the greatest gaps, not to reallocate from within the current funding pool.

Case studies

The full report contains six case studies that show the range of impact and potential for research for implementation.

Case study 1: Drug packaging increases access to malaria treatment
Case study 2: Reducing deaths with bednets
Case study 3: Two approaches to managing fever, a symptom shared by three diseases—malaria, pneumonia and diarrhea
Case study 4: Ensuring appropriate health care use during malaria vaccine introduction
Case study 5: Reaching malaria elimination through strengthened national research capacity
Case study 6: Increasing access to new insecticidal products

This summary includes Case study 6 from the full report, a recent example of research for implementation. All six case studies are available at: **www.malariavaccine.org/resources/reports/investigating-second-valley-of-death-malaria-rd**

Case study: Increasing access to new insecticidal products

THE PROBLEM

More than 80% of the reduction in malaria prevalence seen in Africa since 2000 has been attributed to vector control interventions—specifically the indoor residual spraying (IRS) of insecticides inside homes and the use of insecticide-treated nets.[15] Unfortunately, insecticide resistance is spreading and threatening this control.[16] New insecticide products need to be developed and used.[17, 18, 19] Several third-generation indoor residual sprayin (3GIRS) products are currently pre-qualified by the World Health Organization (WHO) for malaria vector control. However, the new products are more expensive; as a result, uptake has been slow, overall IRS coverage is low, and market stability remains a concern.

THE APPROACH

The Next Generation IRS (NgenIRS) project is a market-shaping initiative to expand the use of new IRS products in Africa. The project is designed to overcome 5 main conditions that create a challenging market: 1) limited demand; 2) market instability; 3) limited competition; 4) high prices; and 5) absence of a strong evidence base showing cost-effectiveness and impact.

The project provides copayments that reduce prices for national malaria control programs, thereby allowing them to increase the volume of product that they procure. In addition, the project provides consolidated forecasts and volume guarantees to manufacturers to address volatility in the market and the manufacturers have reduced prices in response to the greater certainty of demand.

THE IMPACT

Malaria programs and implementation partners have been able to procure over 4 million units of 3GIRS as prices dropped from $23.50 per unit to $15.00 per unit. Over 1 million additional units have been procured by partners outside of the co-payment mechanism at a significant discount, in return for volume guarantees to manufacturers; this shows the extended impact of the market-shaping intervention.

Programs increased coverage, protecting an estimated 15 million more people than would have been possible if they were paying full price. The improved market has supported WHO pre-qualification listing of new 3GIRS products; a second insecticide was included in the project in 2018 after prequalification listing in 2017. Two additional products are currently under advanced WHO evaluation. The inclusion of a second 3GIRS product created needed competition in the marketplace; it also has allowed malaria programs to invest in sub-national rotation as part of their insecticide-resistance management strategies.

The evidence thus far from observational analyses in Ghana, Mali, and Zambia, along with a randomized control trial in Mozambique, have shown a 22 to 40% reduction in malaria cases attributed to IRS. Further outcomes of these studies will be disseminated through journal publications, conference presentations, and workshops with key country- and global-level stakeholders in 2018 and 2019.

PROJECT FUNDERS AND IMPLEMENTERS

NgenIRS country partners include: Benin, Burkina Faso, Ethiopia, Ghana, Kenya, Madagascar, Malawi, Mali, Mozambique, Rwanda, Tanzania/Zanzibar, Uganda, Zambia and Zimbabwe. Unitaid and the Innovative Vector Control Consortium have partnered with the US President's Malaria Initiative, Abt Associates, PATH, and the Global Fund to Fight AIDS, Tuberculosis and Malaria to work with industry and malaria programmes in Africa to increase the uptake of 3GIRS products. The project is funded by Unitaid.

A malaria spray operator in a village in Rwanda, talking to the householders before spraying their home. © Photo: Innovative Vector Control Consortium, 2016

Spraying the walls of a house in a village in the Ashanti region of Ghana to control mosquito vector populations and minimize contact between infected mosquitoes and people. © Photo: Innovative Vector Control Consortium, 2018

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Both this summary and the full report:

Bridging the gaps in malaria R&D

An analysis of funding—from basic research and product development to research for implementation

Can be found online here:
www.malariavaccine.org/resources/reports/investigating-second-valley-of-death-malaria-rd

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