U.S. PRIORITIES FOR MALARIA

By David Bowen and Hannah Kaye

Synopsis

Increased funding and political support for efforts to control malaria have resulted in dramatic declines in related morbidity and mortality. These gains are fragile, however, and could be reversed if success slows momentum.

The U.S. government has played an enhanced leadership role in this effort since 2005, when President George W. Bush created the President’s Malaria Initiative and enhanced contributions to the Global Fund. The Obama administration has increased support for both of these programs. Alongside the government, U.S.-based entities, including private companies, nonprofit organizations, and philanthropic institutions, have provided critical funding, innovation, and expertise.

Financial and programmatic continuity are required for ongoing progress, along with new efforts to maximize use of existing interventions and develop necessary new tools. Bed nets used for malaria prevention last only three years and must be replaced. Rapid, inexpensive diagnostic tests must be used more consistently to confirm suspected malaria cases and avoid overuse of antimalarial drugs. Lack of regulatory and enforcement capacity must be addressed to reduce availability of counterfeit and substandard medicines. Emerging drug and insecticide resistance (and the current lack of second-line options) threaten future progress, and strategies and technical expertise for tracking, containing, and responding to resistance are essential.

To reflect current realities and complexities, strategies and success metrics will have to emphasize solidifying progress rather than the rapid case decreases measured a decade ago. Programmatic improvements including enhanced surveillance capacity; greater availability, accessibility, and affordability of medicines and diagnostics; and increased attention to border areas and highly vulnerable populations are needed alongside innovative, sustained funding and new partnerships. Malaria investments will also have to balance existing needs with the urgency of developing tools for the future.

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Introduction

Malaria, an infectious mosquito-borne disease, has afflicted humanity since before the dawn of history. Infected people initially experience fever, chills, and flu-like illness; without treatment, their symptoms can intensify to anemia, organ failure, cerebral edema, and death. In 2010 there were an estimated 219 million cases of malaria per year and 660,000 fatalities; 91 percent of these fatalities were in sub-Saharan Africa. The disease remains one of the biggest killers of children under five.

Beyond the health challenge and devastating loss of life, malaria poses a serious obstacle to stability and economic growth. Africa is estimated to lose at least $12 billion per year due to the direct costs of malaria, but indirectly loses much more: Malaria is a leading cause of school absence, and a 2005 survey found that nearly three-quarters of companies in Africa reported that malaria was negatively affecting their business. Even though simple, effective tools exist to prevent and treat the disease, it absorbs 40 percent of health-system capacity. A group of African military leaders recently concluded that malaria is the number-one concern for their troops, many of whom are involved in peacekeeping. Malaria’s impact is thus severe for societies and human security as a whole.

Over the past decade, governments, the private sector, nonprofit organizations, faith-based organizations, and other entities have significantly increased efforts on malaria control, using a suite of interventions that include long-lasting insecticide-treated nets (LLINs), indoor residual spraying (IRS), intermittent preventive treatment for pregnant women (IPTp), and artemisinin combination therapies (ACTs). These efforts have shown that progress can be swift and cost-effective: after significant scale-up of programs funded in large part by the United States and other international donors, estimated malaria deaths dropped from 755,000 annually in 2000 to 660,000 in

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4. One example of this finding is from the World Malaria Report 2012, xiii, which notes that “Malaria is strongly associated with poverty. Estimated malaria mortality rates are highest in countries with a lower GNI per capita.”
10. An ACT is a medication in which a compound derived from the Chinese wormwood, Artemisia annua, is combined with a drug from a different class, such as lumefantrine or mefloquine.
2010\textsuperscript{11} (see Figure 1). The WHO estimates that, without these investments, if the malaria incidence and mortality rates estimated for 2000 had remained unchanged over the decade, 274 million more cases and 1.1 million more deaths would have occurred between 2001 and 2010.\textsuperscript{12}

Today, 36 of the 99 remaining endemic countries are moving from controlled low-endemic malaria to elimination, though only four of these countries are in Africa.\textsuperscript{13} Investing in malaria is bringing benefits far beyond health improvements. A 2011 study found that companies achieved a 28 percent return\textsuperscript{14} when investing in malaria prevention programs for their employees, with a 94 percent reduction in malaria-related work absence.\textsuperscript{15} An increasing range of companies, particularly in the oil and gas production, mining, and consumer goods sectors, are recognizing the need to invest in malaria control, not only as a humanitarian priority but as a business decision, and are making significant contributions to the fight.

Yet, these gains are still fragile. Status quo program implementation, lack of research and development, emerging drug and insecticide resistance, and reduced resources could all contribute to a dramatic reversal in the progress that has been achieved so far, with devastating consequences. A renewed commitment to malaria could support even more progress toward elimination and, ultimately, eradication. The growing list of countries advancing through pre-elimination and elimination stages demonstrates that this achievement is possible, despite the challenges.

\begin{figure}
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\includegraphics[width=\textwidth]{malaria_deaths.png}
\caption{Global Malaria Deaths (in thousands) \textit{Source: World Malaria Report 2011/12}}
\end{figure}

\textsuperscript{11} World Health Organization, \textit{World Malaria Report 2011}.
\textsuperscript{12} World Health Organization, \textit{World Malaria Report 2012}, ix.
\textsuperscript{14} Roll Back Malaria Partnership, \textit{Business Investing in Malaria Control: Economic Returns and a Healthy Workforce for Africa}, 9.
\textsuperscript{15} Ibid.
Policy Developments under the First Obama Administration

The United States has long viewed malaria control as in the national interest. Indeed, the Centers for Disease Control and Prevention (CDC) was originally established to fight malaria in the United States.16

In 2005, recognizing the strategic value of global reductions in malaria, President George W. Bush launched the President’s Malaria Initiative (PMI), an interagency effort housed at USAID, co-implemented with CDC, and carried out in partnership with DOD, NIH, and other agencies, through which the U.S. government substantially increased its focus on malaria control.

With bipartisan congressional support, PMI has grown from $30 million and 15 countries in FY 2006 to a peak of $650 million in FY 201217 and 19 countries.18 The Obama administration has set ambitious targets for future success. PMI has now been directed to “achieve Africa-wide impact by halving the burden of malaria in 70 percent of at-risk populations in sub-Saharan Africa.”19

An independent, external evaluation of PMI’s first five years concluded that PMI “quickly reoriented a problematic U.S. government malaria program, took it to a large scale quickly, efficiently, and effectively complemented the larger global malaria program, and contributed to the reduction in child mortality.”20

The Obama administration has also supported the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM). In 2012, the GFATM funded an estimated 40 percent of global malaria programs worldwide,21 with the U.S. government providing nearly 25 percent of its funding and actively engaging in programmatic and governance reforms. Funding levels for the GFATM have risen since FY 2007, reaching $1.3 billion in FY 2012—a significant increase in a climate of fiscal austerity.

All these initiatives are part of the overarching Global Health Initiative, begun by the Obama administration in 2009 as an effort to coordinate sometimes-disparate global health programs to maximize their impact around a theme of improving maternal and child health. Although the administrative structure of the Global Health Initiative has changed since its inception, it remains a conceptual framework for the administration’s global health efforts.

Ongoing Challenges

The successes in combating malaria these past 10 years have resulted in a profoundly changed landscape—one that holds great promise, but also peril. Just as the results of successful antimalarial efforts are quickly apparent, so are the costs of backsliding. Successful efforts to control malaria

19. Ibid., 3.
20. Ibid., 4.
give rise to an increasing population of people in formerly malaria-endemic areas who have little exposure to the disease, and thus have little or no malaria resistance. If malaria returns to these areas, these malaria-naïve populations are at extreme risk for illness and death.

When countries deprioritize malaria control after a period of success, the disease’s rebound can be swift and severe. For example, WHO cut funding and staff from its malaria control program in Swaziland after the country had all but eliminated malaria in the late 1950s, and epidemics soon followed. India, Sri Lanka, and Zanzibar also experienced surges in malaria after donor funding was withdrawn.

**A Changed Landscape, New Challenges.** In many ways, today’s most pressing anti-malaria challenges are the by-products of success.

For example, only 3 percent of African households owned insecticide-treated bed nets in 2000; but thanks to mass distribution campaigns, nearly 53 percent do so today. These nets do not provide permanent protection, since the insecticide loses potency within three to four years, and nets themselves can get worn out, ripped, or torn sooner. As a consequence, millions of LLINs must be replaced, now or very soon.

Programs must now grapple with how to replace worn-out nets without incurring the unnecessary cost of replacing nets that still function. Particularly as countries achieve national progress, donors and affected countries alike will need to focus on improvements in subnational pockets/regions not performing as well as the nation as a whole. Addressing these areas of persistent challenge may involve additional attention to issues such as cross-border transmission, vulnerable populations, delivery bottlenecks, and lack of health workers.

The effectiveness of malaria drugs and insecticides is also under pressure as resistance emerges to the relatively few approved products for treatment. All of the ACTs recommended by WHO rely on the same key ingredient, artemisinin, and only one class of insecticide, pyrethroids, is approved for use in LLINs. Four classes of insecticides are approved for indoor residual spraying, but pyrethroids are the safest, most effective, and least expensive, and thus used in the majority of IRS programs, including those in the highest-burden areas.

In recent years, several worrying forms of resistance have emerged, which could cripple programmatic effectiveness, drive up costs, and reverse global progress: resistance of the malaria

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23. Ibid., 3.
26. Ibid., 41.
29. Wilson and Aizenman, “Value for Money in Malaria Programming,” 42. Also note an interesting example: KwaZulu-Natal switched from DDT to deltamethrin for IRS in 1996, causing malaria rates to rise fourfold over four years; when studies showed local resistance, the program switched back and experienced a 91 percent drop in malaria cases, 41–42 citing 94, 5, 96.
parasites to artemisinin has been found in limited areas within four countries in Southeast Asia so far; and resistance of the malaria vector (mosquitoes) to the insecticides approved for public health programs has been identified in 64 countries with ongoing malaria transmission.

While progress is being made against *Plasmodium falciparum*, one species of the malaria-causing parasite, attention is also needed on *Plasmodium vivax*, another species associated with high morbidity and which, unlike *P. falciparum*, has a dormant stage in the human liver that can shelter it from antimalarial drugs, and can cause recurring bouts of disease in infected individuals.

**Quality and Surveillance.** One factor contributing to drug and insecticide resistance is a lack of surveillance and enforcement capacity to ensure that cases are tracked and reported. The WHO has banned artemisinin monotherapies (i.e., those that lack the additional active elements found in combination treatments) since 2007, because these drugs have limited efficacy and build resistance to artemisinin, but as late as November 2012, 16 countries were still allowing use of these products, and 28 pharmaceutical companies were manufacturing them. Low-quality or counterfeit drugs also reach markets, and few affected countries have adequate capacity to regulate, monitor, and enforce quality standards.

In addition to ensuring the quality of antimalarial commodities, in-country programs also face the challenge of adequate training and monitoring for those prescribing and using drugs. Many practitioners and patients still treat malaria preemptively, based on the appearance of symptoms before diagnosis. In 2010, the WHO recommended that all suspected malaria cases be confirmed prior to treatment. Though the proportion of suspected malaria cases receiving a diagnostic in the public sector increased in much of Africa from 20 percent in 2005 to 47 percent in 2011 and globally from 68 percent to 77 percent, many fevers are still treated preemptively and diagnostic testing appears to be less available in the private sector than in the public sector. This can lead to overuse of malaria drugs, as well as improper treatment for patients with non-malaria fever cases such as pneumonia. Better use of diagnostics could also have cost implications, as the need for malaria treatment would be dramatically reduced if all suspected cases were tested and only confirmed cases treated with antimalarial drugs.

Finally, the need to develop and integrate new tools has taken on new urgency. The interventions developed to combat malaria are effective and low-cost, but all treatments eventually lose effectiveness as diseases and vectors adapt to them. Enhancing diagnostic capacity, in addition to meeting the urgent need for the development of new drugs, will be essential to progress, by ensuring that the potency of antimalarial drugs is not squandered through misuse.

An effective malaria vaccine would be a key addition to the set of interventions used to combat malaria, but it has proven an elusive goal. After decades of unrealized hopes, a partnership consisting of GlaxoSmithKline, PATH (with funding from the Bill & Melinda Gates Foundation), and 11 African research centers is now testing the RTS,S vaccine candidate in a large-scale clinical trial. Results published in 2011 showed a 50 percent reduction in malaria cases over one year among toddlers enrolled in the trial. Later results for a younger cohort in the same trial, however, showed that the vaccine was somewhat less efficacious, reducing the number of cases by approximately one-third for this group. Further trial results, expected in 2014, will be essential in determining whether RTS,S can make a major contribution to malaria control.

Policy Recommendations

1. Improve the use of rapid diagnostics for case management.

Diagnosis of malaria has historically been complicated and slow, and with a high prevalence of the disease, presumptive treatment was standard. As malaria rates fall, however, and patients’ fevers are less likely to be caused by malaria, it is important to treat only confirmed malaria cases so that patients receive appropriate treatment and antimalarials are not overused.

Now, researchers have developed cheap, easy-to-use, rapid diagnostic tests (RDTs) that detect true malaria cases. In 2005, fewer than 200,000 RDTs were in use, but by 2011, that number had skyrocketed to more than 50 million. Continuing to improve use of RDTs remains essential, particularly in areas that have significantly reduced their malaria burden and where rates of over-treatment are consequently likely to be high. More diagnostics are needed at the community health worker level in particular, along with training and policies to ensure they are used properly.

Beyond expanding access to diagnostics, the PMI should improve support for efficient, strategic case management to ensure that patients presenting with fevers not caused by malaria receive appropriate treatment. It is estimated that current malaria surveillance systems detect only around 10 percent of the estimated global number of cases. Enhanced surveillance is thus a critical component of case management, and PMI should work with other donors and partners to develop consistent standards for identifying malaria cases to improve completeness and consistency of reporting that can be used to better design and carry out programs.

2. Innovate finance to stretch available resources.

In an era of fiscal constraints, creative approaches to financing take on special importance. New sources of funds, such as service fees on airline tickets or financial transactions, are beyond the scope of this paper, but the high risk of resurgence over the next few years has spurred an urgent need to do more with less. New approaches to financing, both at the global and national levels, are needed to help address funding gaps in the short- and medium-term that threaten the gains of recent years. As its major funder, the United States should work closely with the World Bank to help formulate new mechanisms, such as a “malaria bond” or performance-based forgivable loans. The United States should also support efforts to catalyze country-generated financing, and work with the World Bank, private sector, and affected countries to incentivize affected countries

39. Ibid., v and 51.
40. Ibid., 51.
to consolidate and expand upon hard-won progress against malaria. Such mechanisms could have the additional benefit of providing smoother and more predictable funding flows that are important for adequate program planning.

3. Adapt to reflect the changing malaria-control landscape.

The landscape of malaria control has changed markedly in a decade, with widespread deployment of malaria interventions, new tools, and a changed profile of the epidemic. These changes require similar adjustments in the ways the United States fights the disease.

One aspect of this adjustment is the need for new measures of success. Measuring success on more than just reducing the number of cases will help ensure that funding rewards countries that are excelling not only at initial control but in maintaining their gains. When the global scale-up in malaria control began, the burden was so high that programs necessarily focused on case reduction. Where countries are at high risk of disease resurgence or where the risk of spreading resistance is elevated, funding decisions should also take into account measures such as maintenance of low case burden to ensure that gains are consolidated. The U.S. government, acting through its representative on the GFATM Board, should ensure that GFATM properly takes into account these measures as the Fund implements a sweeping reform of its grant structure. In addition, funding allocations for countries should also consider risks of cross-border transmission, or special risks in subnational regions. Finally, new research should focus on the best ways to combat \textit{P. vivax}, as this species assumes greater importance in the epidemic.

4. Invest in future success.

To improve outcomes and avoid resistance, new tools, methods, and combinations of interventions must be developed and brought to scale. Federal agencies conducting malaria research should ensure that their research portfolios take into account the changing landscape of the malaria epidemic, particularly the acute need for better strategies and tools to contain drug and insecticide resistance. It will also be important to urge coordination and cooperation across sectors; for example, research sharing with the agricultural sector could enhance efforts to develop new insecticides without excessive additional cost.

5. Strengthen safeguards against substandard products.

PMI continues to prioritize efforts within its programs to ensure that substandard or counterfeit drugs do not enter the malaria commodity supply chain. Despite reductions in the number of manufacturers marketing monotherapies, substandard and counterfeit drugs continue to put patients at risk and increase the risk of resistance. The Obama administration should make it a priority to raise these issues in bilateral diplomatic talks with the manufacturing country of the origin's government. The United States can also enhance its work with the international global health, development, and diplomatic community to strengthen partner countries’ drug regulatory and enforcement regimes through governance programs. To assist in this effort, the administration should provide adequate support to improve the capacity of the Food and Drug Administration and other agencies to provide technical assistance to aid such efforts. Just as important is renewed effort to ensure that malaria-endemic countries no longer permit the sale of monotherapies. Ultimately, the continued allowance of such sales should be taken into account in determining funding allocations.
While drug quality has rightly attracted significant attention from policymakers, the need to ensure the quality of LLINs should not be overlooked. PMI should continue to stress best value (i.e., a measure that properly takes into account cost per year of effective protection) in addition to up-front cost, in its procurement decisions, and work with the GFATM to see that these quality criteria are broadly adopted.

Conclusion

U.S. leadership—political, financial, and technical—has made possible a decade of dramatic progress against malaria, and enabled opportunities for economic growth, stability, and education that had previously been limited by the ravages of this devastating disease. All government partners in the PMI initiative have contributed unique strengths in program support, research, and capacity development that have been leveraged for even higher impact by the decision to invest the U.S. global malaria coordinator with the clear authority to lead the U.S. malaria effort.

With creative approaches to ensuring drug quality, proper use of diagnostics, and sustained financial and political commitment from governments, communities, and industry alike, the United States can ensure this success continues—and usher in the day when malaria no longer threatens or obstructs human health and development around the world.

For Additional Information:

- Roll Back Malaria: www.rbm.who.int
- President’s Malaria Initiative: www.pmi.gov
- Malaria No More: www.malarianomore.org