Malaria Elimination and Eradication

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INTRODUCTION

The world has made tremendous progress in the fight against malaria in the past 15 years. According to the *World Malaria Report*, malaria case incidence was reduced by 41 percent and malaria mortality rates were reduced by 62 percent between 2000 and 2015 (WHO 2016c). At the beginning of 2016, malaria was considered to be endemic in 91 countries and territories, down from 108 in 2000.

Despite this progress, malaria continues to place a heavy toll on the world. In 2015, 212 million cases occurred globally, leading to 429,000 deaths, most of which occurred in children under age five years in Africa. These estimates are likely to be conservative, as adult deaths from malaria might well be underestimated in Africa and India (Adjuik and others 2006; Bawah and Binka 2007; Dhingra and others 2010; Gupta and Chowdhury 2014).

More than 100 countries have eliminated malaria in the past century. Of the 106 countries with ongoing transmission in 2000, 57 reduced malaria incidence more than 75 percent by 2015, in line with the World Health Assembly target for 2015 of reducing the malaria burden by 75 percent. An additional 18 countries reduced incidence by more than 50 percent (WHO 2015e), also achieving target 6C of the Millennium Development Goals, which called for

halting and beginning to reverse the global incidence of malaria by 2015.

An increasing number of countries are moving toward the elimination of malaria. Since 2000, 12 countries have eliminated malaria; 4 were certified as malaria free by the World Health Organization (WHO) between 2007 and 2013 (Armenia, Morocco, Turkmenistan, and the United Arab Emirates); an additional 8 moved into the WHO's prevention-of-reintroduction phase after sustaining at least three years of zero local malaria transmission (Argentina, the Arab Republic of Egypt, Iraq, Georgia, the Kyrgyz Republic, Oman, the Syrian Arab Republic, and Uzbekistan); and 5 interrupted local transmission (Azerbaijan, Costa Rica, Paraguay, Sri Lanka,[1] and Turkey). The WHO European Region reported zero indigenous cases for the first time in 2015, in line with the goal of the Tashkent Declaration to eliminate malaria from the region by 2015.

According to the WHO (2016a), an additional 21 countries are in a position to achieve at least one year of zero indigenous cases of malaria by 2020.[2] These dramatic declines can be attributed to the scale-up of effective malaria control tools and technologies coupled with renewed political leadership and financial commitment.

Bolstered by these successes, most national malaria programs now consider elimination to be an

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Table 12.1 Global Milestones and Targets for Elimination

Goal	Milestones		Target
	2020	**2025**	**2030**
Reduce malaria mortality rates globally compared with 2015.	At least 40%	At least 75%	At least 90%
Reduce malaria case incidence globally compared with 2015.	At least 40%	At least 75%	At least 90%
Eliminate malaria from countries in which malaria was transmitted in 2015.	At least 10 countries	At least 20 countries	At least 35 countries
Prevent reestablishment of malaria in all countries that are malaria free.	Reestablishment prevented	Reestablishment prevented	Reestablishment prevented

Sources: RBM Partnership 2015; WHO 2015a.

attainable goal, and the idea of eradication is once again on the global health agenda. Many countries have developed national elimination goals, and regional networks have been formed to facilitate collaboration (Newby and others 2016). Leaders from the Asia Pacific Leaders Malaria Alliance and the African Leaders Malaria Alliance endorsed regional goals for malaria elimination by 2030 in November 2014 and January 2015, respectively, galvanizing support for elimination and eradication (APLMA 2015; United Nations 2015).

In this context, two new global malaria policy and advocacy documents supporting elimination and eradication were released in 2015: the Roll Back Malaria (RBM) Partnership's *Action and Investment to Defeat Malaria 2016–2030* and the WHO's *Global Technical Strategy for Malaria 2016–2030*. The *Global Technical Strategy* (GTS), which the WHO ratified in May 2015, calls for at least another 40 percent reduction in malaria-related mortality and morbidity between 2015 and 2020. Other goals and targets are illustrated in table 12.1. A third document, launched in September 2015, *From Aspiration to Action: What Will It Take to End Malaria?*, outlines the resources and strategies needed for global eradication by 2040, calling by 2020 commit to eradication in the next five years (Gates and Chambers 2015).

Despite these advances, malaria elimination and eradication face significant technical, operational, and financial challenges. About 3.2 billion people remain at risk of malaria; in 2015 alone, there were an estimated 214 million new cases of malaria and more than 400,000 malaria-related deaths. Global progress in malaria control and elimination is marked by vast disparities between and within countries, with vulnerable groups that have poor access to health services continuing to be marginalized. The Sub-Saharan Africa region shoulders the heaviest burden, with two countries—the

Democratic Republic of Congo and Nigeria—accounting for more than 35 percent of global malaria deaths. In these areas, malaria control programs aim to maximize the reduction of malaria cases and deaths; elimination will likely require more potent tools and stronger health systems.

A few countries that have successfully reduced malaria transmission are struggling to maintain their gains. An increased number of cases has recently been reported from a number of countries, including Cambodia, Djibouti, Madagascar, Uganda, and República Bolivariana de Venezuela (WHO 2015e). Furthermore, as the global malaria burden declines, emerging biological threats have the potential to critically weaken malaria responses in several parts of the world. In 2014, 60 countries reported resistance of mosquitoes to at least one insecticide used in vector control strategies; resistance of parasites to artemisinin, the cornerstone of malaria chemotherapy, has been detected in five countries in the Greater Mekong subregion, posing a serious threat to global health security.

This chapter summarizes the literature on malaria elimination; describes the progress made; and discusses malaria epidemiology, interventions, and challenges. In addition, it presents empirical information on financing and economics, including cost information from various settings. It concludes with a discussion of the economic basis for eradication and recommendations for research.

WHAT ARE ELIMINATION AND ERADICATION?

In areas of moderate to high transmission that are implementing malaria control, interventions are deployed on a large scale to reduce the public health burden of the disease. In elimination settings, targeted interventions

aim to interrupt local transmission in the specific places where it becomes increasingly concentrated, that is, small geographic areas or special subpopulations that may be harder and costlier to reach. The key decisions facing policy makers in low- and moderate-transmission settings are when to embark on malaria elimination (Sabot and others 2010); which interventions to implement and where and when; and at what levels of intensity and reach. Critical to this debate are the political and financial commitments that are needed long after the disease stops being a public health burden.

Malaria elimination involves stopping indigenous transmission through active control measures (Cohen and others 2010; Smith and others 2009). The complete absence of local incidence is very unlikely to be achieved in places with high intrinsic potential for transmission and elevated importation of cases (Cohen and others 2010). For example, even the United States, a relatively low transmission risk area, identified 156 locally acquired cases between 1957 and 2003 (Filler and others 2006). Even countries that do not contiguously border endemic neighbors experience considerable importation annually: Sri Lanka reported 49 confirmed imported malaria cases in 2014, and in Tanzania, Zanzibar's estimated importation of 1.6 cases per 1,000 residents could potentially produce 1,300 incident cases (Le Menach and others 2011). Transmission from imported cases may lead to first degree *introduced* cases; a second degree of transmission from an introduced case produces an *indigenous* case: both are products of *local* transmission. Elimination accordingly requires preventing all indigenous cases, but introduced cases may continue to occur sporadically.

As more countries and regions eliminate malaria and implement measures to prevent reintroduction, fewer imported infections will occur, and eradication will become increasingly feasible. See box 12.1 for the WHO definitions of control, elimination, and eradication.

Box 12.1

Definitions of Control, Elimination, and Eradication

The path to malaria-free status is characterized by four distinct programmatic phases: control, pre-elimination, elimination, and prevention of reintroduction. The terms *elimination* and *eradication* are often used interchangeably. For example, *eradication* was previously used to describe what is now defined as elimination (Feachem and others 2010). To compare programs across these phases, it is important to adhere to agreed-upon terms and definitions.

Malaria control is the reduction of disease incidence, prevalence, morbidity, or mortality to a locally acceptable level as a result of deliberate efforts. Continued intervention is required to sustain control.

Malaria elimination is the interruption of local transmission (that is, reducing the rate of malaria cases to zero) of a specified parasite in a defined geographic area. Continued measures are required to prevent the reestablishment of transmission.

WHO certification of elimination[a] is the WHO certification of a country's malaria-free status. It confirms to the international community that the country, at that time, has halted local transmission of malaria by *Anopheles* mosquitoes and has created an adequate system for preventing reestablishment of the disease. The WHO grants this certification when a country has proved, beyond reasonable doubt, that the chain of local malaria transmission by *Anopheles* mosquitoes has been interrupted nationwide for at least three consecutive years. Certification of malaria elimination is managed by the WHO Global Malaria Programme. The process is voluntary and can be initiated only after a country has submitted an official request to the WHO. The burden of proof falls on the country requesting certification. The final decision on granting a certification of malaria elimination rests with the WHO director-general.

Malaria eradication is a permanent reduction to zero of the worldwide incidence of infection caused by human malaria parasites as a result of deliberate efforts. Once eradication has been achieved, intervention measures would no longer be needed.

Source: WHO 2016a.
a. Since the early 1960s, the WHO has maintained an official register of areas where malaria elimination has been achieved. The WHO also maintains a supplementary list to the official register, listing countries where malaria never existed or disappeared years or decades ago and where full WHO certification of malaria elimination is not needed. The first supplementary list was published in 1963 and included 23 countries. The most recent list was published in 2012 and included 62 countries (WHO 2012d).

PROGRESS TOWARD MALARIA ELIMINATION

Elimination in the Twentieth Century

Until the mid-nineteenth century, malaria was endemic in most countries across the globe. Countries that did not have malaria included the Pacific islands east of the longitude of Vanuatu (the Buxton line) (Mendis and others 2009), which have no *Anopheles* mosquitoes; or countries that were too high in elevation or too cold in temperature (map 12.1).

Between 1900 and 1945, only nine countries in Europe eliminated malaria (Feachem, Phillips, and Targett 2009). Sparked by the availability of chloroquine for treatment and dichloro-diphenyl-trichloroethane (DDT) for vector control, the WHO launched the Global Malaria Eradication Program (GMEP) in 1955 to interrupt transmission in all endemic areas outside of Africa (Najera 1999). The program relied on vector control—mainly indoor residual spraying—and systematic detection and treatment of cases. The campaign succeeded in eliminating malaria in 37 of the 143 countries or economies where it was endemic in 1950 (Wernsdorfer and Kouznetzov 1980), including some lower-income areas with tropical climates such as Maldives; Mauritius; Réunion; Taiwan, China; much of the Caribbean; Brunei Darussalam; most of China; Hong Kong SAR, China; Singapore (Feachem and others 2010).[3] In many other countries, the burden of disease and deaths from malaria was greatly reduced. For example, in India, the number of malaria cases declined from an estimated 110 million in 1955 to fewer than 1 million in 1968, and in Sri Lanka, the incidence of malaria declined from an estimated 2.8 million cases in 1946 to just 18 cases in 1966 (Mendis and others 2009).

However, failure to sustain strong funding for the program, particularly in the face of increasing costs due to mounting drug and insecticide resistance, led to the effective end of the GMEP in 1969 (WHO 1969) when the World Health Assembly recommended that countries not yet ready for "eradication" focus on controlling malaria as a first step toward the ultimate goal of getting rid of malaria altogether. Multilateral agencies withdrew their support for malaria programs in favor of general health programs. In the ensuing years, although most countries that had eliminated malaria continued to remain malaria free, the scaling back of control efforts in malarious countries led to a global resurgence of the disease during the 1970s and 1980s and a complete reversal of progress in some countries, such as Sri Lanka and Pakistan (Abeyasinghe and others 2012; Cohen and others 2012).

The experience of the GMEP provides critical lessons for contemporary elimination programs about the need to maintain vigilance and sustain investments during the latter stages of elimination efforts.

Elimination in the Twenty-First Century

The adoption of the Global Malaria Control Strategy in 1992 (WHO 1993) and the launch of the Roll Back Malaria initiative in 1998 (Nabarro and Taylor 1998) stimulated increased interest and financial investment in malaria control. Increased investment in research and development resulted in highly effective malaria control tools—notably, long-lasting insecticide-treated nets (LLINs), rapid diagnostic tests, and artemisinin-based combination therapies (ACTs). The creation of the Global Fund to Fight AIDS, Tuberculosis, and Malaria; the President's Malaria Initiative; and other financing mechanisms allowed for the wide-scale deployment of these new tools. The first Global Malaria Action Plan for a malaria-free world 2008–2015 served as a valuable guide for countries and partners to mobilize resources. Between 2005 and 2014, global investment for malaria control increased from US$960 million to US$2.5 billion annually, leading to dramatic declines in the global malaria burden and rapid shrinking of the malaria map. With the end of the Millennium Development Goals in 2015 and the transition to the era of the Sustainable Development Goals, the malaria community has once again committed to the vision of a malaria-free world.

Table 12.2 summarizes the countries and territories that eliminated malaria between 1900 and 2015.

Currently 35 countries are moving from low-endemic malaria to elimination (Newby and others 2016). These countries fit into one of two categories: (1) countries that have assessed the feasibility of elimination, declared a national evidence-based goal, and launched a malaria elimination strategy; or (2) those that are strongly considering an evidence-based national elimination goal as determined by expert opinion, have made substantial progress in spatially progressive elimination (by eliminating malaria from specific islands or geographic areas), and are greatly reducing malaria nationwide. These 35 countries have elimination goals ranging from 2013 to 2035, with the majority aiming for, and likely to achieve, elimination by 2020 (annex 12A).
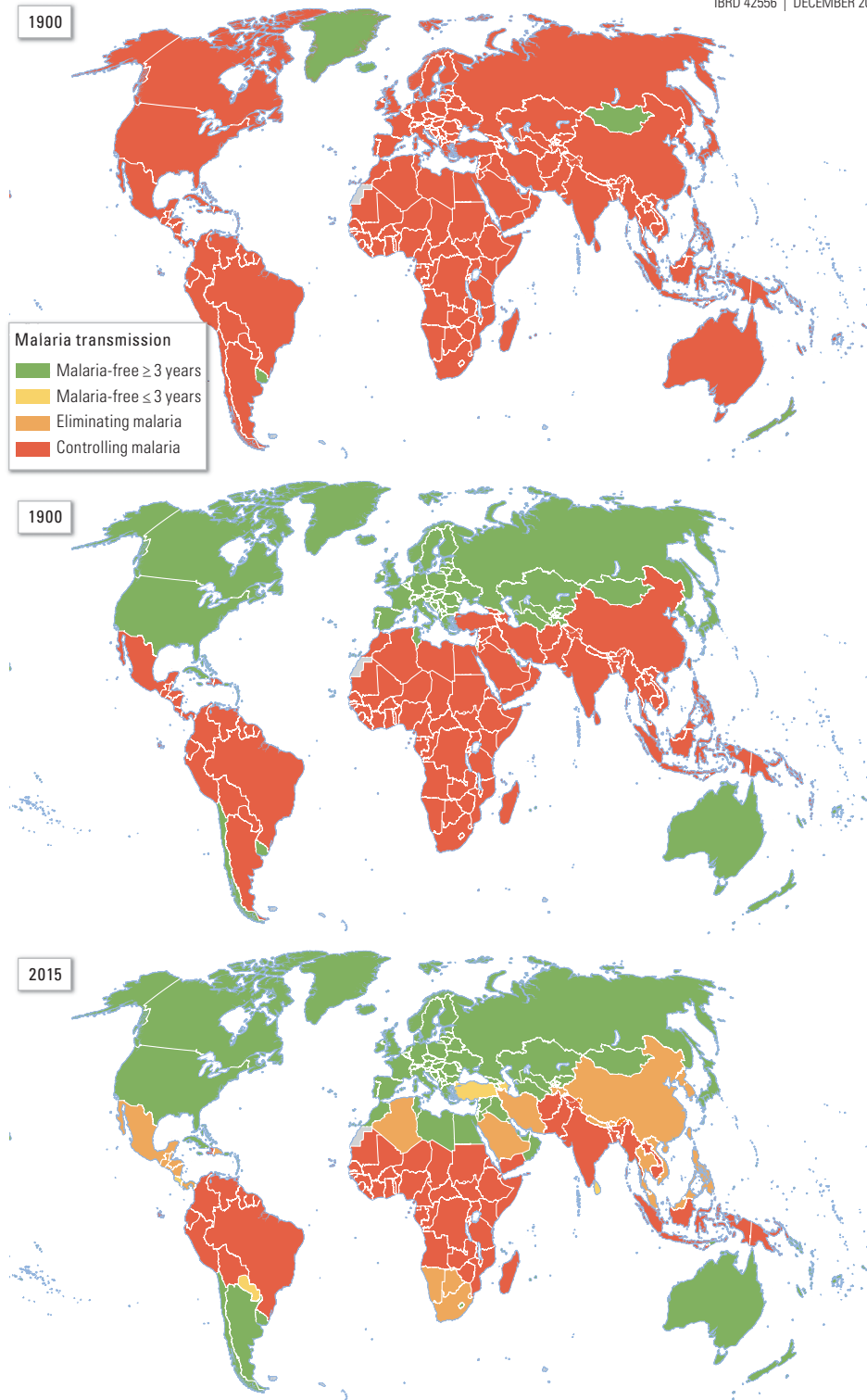
Five countries—Argentina, the Kyrgyz Republic, Paraguay, Sri Lanka, and Uzbekistan—recently achieved three consecutive years of zero local transmission. All but Uzbekistan have initiated the WHO process for malaria-free certification. Three other countries have achieved zero local transmission but have not yet sustained it for three consecutive years: Azerbaijan, Costa Rica, and Turkey.

Lessons Learned and Planning for Success

Lessons learned from the GMEP highlight the fact that a single strategy is unlikely to be successful everywhere

Map 12.1 Malaria Transmission Worldwide, 1900, 1990, and 2015

1900

Malaria transmission
- Malaria-free ≥ 3 years
- Malaria-free ≤ 3 years
- Eliminating malaria
- Controlling malaria

1900

2015

Source: Global Health Group 2016, unpublished data.

given the complexities of malaria transmission systems, and given that a long-term commitment with a flexible strategy that includes community involvement, integration with health systems, and the development of agile surveillance systems with supporting infrastructure is needed (Najera, Gonzalez-Silva, and Alonso 2011). A review conducted at the GMEP's conclusion cited the lack of robust assessments to determine the feasibility of malaria eradication programs (WHO 1968; see box 12.2), including an assessment of the technical and operational evidence and government commitment to sustain funding. Attempting to eliminate malaria before it is feasible to do so can raise expectations, damage the credibility of the public health sector (Moonen and

others 2009), and require prolonged expenditure (Sabot and others 2010). Reducing transmission without sufficiently sustainable interventions to maintain those reductions may also lead to epidemics and resurgence. Out of 49 discontinued programs during GMEP, resurgence was reported in 36 programs following cessation, usually because of an inability to maintain sufficient financial resources (Cohen and others 2012). Countries should assess the technical, operational, and financial feasibility of achieving their goals (discussed further in the section titled Prospects for Malaria Eradication) before embarking on a costly restructuring of their programs (Moonen, Cohen, Tatem, and others 2010; WHO 2014a).

Table 12.2 Number of Countries and Territories That Eliminated Malaria, by Region, 1900–2015

Indicator	Americas and Caribbean	South Asia and East Asia and Pacific	Europe and Central Asia	Middle East and North Africa	Sub-Saharan Africa	Total
Total number of countries	46	39	58	23	45	211
Malaria free						
1900	2	13	3	1	1	20
1900–49	0	0	9	0	0	9
1950–78	23	5	35	4	1	68
1979–90	0	1	2	2	1	6
1991–2015	2	1	9	6	0	18
Total number of malaria-free countries	27	20	58	13	3	121

Box 12.2

Challenges to Elimination: Select Examples

Despite the recent successes in eliminating malaria, challenges remain. The following discussion highlights these challenges and provides examples of some actions taken to overcome them:

- *Lack of sustained funding.* India implemented a widely successful program through DDT spraying that reduced the malaria burden from an estimated 100 million annual cases in the early 1900s to about 100,000 cases in 1965. However,

when U.S. assistance ended, India was unable to maintain its vector control activities. Resurgence over the next decade led to nearly 6 million cases. A key priority identified in India's current *National Framework for Malaria Elimination 2016–2030* is funding its elimination plan with sustained domestic resources and innovative financing models, including cost-sharing partnerships and integration with other government departments (Government of India 2016).[a]

box continues next page

Box 12.2 (continued)

- *Political instability and conflict.* By 1975, malaria was eliminated throughout the former Soviet Union. However, after its collapse in the early 1990s, efforts were disrupted by a lack of funding. Civil wars broke out in several of the former territories, such as Azerbaijan and Tajikistan, contributing to resurgence and reintroduction. Overall strengthening of national health systems and creation of national malaria control programs in 1998 and 1997, respectively, after gaining independence and achieving political stability allowed the malaria situation to be brought under control rapidly in both countries.
- *Weak program vigilance.* Mauritius achieved malaria-free certification in 1973. However, when the program was integrated into preventive health services, the malaria surveillance system was weakened. Vector control activities and screening were reduced, contributing to resurgence associated with an influx of migrant workers. Through the combination of an active surveillance program that screened visitors from malarious areas, an integrated vector management strategy, and a strong health system for detecting and responding to missed cases of imported or introduced malaria, Mauritius has remained malaria free since 1998.
- *Drug and insecticide resistance.* With few replacement options, drug and insecticide resistance is a major threat to elimination. Multidrug resistance emerged and spread rapidly within and outside the Greater Mekong subregion (Cambodia, the Lao People's Democratic Republic, Myanmar, Thailand, Vietnam, and China's Yunnan Province), threatening effective treatment everywhere. In the Greater Mekong subregion, the WHO is leading an urgent, multipartner effort to eliminate *P. falciparum* transmission by 2025.

    At the same time, resistance to pyrethroids, the active ingredients used in insecticide-treated nets, is expanding rapidly in Sub-Saharan Africa. In 2014, 27 countries had reported insecticide resistance (Strode and others 2014). To combat insecticide resistance, the Innovative Vector Control Consortium and UNITAID have recently partnered to improve access to new insecticides for indoor residual spraying in 16 countries across Africa. Their US$65 million Next Generation Indoor Residual Spray Project will work with multiple partners to make alternative insecticides more affordable.
- *Importation.* Four countries in southern Africa—Botswana, Namibia, South Africa, and Swaziland—are seeking to eliminate indigenous transmission within the next five years, but many of their neighbors have much higher malaria burdens. Mobile (moving within a country or coming back from abroad) and migrant (coming from elsewhere into the area) populations are primary sources of imported cases, driving secondary transmission. As a result, the number of cases and deaths between 2012 and 2013 rose in all four countries. Cross-border initiatives are essential to addressing these challenges.

    In September 2015, the Global Fund approved US$17.8 million for the eight countries in southern Africa (Angola, Botswana, Mozambique, Namibia, South Africa, Swaziland, Zambia, and Zimbabwe) termed the "Elimination 8" or "E8," designed to serve as a platform for joint planning, negotiation, and accountability toward a regionally synchronized malaria elimination effort. The main thrust of the E8 regional program is to expand access to early diagnosis and treatment for mobile and underserved populations and to enhance surveillance in the border areas.
- *Weak health systems and program capacity.* The Solomon Islands and Vanuatu have had difficulty maintaining robust malaria elimination programs as a result of weak health systems and limited program capacity to deliver effective diagnosis and treatment to populations in remote areas. Both have experienced periodic spikes in cases that have proved challenging to bring under control.

Sources: Cohen and others 2012; Manguin, Carnevale, and Mouchet 2008; Tatarsky and others 2011.

a. Sustaining domestic and international funding as the malaria burden declines is a serious concern for most malaria-eliminating countries, 15 of which are now upper-middle income and thus no longer eligible for donor funding.

CHALLENGES AND THREATS TO SUCCESS

In contrast to previous attempts at eradication, current efforts explicitly acknowledge that malaria eradication requires a long-term effort incorporating multiple activities and embracing multiple interventions, disciplines, approaches, and organizations. Success will be built largely on a series of effective national and subregional elimination programs, driving global eradication from the bottom up, with countries integrating malaria surveillance, transmission interruption, and treatment programs into their national health systems. Nevertheless, challenges exist.

Eliminating *P. vivax*

In countries where both *P. falciparum* and *P. vivax* are transmitted (mainly outside of Sub-Saharan Africa), as *P. falciparum* malaria declines, the proportion of infections due to *P. vivax* often rises.

P. vivax accounts for more than 70 percent of malaria cases in low-transmission countries (those with fewer than 5,000 cases). Elimination is more difficult for *P. vivax* than for *P. falciparum* because of the presence of persistent liver-stage infections (hypnozoites), the dormant form of the parasite responsible for relapses after months or even years. In addition, gametocytes appear earlier in *P. vivax* than in *P. falciparum*, making onward transmission more likely and more challenging to contain, because eliminating *P. vivax* requires repeated blood-stage treatment or reliable approaches for dealing with the hypnozoite. *P. vivax* therefore persists as the main challenge to malaria elimination, particularly in the late stages.

Despite these difficulties, *P. vivax* has been eliminated in many countries, including China, Mexico, Morocco, Turkey, Turkmenistan, and most recently Sri Lanka, through well-organized deployment of vector control and effective treatment (El Khyari 2001; Shamuradova and others 2012). In 2015, the WHO published a technical brief on the control and elimination of *P. vivax* highlighting the need for international donors and governments to invest in additional measures to control, eliminate, and prevent its reestablishment (WHO 2015c).

Reaching High-Risk Populations

In malaria-eliminating settings, parasite reservoirs are increasingly clustered in high-risk populations or in geographically restricted foci of transmission (Sturrock and others 2013). As transmission decreases, incidence shifts from young children and pregnant women to all age groups, including older children and men. In Asia, this shift is exacerbated by occupational and behavioral risk factors—such as collecting firewood, farming, hunting, or fighting in armed conflict—that put these

groups in contact with infective vectors (Bhumiratana and others 2013; Chuquiyauri and others 2012; Hiwat and others 2012; Ngomane and de Jager 2012; Tobgay, Torres, and Na-Bangchang 2011). Adult men often act as parasite reservoirs, with many low-density asymptomatic infections that, if left untreated and carried for long periods, contribute to seasonal transmission outbreaks and epidemics (Harris and others 2010). High-risk populations, such as ethnic or political minorities or mobile tribes, are also often hard to reach. These groups rarely seek treatment and face substantial barriers to accessing health care, including service delivery, and may be missed by disease surveillance systems (Hiwat and others 2012).

As local transmission declines, the threat of secondary transmission from importation becomes increasingly important. The greatest risk for importation is from travel to and from neighboring or well-connected high-endemic areas (Cohen and others 2012; Tao and others 2011; Tatarsky and others 2011). Knowledge of the dynamics of population migration, both domestic and international, and cross-border transmission is crucial for developing appropriate surveillance and response mechanisms. Researchers have used mobile phone data to infer patterns of human movement (Tatem and others 2014; Wesolowski and others 2012) and identify sources and sinks of transmission; some programs are implementing spatial decision support systems (Le Menach and others 2011; Marston and others 2014; Tatem and others 2014).

In some elimination settings, at a given time many malaria infections either are asymptomatic or cause only minor symptoms (Lindblade and others 2013). Passive surveillance misses those individuals who act as parasite reservoirs that are infectious to mosquitoes, causing onward transmission (Sturrock and others 2013). A substantial proportion of infections may also be subpatent or submicroscopic, that is, the density of parasites is lower than the threshold for detection by microscopy or rapid diagnostic tests. These infections account for 20 percent to 50 percent of all transmission occurrences in low-endemic settings (Mosha and others 2013; Okell and others 2012). Draining this asymptomatic reservoir is thus important for elimination. There is, however, growing certitude that curing all symptomatic infections will automatically shrink this asymptomatic reservoir.
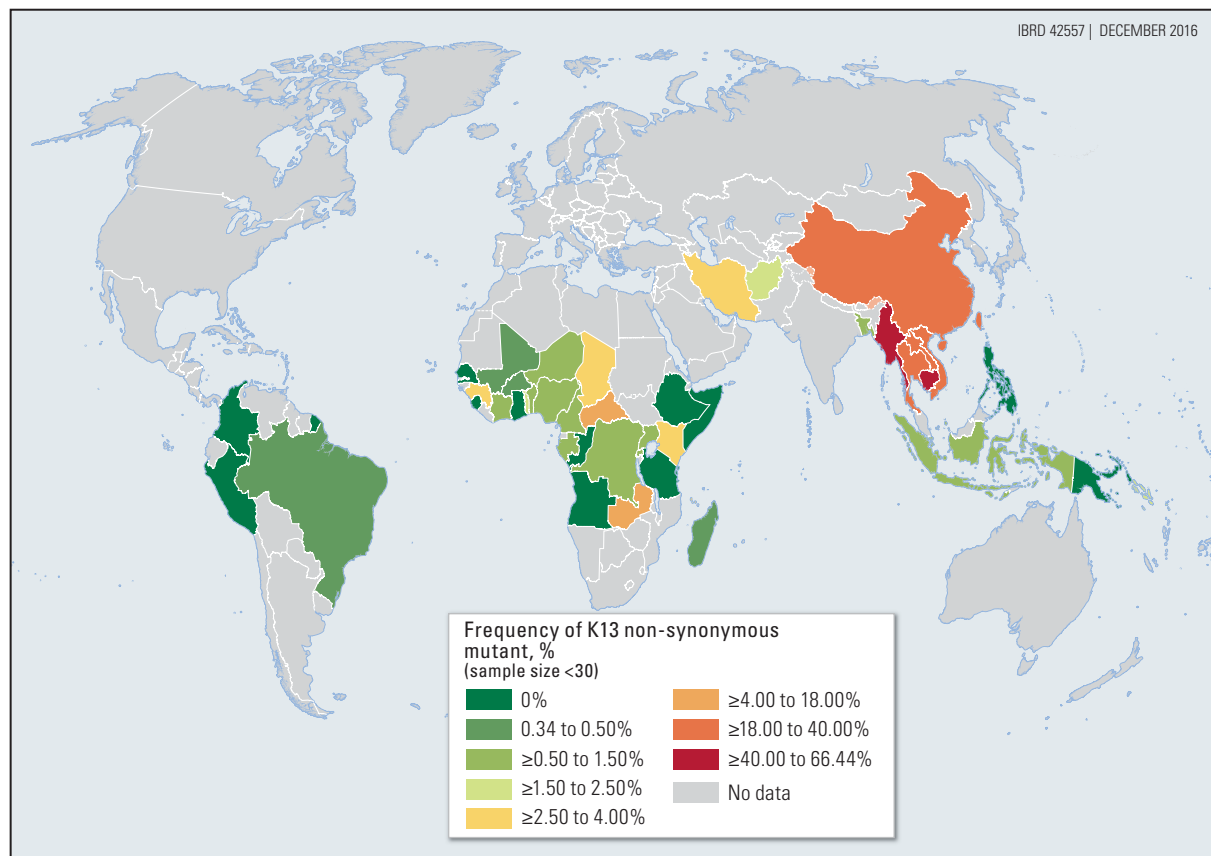
Addressing Artemisinin Resistance

Resistance of parasites to artemisinin derivatives, the mainstay of malaria treatment, is a mounting problem. Delayed parasite clearance times following artemisinin monotherapy or ACT were first detected in Western Cambodia in 2007 and soon after along the Thai-Burmese,

the Thai-Cambodian, and the Cambodian-Vietnamese borders (Carrara and others 2013; Dondorp and others 2009; Hien and others 2012; Phyo and others 2012). *Plasmodium falciparum* artemisinin resistance is evident in five countries in the Greater Mekong subregion (WHO 2015b), most recently in Myanmar, just 25 kilometers from the Indian border (map 12.2). Delayed parasite clearance times are correlated with some specific mutations (580C→Y, 539R→T, 543I→T, 493Y→H, and 446F→I) in the propeller domain of a Kelch protein gene located on chromosome 13 (PF3D7_1343700) (Ariey and others 2014; Straimer and others 2015). K13 mutant parasites associated with artemisinin resistance are currently prevalent throughout mainland South-East Asia from southern Vietnam to central Myanmar (Ashley and others 2014; Ménard and others 2016; Takala-Harrison and others 2015).

This development has major implications for malaria elimination: First, parasites susceptible to artemisinin will be eliminated earliest, and the remaining parasites in low-transmission areas will be resistant and the hardest to kill (Maude and others 2009). Second, artemisinin-resistant parasites are selected for concomitant resistance to ACT partner drugs, resulting in high late-treatment failure rates, as observed in Cambodia with dihydroartemisinin-piperaquine (Amaratunga and others 2016; Duru and others 2015; Leang and others 2013; Leang and others 2015; Lon and others 2014; Saunders and Lon 2016; Spring and others 2015) and along the Thai-Myanmar border with artesunate-mefloquine (Carrara and others 2013). Although innovative compounds with different modes of action are in development, they will not be ready for deployment before 2020 (Wells and Hooft van Huijsduijnen 2015; Wells, Hooft van Huijsduijnen, and Van Voorhis 2015). Therefore, novel strategies and regimens using available antimalarial drugs need to be further evaluated. These strategies may include drug rotation between different ACTs, extension of the three-day ACT course to five or seven days, and the triple combination of artemisinin derivatives with two partner drugs in a three-day therapy.

Map 12.2 Frequency Distribution of the Wild-Type K13 Allele in Asia and Worldwide

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Frequency of K13 non-synonymous mutant, % (sample size <30)
- 0%
- 0.34 to 0.50%
- ≥0.50 to 1.50%
- ≥1.50 to 2.50%
- ≥2.50 to 4.00%
- ≥4.00 to 18.00%
- ≥18.00 to 40.00%
- ≥40.00 to 66.44%
- No data

Source: Ménard and others 2016.

The WHO (2012a, 2015d) has labeled multidrug-resistant malaria in the Greater Mekong subregion as a regional public health disaster with the potential for severe global consequences. In March 2015, the WHO concluded that eliminating malaria in this subregion is the only way to extend the lifespan of artemisinin derivatives as an effective treatment and outlined a strategy for elimination by 2030 (WHO 2015d).

The potential spread of artemisinin resistance poses a substantial risk to global health security and economic development. Widespread resistance could increase global malaria mortality by an estimated 25 percent, with an annual economic impact of more than US$0.5 billion (Lubell and others 2014). These increases in mortality and in costs could undermine years of investments, making the case for preventing the spread of resistance even more compelling. Geospatial and temporal mapping of the emergence and spread of parasite resistance allows policy makers to mobilize resources efficiently and to adopt more efficacious treatment regimens (Ashley and others 2014; Ménard and others 2016; Takala-Harrison and others 2015).

MALARIA ELIMINATION INTERVENTIONS AND STRATEGIES

Elimination and control rely on similar interventions: high-quality case management, vector control, and surveillance. However, while high coverage rates are desirable in control programs, interventions in elimination programs must be highly targeted and tailored, and the right tool needs to be selected according to vector and human behavior (table 12.3). Redistributing resources toward elimination-specific interventions, such as strengthening surveillance systems to identify and investigate transmission foci, may produce economic efficiencies. However, continued investments in enhanced program and managerial capacity are needed.

Table 12.3 Key Differences between Interventions for Malaria Control and Elimination

Indicator	Malaria control	Malaria elimination
Epidemiological setting	High and medium transmission	Low transmission, localized, and seasonal
Population at risk	Entire population(s) considered to be at risk	Populations living in transmission foci, high-risk groups, migrants, and mobile populations
Vector control		
Long-lasting insecticide-treated nets	Widespread coverage	At-risk areas and populations; travelers to endemic areas
Indoor residual spraying	Widespread coverage	At-risk areas and populations
Larval control		
Larviciding	Appropriate in specific circumstances where breeding sites can be identified and regularly targeted; supplement to insecticide-treated nets and indoor residual spraying; may be better suited to urban areas	Appropriate in specific circumstances where breeding sites can be identified and regularly targeted
Environmental management	Not feasible in most high-transmission settings where the specific cases cannot be targeted	Feasible in targeted areas
Case management		
Diagnosis	All suspected cases should undergo diagnostic testing with rapid diagnostic tests or microscopy; goal is to have a confirmed diagnosis; clinical diagnosis not recommended; diagnosis should distinguish between parasite species; quality assurance protocols should be implemented	Rapid diagnostic tests, microscopy, or both with confirmatory diagnostics; quality assurance protocols implemented; highly sensitive molecular diagnostic (polymerase chain reaction, loop-attenuated isothermal amplification) may be considered for quality assurance; diagnostic should distinguish between parasite species
Treatment	*P. falciparum*: ACT	*P. falciparum*: ACT plus single low dose primaquine (0.25mg/kg)

table continues next page

Table 12.3 Key Differences between Interventions for Malaria Control and Elimination (continued)

Indicator	Malaria control	Malaria elimination
	P. vivax:	*P. vivax:*
	Blood-stage infections, chloroquine-sensitive areas: Chloroquine or ACT	Chloroquine-sensitive areas: Chloroquine or ACT for blood-stage infections plus primaquine (0.25–0.5 mg/kg) for 14 days to ensure clearance of liver-stage infection (gametocytes)
	Blood-stage infections, chloroquine-resistant areas: ACT or quinine during pregnancy	
	To prevent relapse: primaquine (0.25–0.5 mg/kg) for 14 days	Prophylaxis for travelers
	G6PD deficiency: primaquine 0.75 mg/kg once a week for 8 weeks	
	Prophylaxis for travelers	
	Intermittent preventive treatment for pregnant women and infants	n.a.
Mass drug administration	Seasonal malaria chemoprevention	High-risk groups in geographic or demographic clusters Trials have used DHA/PIP and artemether lumefantrine accompanied by single low dose of primaquine.
Surveillance		
Passive	Monthly reporting of aggregate, confirmed cases to a central level	Rapid or weekly reporting, ideally electronically, of individual cases classified by origin to a central level
Active	Not feasible because of high number of cases	Includes case investigation, reactive case detection, proactive case detection (which may include mass screening), and foci investigation
Program management		
Program structure	Increased investment in integrated programming in the general health system	Vertical programming investment needed; flexibility needed between vertical and integrated systems
Human resources	Large teams of dedicated staff for specific interventions; specialized skills training	Dedicated managers; basic skills maintained among cadre of integrated staff
High-level commitment	National reduction of disease burden (morbidity, mortality)	National or subnational goals of elimination; may feed into regional elimination goal; regional collaboration encouraged for controlling imported cases

Source: Gosling and others 2014; RBM Partnership 2008; WHO 2012c.
Note: ACT = artemisinin-based combination therapy; DHA/PIP = dihydroartemisinin-piperaquine; mg/kg = milligrams per kilogram; n.a. = not applicable.

Vector Control

Vector control, a key intervention for preventing malaria transmission by *Anopheles* mosquitoes, includes indoor residual spraying with insecticide, use of LLINs, larviciding, and environmental management to remove breeding sites (WHO 2006). The massive gains in malaria control in the past 15 years are attributed largely to the scale-up of these interventions, notably LLINs (Bhatt and others 2015). LLINs have been most widely deployed in Africa, which has the highest proportion of the population at risk of malaria and has malaria vectors most amenable to control with LLINs. The proportion of the population sleeping under LLINs in Sub-Saharan Africa increased from 2 percent in 2000 to an estimated 55 percent in 2015 (WHO 2015e).

However, there are threats to the sustainability of these interventions. First, LLINs must be replaced at least every three years, and maintaining consistent use is difficult, especially when the perceived risks of malaria decline (Hsiang and others 2012). The WHO estimates that as many as 300 million new nets may be required each year to ensure that all populations at risk have access to LLINs in countries where LLINs are the primary vector control strategy (WHO 2015e). Second, mosquitoes are becoming resistant to insecticides: most countries in Sub-Saharan Africa have detected resistance

to pyrethroids, the main class of insecticides for indoor residual spraying and LLINs (Ranson and others 2011). While researchers and product development partners are developing and deploying new insecticides, country malaria programs must implement strategies to mitigate resistance by rotating insecticides and using alternative vector control tools (Hemingway and others 2016).

Residual Transmission and New Tools for Control

Despite high coverage of LLINs and indoor residual spraying, transmission persists in many areas because of *residual transmission,* defined as transmission sustained by vectors that evade contact with these two indoor interventions and that rest outdoors and bite humans or animals (Killeen 2014). Residual transmission poses a particular challenge to elimination and eradication and requires efficient tools to target malaria vectors.

Measures such as topical and spatial insect repellants (Ogoma, Moore, and Maia 2012; Wilson and others 2014), insecticide-treated hammocks (Magris and others 2007), and insecticide-treated textile products (Kimani and others 2006; Rowland and others 1999; Thang and others 2009) may be more effective for protecting individuals outdoors (Katz, Miller, and Hebert 2008). Innovative indoor methods such as durable wall liners and insecticidal paint could replace indoor residual spraying, and mosquito-proofed housing (using window screens) and housing modifications (closing eaves and using insecticide-treated eave tubes) may be effective supplemental interventions (Ngufor and others 2014; Oxborough and others 2015; Tusting and others 2015). Space spray and attract-and-kill mechanisms could target adult vectors outdoors, and topical and systemic insecticide treatments for livestock can be effective for vectors that also feed on animals (Matowo and others 2013; Poché and others 2015; Pooda and others 2015; Rowland and others 2001; Shono and others 1991). Researchers are also examining new approaches such as attractive toxic sugar baits and swarm spraying to exploit intrinsic mosquito sugar feeding and mating behaviors, respectively (Müller and others 2010; Qualls and others 2015).

More aggressive approaches to targeting immature stages of vectors, including aerial and ground larviciding and breeding source reduction through environmental management, are the mainstays of mosquito control programs in high-resource settings such as Australia and the United States and can be considered for malaria control and elimination in lower-resource settings (Floore 2006). Research to develop genetic and biological control of adult malaria vectors is ongoing and may be one of the long-term solutions for malaria eradication (Blanford

2012; Helinski and others 2008; Howard and others 2011). As an example, work to develop gene drive systems that either suppress or replace vector populations is proceeding (Hammond and others 2016).

Ultimately, the use of an integrated approach to vector control based on entomological surveillance to understand and target unique vector behaviors and the development of new tools to target different mosquito life stages, habitats, and behaviors are essential for the effective control of malaria vectors (Durnez and Coosemans 2013).

Entomological Surveillance and Integrated Vector Management

Robust entomological surveillance and monitoring is critical to guiding vector control interventions. Information on local vector species, their behaviors, and their susceptibility to insecticides as well as on coverage, usage, quality, and durability of vector control tools is needed to inform decision making and shape local vector control strategies. Entomological expertise was the backbone of successful elimination programs in the past (Mauritius, Sri Lanka, and the United States) and should inform and direct future vector control strategies (Tanner and others 2015).

Evidence-based programming and decision making and entomological intelligence are key components and the foundation of integrated vector management (IVM). IVM is an approach to integrated vector control that optimizes available resources and encourages ecological soundness and sustainability. Other features of the IVM approach include multisectoral collaboration, community and stakeholder engagement, and integrated tools and structures to control disease vectors more effectively and efficiently (WHO 2012b).

Maintenance of Low Transmission

The rate of progress toward elimination and the level of interventions required to interrupt transmission depend on the strength of the health system to detect and respond to cases; the level of investment in malaria programs; and various other factors, including biological determinants, the environment, and the social, demographic, political, and economic realities in the particular country. Two important factors determine the risk of reestablishment of malaria: vulnerability and receptivity. Vulnerability is determined by the importation rate of malaria into malaria-free areas; receptivity is the probabilistic risk of local mosquitos and strategies needed for global becoming infected with malaria parasites and subsequently transmitting the infection to humans. In Canada, Europe, and the United States, vulnerability is high, but receptivity is low. Thousands of imported

malaria cases arrive each year, but local mosquitoes rarely become infected and transmit the infection onward. In contrast, the risk of reestablishment is high in countries where both vulnerability and receptivity are high, such as Oman and Sri Lanka, which have previously had high rates of transmission and also receive visitors infected with malaria. In these settings, imported cases must be detected rapidly to prevent onward transmission to the local community.

The success of achieving and sustaining elimination is largely dependent on the receptivity of an area to malaria or "the abundant presence of anopheline vectors and the existence of other ecological and climatic factors favouring malaria transmission" (WHO 2007, 84). Vector control is a key strategy for reducing vectorial capacity—the efficiency of the vector in transmitting malaria based on mosquito density, survival, human biting rates, and parasite incubation period (Brady 2016). In addition, understanding the ecological and climatic factors that cause an increase in receptivity and responding with tailored, effective vector control will be critical to elimination and eradication.

Diagnosis and Treatment

At present, the WHO considers quality-assured microscopy the gold standard for diagnosing clinical malaria. However, microscopy and RDTs are less sensitive at detecting low-density and subpatent infections, which can contribute a sizable proportion of secondary cases and onward transmission. Nucleic acid amplification techniques such as polymerase chain reaction are more sensitive than microscopy and RDTs and are increasingly being used in epidemiological studies; however, they are not yet field friendly and require considerable start-up costs and staff training. Lab-based polymerase chain reaction assays through pooling techniques can provide a high-throughput approach for detecting low parasitemias (Hsiang and others 2012; Imwong and others 2014). However, they do not provide immediate results, and conducting them is capital intensive. Similarly, loop-attenuated isothermal amplification can detect all species of infection at low density and high throughput, is available at a relatively low marginal cost, and involves less lab equipment, but it still requires staff capacity (Surabattula and others 2013). The WHO recommends that the use of highly sensitive diagnostic tools should be considered only in low-transmission settings where malaria diagnostic testing and treatment are already widely used (WHO 2014b).

ACT is the frontline therapy for uncomplicated *P. falciparum* and has been widely deployed globally. The WHO currently recommends five ACT combinations,

and a few others are in the pipeline, although they are not expected to be available in the near future.

Eliminating countries also face significant threat from *P. vivax*. Despite long being regarded as benign, acute cases can have severe consequences. *P. vivax* infections are treated with chloroquine in areas where it remains effective (treatment failure with chloroquine for *P. vivax* malaria has been observed in 24 countries and confirmed in 10 countries) or with ACT where it is not. Primaquine, the only medicine currently available to treat hypnozoites, requires a long course of treatment (7–14 days or even 8 weeks), and poor adherence can lower its efficacy (John and others 2012). Furthermore, the risk of life-threatening hemolysis in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, a common blood disorder present in about 8 percent of the population in malaria-endemic areas (Howes and others 2012), limits its use. A reliable point-of-care test to detect G6PD deficiency is not yet widely available (Baird 2015). Tafenoquine, a promising single-dose medicine against hypnozoites and relapses, is likely to be available in 2018 (Eziefula and others 2012; Llanos-Cuentas and others 2014), but it has severe side effects in G6PD-deficient patients. Therefore, solving the problem of G6PD diagnosis and making more sensitive, field-deployable diagnostics more widely available have great potential for eliminating *P. vivax*.

Mass Drug Administration

Interest in the empiric administration of a therapeutic antimalarial regimen to an entire population at the same time, otherwise known as mass drug administration (MDA), has recently been renewed. Proactive MDA has been successfully deployed against several infectious diseases, including lymphatic filariasis, onchocerciasis, schistosomiasis (Hotez 2009), and malaria (Bruce-Chwatt 1959; Newby and others 2015; Poirot and others 2013). The goal is to interrupt transmission by treating all parasitemia in the population. MDA can potentially reduce malaria mortality and morbidity through its direct therapeutic effect on individuals who receive a treatment dose of antimalarials. It also can reduce transmission rates by reducing parasitemia prevalence and interrupting various stages of the parasite lifecycle, and it can inhibit the sporogonic cycle in the mosquito, reducing its vectorial capacity. If every member of a given population were treated by antimalarial MDA, the prevalence of asexual parasites in the population would immediately decline.

However, knowledge gaps remain, especially regarding optimal size of the target population, methods to improve coverage, selection of drug-resistant parasites, and

primaquine safety. Malaria elimination programs will likely use MDA in targeted ways to accelerate the impact of vector control and ongoing diagnosis and treatment. Current trials use a full course of dihydroartemisinin-piperaquine or artemether-lumefantrine and a single low dose of primaquine (Eckhoff, Gerardin, and Wenger 2015; White 2013). A key issue is that medicines such as ACTs and primaquine have been registered by drug regulatory authorities based on a clinical indication and a demonstrated risk-benefit ratio in symptomatic patients. The evidence base for its use in asymptomatic or noninfected subjects will need renewed attention. In addition, many medicines considered for MDA are not known to be safe in the first trimester of pregnancy, which presents additional problems if the medicines are deployed in Africa, where pregnancies are rarely reported in the first trimester.

The long-term use of MDA in low-transmission settings faces several challenges. The optimum combination of products and the timing, frequency, and duration of use will depend on the endemicity, seasonality, and rate of importation (Newby and others 2015). For example, MDA, preferably using treatments with a long half-life, is sensible where populations are static and the risk of importation is low (Cohen and others 2013; Gosling and others 2011). To minimize drug pressure on ACTs, a complete course of treatment is needed, and the regimen used for MDA should differ from frontline treatment. At least three "rounds" of administration are needed to affect transmission (Maude and others 2012), requiring adequate resources and political commitment.

The WHO has issued guidelines for implementation of MDA in different epidemiological settings (WHO 2016a). The WHO recommends the use of MDA for the elimination of *P. falciparum* malaria in areas approaching interruption of transmission where there is good access to treatment, effective implementation of vector control and surveillance, and minimal risk of reintroduction of infection, as well as for epidemic control and in exceptional circumstances such as complex emergencies. Like most interventions, MDA is designed to accompany other interventions, including active surveillance and vector control.

Epidemiological Surveillance

Robust and responsive surveillance systems that identify and eliminate transmission foci are critical for the success of malaria control and elimination. (Ohrt and others 2015). An ideal malaria elimination surveillance system swiftly collects and transmits data about individual cases, classified by the origin of infection; integrates it with information on program activities; and analyzes

the information on an ongoing basis to guide rapid response strategies.

In elimination settings, the WHO recommends investigation of all malaria cases to determine if they are imported or the first- (introduced) or second- (indigenous) degree results of local transmission. Passive detection of cases must be complemented with some form of active case detection. Active case detection might take the form of mass screening of high-risk individuals (GHG 2013; Smith Gueye and others 2013; WHO 2013), targeted testing of specific high-risk groups, or household visits seeking febrile or infected individuals. Active case detection typically costs more than passive surveillance; however, the relative cost-effectiveness has not been assessed (Sturrock and others 2013). Less-demanding approaches are being explored, such as surveying children in vaccination clinics, women in antenatal clinics, or children attending school.

Some programs proactively screen at-risk populations on a periodic basis or screen the contacts of index cases for related infections (Moonen, Cohen, Snow, and others 2010; Wickremasinghe and others 2014). For example, migrant laborers and returning military may be screened when entering a malaria-eliminating country, or a village may be screened before and during the malaria season to detect cases before transmission begins. Focal screening and treatment of high-risk communities and mass screening and treatment of whole populations may be used, but these approaches miss infected subjects who are not screened (Hoyer and others 2012) or persons with subpatent infections. In islands or in countries with few entry points, visitors from endemic areas can be screened to prevent reintroduction; however, such screening is difficult to sustain. For any of these methods to be effective, diagnostic tests have to be reliable and able to detect low levels of infection, or presumptive treatment (treatment without a diagnostic test) can be used (WHO 2014b).

Use of serology to measure past exposure could help identify at-risk populations, especially in low-transmission settings where infections are relatively rare (Hsiang and others 2012). Combining serology with conventional diagnostic testing in geospatial models to produce accurate risk maps at finer scales can improve the targeting of interventions (Corran and others 2007; Hsiang, Greenhouse, and Rosenthal 2014; Kelly and others 2012; Lindblade and others 2013; Sissoko and others 2015; Sturrock and others 2014).

Malaria should be made a notifiable disease (required by law to be reported to government authorities) once incidence is low enough that malaria surveillance teams can investigate and report every individual case (Moonen, Cohen, Snow, and others 2010). China and Swaziland

have made malaria a notifiable disease to try to increase reporting and encourage more sectors to use the surveillance system (Cohen and others 2013; Hemingway and others 2016). Other approaches to capturing cases that present outside the public sector include restricting access to antimalarials and incorporating private health facilities into the surveillance system (Moonen, Cohen, Tatem, and others 2010).

After elimination has been achieved, passive surveillance at health facilities, including in the informal private sector, is needed to detect and treat introduced infections.

Vaccines

Malaria vaccines include pre-erythrocytic vaccines that aim to prevent blood-stage infection, blood-stage vaccines that clear parasitemia and prevent clinical disease, and transmission-blocking vaccines that prevent infection of mosquitoes and interrupt transmission (Horton 2015). RTS,S, a pre-erythrocytic vaccine to prevent clinical *P. falciparum* in children, is the first malaria vaccine to have completed a Phase 3 clinical trial and was approved by the European Medicines Agency in June 2015. Clinical trials demonstrated a vaccine efficacy for clinical malaria of 28 percent in children ages 5–17 months, but only 18 percent in infants, the target population (RTSS Clinical Trials Partnership 2015) and 36 percent and 26 percent, respectively, after a booster dose administered 18 months after the primary series. In January 2016, the WHO released a position paper recommending further evaluation of the malaria vaccine in a series of pilot implementations before considering wider country-level introduction (WHO 2016b).

An ideal vaccine would be more effective than RTS,S at protecting individuals against infection and at stopping transmission of both *P. falciparum* and *P. vivax* (Nikolaeva, Draper, and Biswas 2015; Tran and others 2015). Such combinations will likely not be commercially available for at least another decade.

Program Management

Reorienting a program from control toward elimination involves retraining staff, developing strong surveillance capacity, building a data architecture that can monitor and direct activities, instituting managerial practices that ensure a capable and ready workforce, and changing program tasks from curative services to preventive community action. These activities involve securing political and financial commitment for at least 6–10 years after elimination has been achieved, as demonstrated by the experiences of Turkmenistan and Sri Lanka, described in boxes 12.3 and 12.4 (Feachem and others 2010).

Box 12.3

Eliminating Malaria in Turkmenistan: Going the Last Mile

Key lessons learned:

- Use regional goals to drive country progress.
- Build and sustain human resource capacity.
- Maintain a dedicated budget even as priorities shift.

Turkmenistan eliminated malaria in the 1950s during the Global Malaria Eradication Program. Over the next four decades, imported cases were detected rapidly through a robust surveillance system. However, population movement after the dissolution of the former Soviet Union in the 1990s led to increases in local vulnerability and imported cases that escaped detection. Two *P. vivax* outbreaks (1998–99 and 2002–03) spurred the Turkmenistan Ministry of Health and Medical Industry to reorient its program toward eliminating transmission. The goal was reinforced by the 2005 Tashkent Declaration, a commitment to achieving regional elimination by 2015 (WHO 2005). The last local malaria case in Turkmenistan was documented in 2004.

After securing high-level political and financial commitment, a revised elimination strategy was launched in 2007, and malaria-free status was achieved in 2010 (WHO 2010). The prevention-of-reintroduction strategy emphasized intensified surveillance at the Afghanistan border, rapid case investigation, and standardized reporting. Even as health priorities shifted away from malaria, Turkmenistan maintained dedicated funding for human resources, surveillance, monitoring and evaluation, and advocacy.

Sources: Turkmenistan Ministry of Health and Medical Industry, WHO, and University of California, San Francisco, Global Health Group 2012; WHO 2005, 2010.

Despite the need for intensified surveillance and response capabilities during the elimination phase, governments and external donors typically reduce funding as incidence declines (Cohen and others 2012). Program activities are often integrated into the local health system to increase efficiency (Liu and others 2013; Tatarsky and others 2011). A review of managerial experiences with disease elimination suggests that dedicated staff should run and oversee some tasks (vector control and rapid case investigation), while local health teams could oversee others (case management, surveillance, and reporting) (Gosling and others 2014).

Regional collaboration can further reinforce collective goals and foster positive cross-border externalities and financing (Barclay, Smith, and Findeis 2012; Gosling and others 2015; Moonen, Cohen, Snow, and others 2010). For a description of regional initiatives, see annex 12B.

ECONOMICS AND FINANCING OF MALARIA ELIMINATION

One of the strongest arguments against eliminating or eradicating any disease involves the costs associated with finding and treating a decreasing number of cases (Lines, Whitty, and Hanson 2007). These final few cases will likely require an outlay of resources that appear to be disproportional to the marginal return. Maintaining a high level of financial support when transmission has been reduced to low levels remains a challenge. Policy makers have to decide whether to maintain control activities indefinitely or whether to actively pursue elimination.

Articulating the costs of elimination and the relative benefits of investment in elimination versus control will help inform these decisions. Three methods can be used to assess the incremental costs and associated benefits of malaria elimination:

- Analyzing the costs and benefits of an elimination program, summarized using a benefit-cost ratio
- Determining the financial cost savings of an elimination campaign relative to alternative scenarios (for example, control or resurgence costs)
- Evaluating the macroeconomic impact of malaria control and elimination against the economic burden that malaria places on society

Costs and Benefits

Since the conclusion of the GMEP in the 1960s, several studies have reported the costs and consequences of malaria elimination and control, but few benefit-cost

Table 12.4 Benefit-Cost Ratios Associated with Malaria Elimination Programs

Country or setting	Study period	Focus (control or elimination)	Benefit-cost ratio	Source
Global	2010–30	Elimination	6.11	Purdy and others 2013
Greece	1946–49	Elimination	17.09[a]	Livadas and Athanassatos 1963
Iraq	1958–67	Elimination	6.3[a]	Niazi 1969
Paraguay	1965	Elimination	2.6–3.3	Ortiz 1968
India	1953–54, 1976–77	Control[b] Control	9.22 4.14	Ramaiah 1980
Philippines	Unspecified	Control[b]	2.4	Barlow and Grobar 1986
Sri Lanka	1947–55	Control[b]	146.3	Barlow and Grobar 1986
	2014	Prevention of reintroduction	14.3	Shretta and others 2016
West Pakistan	1960	Control[b]	4.9	Barlow and Grobar 1986

a. Calculated based on reported benefits and costs.
b. Although the assessments considered these to be control interventions, they were conducted during the Global Malaria Eradication Program era.

analyses have been conducted (table 12.4). Beyond the direct benefits on health, the main economic benefit considered in the studies is increased labor productivity resulting from reductions in absenteeism. Other benefits include gains from the migration of labor into previously malarial areas and lower treatment costs. Most studies assume a 10-year elimination campaign, and only two (Ortiz 1968; Ramaiah 1980) used empirical data.

All studies showed positive benefit-cost ratios, indicating sizable benefits relative to costs. Benefit-cost ratios ranged from 2.4 in the Philippines (Mills, Lubell, and Hanson 2008), 4.14 and 9.22 for control in India (Prakash and others 2003; Ramaiah 1980), 17.09 for elimination in Greece (Livadas and Athanassatos 1963), to 146.3 and 14.3 for control and prevention of reintroduction, respectively, in Sri Lanka (Barlow and Grobar 1986). Of these countries, Greece continues to report outbreaks as a result of imported cases, despite having eliminated malaria, and Sri Lanka is in the process of seeking WHO malaria-free certification (Samaraweera 2015).

Benefits

Many of the economic benefits associated with malaria interventions extend beyond health to include larger macroeconomic and demographic effects. Investments reduce private out-of-pocket expenditures on prevention and treatment (Chuma, Thiede, and Molyneux 2006; Guiguemdé and Guy 2012), increase productivity, and increase agricultural output via reclaimed land (Gallup and Sachs 2001; Mills, Lubell, and Hanson 2008; Utzinger and others 2002). Lower child mortality may reduce fertility (Aksan and Chakraborty 2013), increase literacy and human capital (Lucas 2010), and eventually increase labor productivity. Domestic and foreign investment may be channeled to formerly malarious areas, contributing to fiscal growth.

Comparing the marginal benefits of control to those of elimination is difficult. Elimination can improve health equity because the last remaining foci of infection are often concentrated within poor or marginalized populations (Feachem, Phillips, and Targett 2009). Prevention of reintroduction also protects against resurgences. Furthermore, eliminating malaria within a single country may confer substantial regional externalities and global public good, fostering collaboration. Elimination may also confer threshold benefits by permanently reducing the receptivity of an area to the reestablishment of local transmission (Chiyaka and others 2013; Sabot and others 2010; Smith Gueye and others 2013), but methods to measure the value of the diminished resurgence risk have yet to be established. Some studies have examined the relationship between elimination and tourism demand in the Dominican Republic, Mauritius, and South Africa, but with little success because of confounding factors such as the overall increase in global travel (Maartens and others 2007; Modrek and others 2012). As benefits become less tangible, they are more difficult to measure. Gaining an understanding of the larger set of economic benefits will require better macroeconomic models that quantify the links between elimination and other outcomes (Mills, Lubell, and Hanson 2008).

Costs and Cost Comparisons

Much of the debate regarding elimination concerns the government's costs of delivering services. However, programmatic costs are only part of the picture—individuals, households, and employers also incur costs for treatment and prevention. From a programmatic

perspective, costs increase as control interventions are scaled up, because interventions are often provided for free to increase coverage and to shift costs from individuals to programs.

Analyses of program expenditures are limited to a few studies primarily in Africa and Asia. A systematic literature review identified 21 studies on the costs of malaria elimination with known data sources (Shretta and others 2016). Program expenditures were divided by the cost per capita to account for differences in intended coverage and benchmarked to the first year of data for each country. The reported costs ranged from US$0.18 in Mexico in 1971 (Suarez Torres 1970a) to US$27 in Vanuatu (Kahn and others 2009) (all in 2013 U.S. dollars). Barring a few exceptions, reported costs per capita were generally lowest in East Asia and Pacific and Mexico (Suarez Torres 1970b) and highest in African countries, such as Mauritius (Tatarsky and others 2011), São Tomé and Príncipe (Kahn and others 2009), Swaziland (Kahn and others 2009; Sabot and others 2010), and Zanzibar (Sabot and others 2010). Only Mauritius seeks to prevent reintroduction by screening passengers at ports of entry and using targeted vector control, which may account for the high costs.

Costs for elimination have varied but have generally been low. In the 1960s they were less than US$1 per person-year. Estimates from Nepal and Thailand ranged from US$0.64 to US$1.33 per person-year in the 1980s (in 2006 U.S. dollars) (Mills, Lubell, and Hanson 2008). A retrospective study reports elimination expenditures (including from nongovernmental funders) in Jordan, Lebanon, and Syria of US$0.96, US$0.73, and US$1.69 per person-year, respectively (de Zulueta and Muir 1972). These estimates are lower than those from more recent studies, and it is unclear how directly comparable they are because of variable inputs and the availability of new and more costly tools as well as the rise of new challenges, such as insecticide and artemisinin resistance and human migration (figure 12.1).

Financial Cost Savings of Elimination Relative to Alternative Scenarios

To generate results most relevant to policy, malaria elimination requires a comparison of cost with a counterfactual scenario of malaria control, the costs of which vary substantially with the level of control. Scenarios may encompass a range of alternatives, from a null state of disease without intervention to a state of controlled low-endemic malaria (Sabot and others 2010), to scenarios illustrating the costs of doing "business as usual" with a relatively stable control state punctuated by spikes of epidemics or resurgence when efforts are slowed.

In practice, while an abundance of literature examines the costs of comprehensive control, studies comparing the costs of elimination to the costs of control to determine the financial cost savings of an elimination program relative to control or resurgence are scarce. Nevertheless, once malaria is reduced to a level at which it is no longer a public health threat, reorienting the program from control to elimination is likely to require a significant one-time investment (Sabot and others 2010). One study that projected costs to a 20- to 50-year timeline for Hainan and Jiangsu provinces in China and in Mauritius, Swaziland, and Zanzibar found that elimination is likely to be more costly than control in the short term and is likely to remain more expensive than control at substantially longer timeframes (depending on the inputs of the post-elimination program).
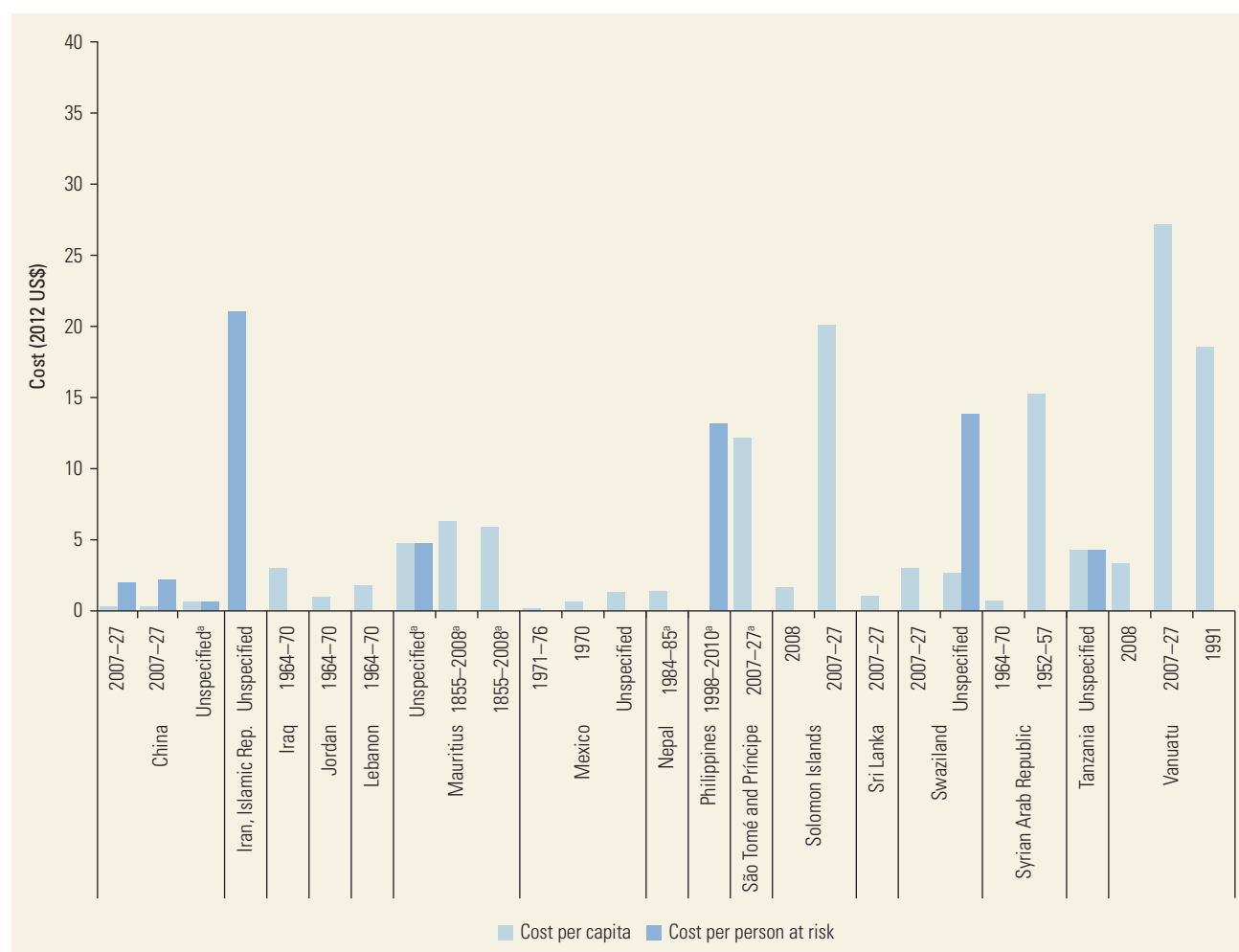
Programs can also be integrated, making disease programs more efficient as well as creating a platform for mobilizing resources, even if malaria is no longer considered a priority. For example, in Singapore, integrating dengue and malaria surveillance facilitated interagency collaboration and reduced transmission of both diseases (Luckhart and others 2010). When transmission decreases and eventually ceases, costs are likely to decline and eventually stabilize as efforts turn to preventing reintroduction primarily through surveillance, vector control, and emergency response. Private out-of-pocket expenditures are also likely to become negligible as the number of cases declines. Two studies (figure 12.2) with empirical data on expenditures over multiple programmatic phases found that expenditures declined when moving from elimination to prevention-of-reintroduction (Abeyasinghe and others 2012; Smith Gueye and others 2014). A study in Sri Lanka estimated the financial cost of prevention of reintroduction activities to cost US$0.37 in 2014 (Shretta and others 2016), less than a quarter of the expenditures in previous years (Abeyasinghe and others 2012).

Elimination should therefore not be justified on the basis of short-term cost savings alone. A focus only on relative cost savings ignores many other factors (for example, population growth, economic development, reductions in malaria in neighboring countries) that could permanently alter the epidemiology of the area, reduce transmission, accelerate the elimination timeline, and decrease costs (Smith and others 2013).

Macroeconomic Gains from Malaria Elimination

Several studies have explored the association between malaria and economic productivity (Audibert, Mathonnat, and Henry 2003; Badiane and Ulimwengu

Figure 12.1 Costs of Malaria Elimination, by Country, Various Years

Sources: China: Jackson, Sleigh, and Liu 2002; Sabot and others 2010; the Islamic Republic of Iran: Rezaei-Hemami and others 2013; Iraq, Jordan, Lebanon, the Syrian Arab Republic: de Zulueta and Muir 1972; Mauritius: Tatarsky and others 2011; Mexico: Suarez Torres 1970a, 1970b; Nepal: Kondrashin 1992; the Philippines: Liu and others 2013; São Tomé and Príncipe: Kahn and others 2009; the Solomon Islands: Beaver 2011; Sri Lanka: Abeyasinghe and others 2012; Swaziland and Tanzania (Zanzibar): Sabot and others 2010; Vanuatu (Aneityum Island): Kaneko and others 2000.
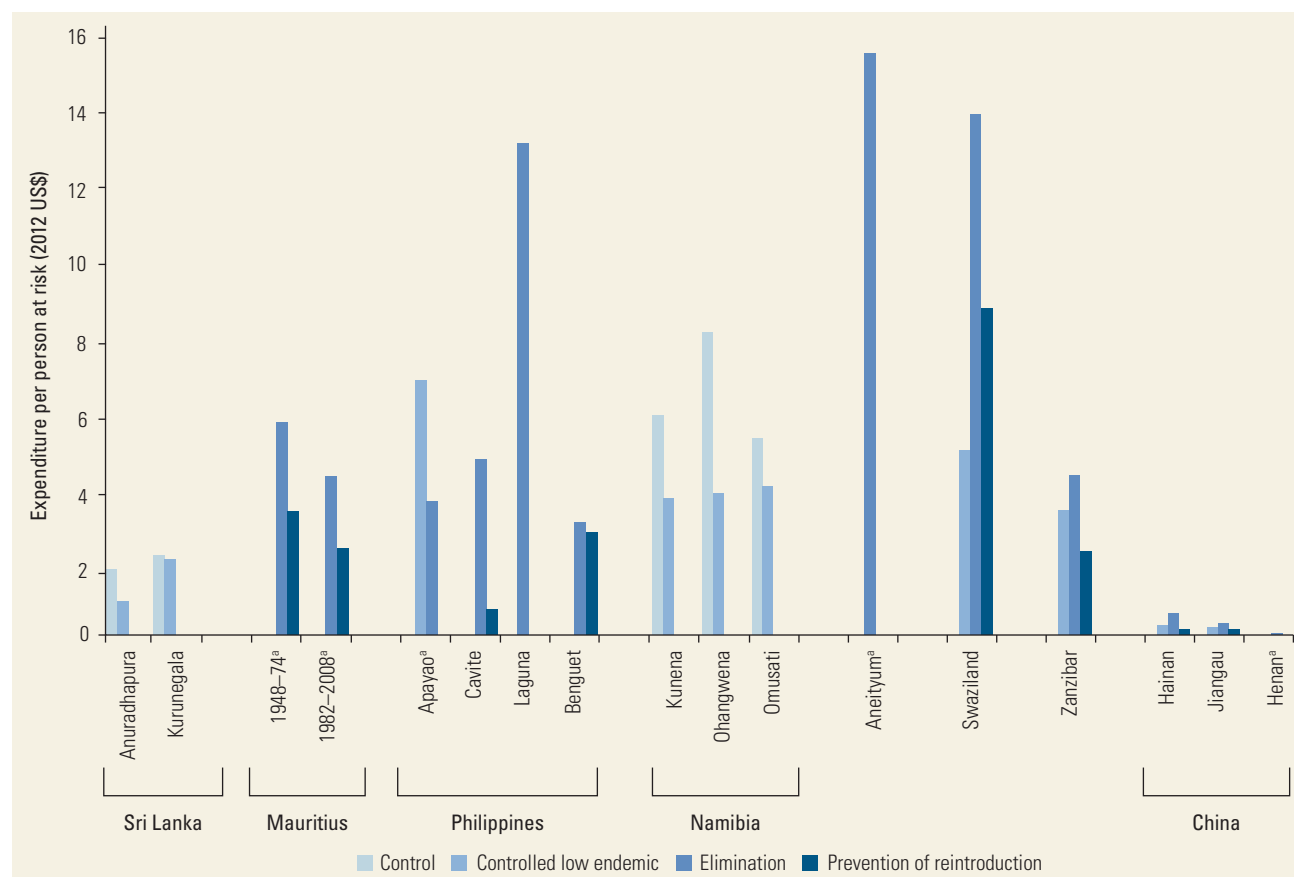
a. Multiple costs per capita were reported in the original article; only the highest cost is presented in the figure.

2013; Girardin and others 2004) and can be used to build the investment case. Khan (1966) estimated the cost of decreased efficiency attributable to malaria for Pakistan at more than US$53 million in 1960, while Dua and others (1997) estimated more than US$347,000 in production losses in one Indian industrial complex in 1985. In the United States in 1914, one day lost to malaria was equal to US$119 in production losses (in 2013 U.S. dollars). Many costs of malaria, such as the long-term effects of chronic malaria infection on lowering educational attainment, have yet to be estimated (Chen and others 2016).

Economic modeling using data from Ghana (Asante and Asenso-Okyere 2003), Uganda (Orem and others

2012), and across several countries (Gallup and Sachs 2001; McCarthy, Wolf, and Wu 2000; Okorosobo and others 2011) found that malaria is associated with losses in gross domestic product (GDP) growth. Using cross-country regressions, Gallup and Sachs (2001) demonstrated that countries with intensive malaria lost 1.3 percent of GDP growth per person per year between 1965 and 1990. Similarly, McCarthy, Wolf, and Wu (2000), using WHO morbidity data, estimated that many high-burden countries lost at least 0.25 percent of GDP growth per year from malaria. GDP losses of between 0.41 percent and 8.9 percent or US$4.2 million have been reported in Africa (Okorosobo and others 2011). The annual monetary cost of these losses was as

Figure 12.2 Malaria Program Expenditures in Select Countries, by Phase

Sources: Sri Lanka: Abeyasinghe and others 2012; Mauritius: Tatarsky and others 2011; the Philippines: Liu and others 2013; Namibia: Smith Gueye and others 2014; Vanuatu (Aneityum Island): Kaneko and others 2000; Swaziland, Zanzibar, and Hainan and Jiangsu, China: Sabot and others 2010; Henan, China: Jackson, Sleigh, and Liu 2002.

a. Multiple costs per capita were reported in the original article; only the highest cost is presented in the figure.

high as US$13.1 million in Mali (Okorosobo and others 2011) to US$10 billion in Nigeria (Okorosobo and others 2011). In Thailand, the economic cost of malaria was valued at US$280 million over five years (Kühner 1971).

Several studies estimated a country's total economic loss by examining expenditures for malaria prevention, control, and treatment, as well as the opportunity cost of caregiving, debility, and premature death. For example, the loss for India was estimated to be between US$856 million and US$1.6 billion a year (Sharma 1996). Losses were estimated to be US$415 million for the Philippines (Barlow and Grobar 1986) and US$133.9 for Pakistan (Khan 1966). However, many of these historical studies are not population based and use secondary sources or expert opinion to calculate the burden of malaria, limiting their contemporary use.

Exposure to malaria in childhood has been associated with lower incomes and a greater likelihood of poverty in adulthood in South America (Barreca 2010;

Bleakley 2003, 2010; Hong 2011). It has also been associated with chronic diseases in later years and an inability to work (Hong 2013), decreased property accumulation in Côte d'Ivoire (Audibert, Mathonnat, and Henry 2003), and decreased spending overall (Somi and others 2009).

The *GTS for Malaria* (WHO 2015a) and Action and Investment to Defeat Malaria (RBM Partnership 2015) use transmission modeling and cost projections to estimate the total cost of reducing the global burden of malaria to 90 percent of its current level by 2030. The estimated cost would be about US$100 billion, resulting in a US$208.6 billion increase in economic output. This figure is in line with a global analysis reporting that malaria reduction and elimination between 2013 and 2035 would produce a benefit whose net present value is US$208.6 billion and a benefit-cost ratio of 6.11 (Purdy and others 2013). Gates and Chambers (2015) estimate that eradication could unlock US$2 trillion in economic

benefits at a cost of about US$90 billion to US$120 billion between 2015 and 2040, yielding a return on investment of about 17:1.
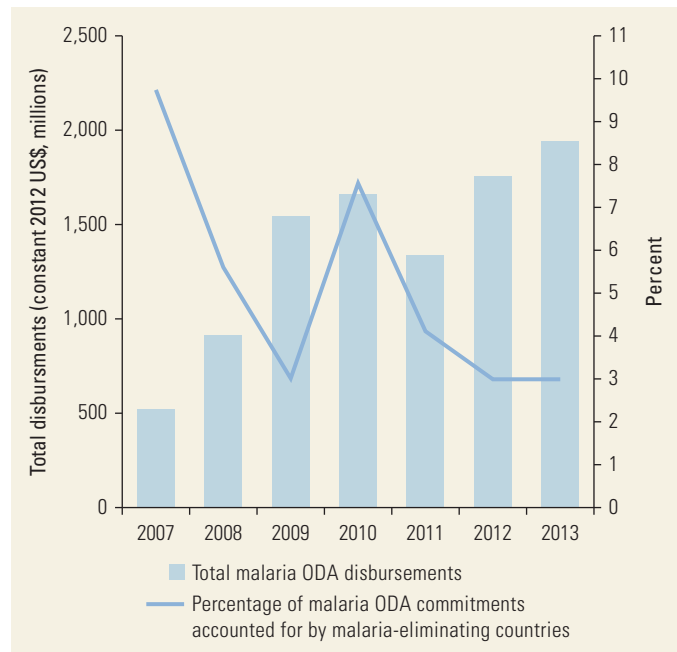
Financing and Efficiency

Development assistance for malaria quadrupled between 2007 and 2013. However, the proportion of development assistance directed toward malaria-eliminating countries declined more than 80 percent and continues to decline (figure 12.3). Securing funding for a disease that occurs infrequently is challenging. Malaria-eliminating countries typically have lower disease burdens and are often middle-income countries; therefore, they are a lower priority for donors. The Global Fund to Fight AIDS, Tuberculosis, and Malaria has historically allocated about 7 percent of its portfolio to malaria-eliminating countries but, under its new funding model, now allocates about 5 percent, representing a projected decrease of 31 percent in national funding allocation—a serious shortfall at a time when maintaining national gains and advancing the elimination agenda are essential (GHG 2014; Zelman and others 2016).

Eliminating countries finance about 80 percent of their malaria programs (CEPA 2013), and this spending has been increasing steadily since 2000. However, spending still falls short of the US$8 billion per year needed to reach the 2030 targets (WHO 2015a).

Greater emphasis is being placed on building the capacity of countries to fund their own programs through increased government spending as well as innovative financing mechanisms. Box 12.5 and annex 12C describe some mechanisms that are being implemented or considered and their applicability to malaria programs.

Figure 12.3 Overseas Development Assistance Commitments for Malaria, 2007–13

Source: Unpublished data from Global Health Group.
Note: ODA = Overseas Development Assistance.

Box 12.5

New Financing Mechanisms to Support Malaria Elimination

Earmarked travel and airline taxes. Given the direct link between travel and the risk of malaria transmission and resurgence in Zanzibar (Le Menach and others 2011), the local government is considering implementing a tax on airplane tickets. A survey finds that visitors are willing to pay a tourist airline tax (Zanzibar Ministry of Health 2012).

Endowment funds. Endowments are created as a permanent financial asset that generates interest into perpetuity or for as long as the funds are invested. Endowments are ideal for financing long-term activities, such as elimination and prevention of reintroduction, but they require a sizable initial investment (Adams and Victurine 2011). Few endowment funds exist in the health sector, and ministries of health would benefit from further guidance on the investment, finance, and legal aspects of this mechanism.

Cash on delivery. Cash on delivery, wherein countries receive funding once they have achieved a predetermined target (Pertakis and Savedoff 2014), has been included in two regional Global Fund grants to provide incentives to some Sub-Saharan African countries to reduce malaria cases to zero or maintain incidence cases below a certain threshold (CEPA 2013). This model could also be used to encourage countries to achieve elimination or maintain malaria-free status.

Efficiency in the portfolio and delivery of interventions will ultimately increase cost-effectiveness. More efficient deployment of resources, however, requires a robust surveillance platform in which high-quality data can be collected and analyzed so that measures of response can be adjusted in a timely manner (box 12.6).

PROSPECTS FOR MALARIA ERADICATION

The benefits of achieving and maintaining elimination include a strong public good component—an incremental contribution to global malaria eradication. While many argue that eradication is unlikely given existing tools (Greenwood 2008; Tanner and de Savigny 2008), particularly for high-burden countries in Africa, the global pipeline for new products has never been stronger, supporting the mounting optimism that global eradication is plausible. The technical and operational feasibility of eradication, the operational complexity, and the political appetite need to be considered when assessing the prospects for eradication.

Technical and Operational Feasibility

Determining feasibility involves assessing both the technical challenge—the transmission intensity and the effectiveness of the tools available to reduce it—and the operational capacity to complete the task. Other disease eradication campaigns suggest that eradication has only been considered after many countries have eliminated the disease. For example, when the goal of smallpox eradication was announced, the disease had been eliminated in all high-income countries and was endemic in only 59 low-income countries (Barrett 2007; Henderson 1987). Similarly, the poliomyelitis eradication initiative was launched in 1998 only after polio had been eliminated in the Americas and all high-income countries, with indigenous transmission remaining in 125 countries (Aylward and others 2003; Bart, Foulds, and Patriarca 1996; Khan and Ehreth 2003). Malaria has been eliminated within many local borders, but the overall burden remains high and widespread. As burdens of *P. falciparum* and *P. vivax* decrease, new strategies to diagnose, treat, and interrupt transmission of lesser-studied malaria species, including *P. malariae, ovale,* and *knowlesi,* will be needed. The true burdens of these species are largely unknown because identification by microscopy or rapid diagnostic tests is not reliable (Baltzell and others 2013; Oguike and others 2011; Steenkeste and others 2010).[4]

Eradication of any species only succeeds if the last carrier of disease is isolated, treated, and prevented from causing further transmission. Understanding of transmission between animal and human hosts relevant for zoonotic reservoirs has only recently gained attention. For example, *P. knowlesi*, carried by the macaque monkey, is increasingly being reported in South-East Asia (Baird 2009; Rajahram and others 2012).

Lessons from other campaigns suggest that for eradication to be feasible, a vaccine or an equivalent means is needed to convey long-term protection, as in the case of smallpox (Barrett 2007, 2013).[5] However, no such measure exists for malaria. Even if other measures could be implemented to confer protection similar to a vaccine, many challenges remain. Drug resistance is on the rise, and pyrethroid resistance has emerged after large-scale distribution of LLINs (John, Ephraim, and Andrew 2008; Trape and others 2011; Tulloch and others 2013).

Operational Complexity

The smallpox and polio eradication campaigns implemented eradication-specific management systems that could be integrated into existing health systems (Aylward and others 2003), used performance indicators to measure management processes, trained adequate

numbers of staff and gave them incentives to execute eradication-specific tasks, developed a robust surveillance system, and expanded financing to support a stronger health care system (Henderson 1987). Through implementation of the smallpox, polio, and guinea-worm programs, innovative breakthroughs were made in organizing large-scale nationwide campaigns; in devising new methods for approaching and mobilizing communities; in developing effective national surveillance networks and using the data to support better strategies; in fostering effective and relevant research programs to facilitate disease control; and in mobilizing support at international, national, and local levels. Lessons learned from these efforts are critical for malaria eradication. Building programs capable of proactively mitigating the risk of transmission requires careful planning rather than reactive emergency response measures.

Political and Financial Commitment

In 1939, Boyd summarized the prevailing public health point of view and emphasized that "malaria control should not be a campaign—it should be a policy, a long-term program. It cannot be accomplished or maintained by spasmodic effort. It requires the adoption of a practicable program, the reasonable continuity of which will be sustained for a long term of years" (Boyd 1939, 5).

The success of malaria eradication will depend on the ability to mobilize collective action. At a minimum, universal political commitment to achieving an agreed-on target is required, as are financial resources to sustain that commitment. Although countries may be willing to eliminate the disease within their borders, the last country to eliminate it has little incentive to do so on its own, given the larger interests of all other countries (Barrett 2004). The smallpox eradication program nearly failed because of lack of political commitment (Barrett 2007), and the GMEP was cut short for the same reason. Although global attitudes have shifted toward malaria elimination and eradication, political and financial support is needed to bolster the goal of global eradication, should that goal be adopted for malaria.

There are concerns that concentrating resources in areas with lower burdens of disease may divert resources from lower-income countries with higher burdens of disease (Shah 2010); however, progress in low-burden countries is likely to drive global progress toward eradication (Newby and others 2016). In addition, because malaria-free countries stand to benefit from eradication, they have an incentive to offer financial assistance if they are assured that the last countries will work toward elimination (Barrett 2007; Taylor, Cutts, and Taylor 1997).

See box 12.7 for future research priorities.

Box 12.7

Priorities for Research

While achievements made in the past 15 years give reason for optimism, some gaps and priorities for research remain (Tanner and others 2015):

- Detection of emergence and spread of drug-resistant parasites using geospatial and temporal mapping of drug resistance
- Epidemiologically and economically effective and efficient mixes of interventions in different contexts
- Serological tests to detect individual-level recent infections
- Sensitive clinical field diagnostic tests
- New tools for eliminating *P. vivax*, including the identification of asymptomatic hypnozoite carriers
- Effective approaches for mass drug administration in different contexts

- Improved vector control strategies that target residual transmission
- Continued research and development for a combination vaccine
- Appropriate models for private sector and community-based surveillance and response
- Capacity building in program and health system management
- Estimates of costs to identify and secure laboratory specimens of malaria parasites and to stockpile diagnostic, treatment, and vaccine production capabilities in the future
- Advocacy for engagement in the eradication agenda
- Sustained investments in malaria elimination and eradication, including innovative financing mechanisms.

CONCLUSIONS

Despite the absence of a highly efficacious vaccine, many countries around the globe have successfully eliminated malaria and prevented its reintroduction. As malaria elimination progresses in more areas, the case for global eradication is likely to become more compelling. Promising new tools are already in the product development pipeline, including radical treatments, sensitive rapid diagnostic tests, and next-generation vector control methods. Piloting the effective use of these innovations will ensure that they can be scaled up safely and effectively. The introduction of game-changing innovations—including anti-infection or transmission-blocking vaccines and novel mosquito control strategies—could substantially accelerate this next phase. As new technologies and advances occur, the cost of elimination may decline as efficiencies are realized and targeting becomes increasingly focused. Elimination may become progressively easier with new drug therapies, simplified treatment regimens, and more effective vaccines. With smallpox, the targeted nature of surveillance and containment and improved needle technology for vaccinations contributed significantly to the success of the eradicaton campaign.

Malaria eradication calls for a long-term investment that will yield dividends over time. If successful, countries would no longer need to implement prevention measures, thereby reaping an "eradication dividend" and accruing substantial economic benefits for all countries. However, eliminating malaria transmission worldwide will require renewed focus in several areas. Strengthening the human resource capacity of programs is essential. Combating the threat of importation will require collaborative regional surveillance efforts that reach communities and the private sector. In addition, as new tools become available, support will be required for their adoption and rapid uptake to combat the effects of drug and insecticide resistance. These actions all require sustained political and financial commitment to ensure success. While increasing numbers of countries are moving toward financing their own programs, external assistance to the last affected countries will be essential—possibly through a dedicated "last-mile fund"—to ensure that the resources required to complete eradication are available in the final phase.

ANNEXES

The following annexes to this chapter are as follows. They are available at http://www.dcp-3.org/infectiousdiseases.

- Annex 12A. Status and Goals of Elimination Countries, by Region
- Annex 12B. Regional Initiatives to Eliminate Malaria
- Annex 12C. Potential Financing Mechanisms for Malaria Elimination

NOTES

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US$1,045 or less
- Middle-income countries (MICs) are subdivided:
  (a) lower-middle-income = US$1,046 to US$4,125
  (b) upper-middle-income (UMICs) = US$4,126 to US$12,745
- High-income countries (HICs) = US$12,746 or more.

1. Sri Lanka obtained WHO certification as a malaria-free country in September 2016.
2. Algeria, Belize, Bhutan, Botswana, Cabo Verde, China, Comoros, Costa Rica, Ecuador, El Salvador, the Islamic Republic of Iran, Republic of Korea, Malaysia, Mexico, Nepal, Paraguay, Saudi Arabia, South Africa, Suriname, Swaziland, Timor-Leste.
3. Despite a highly receptive environment in Taiwan, China, intensive spraying combined with improved housing and socioeconomic conditions, better environmental management, and strong case management reduced morbidity to very low levels, and the WHO certified Taiwan, China, as being malaria free in 1965 (Yip 2000).
4. Polymerase chain reaction testing in African and Asian settings shows a higher proportion of both *P. malariae* and *P. ovale* infections than was previously thought (Baltzell and others 2013; Barrett 2007; Oguike and others 2011).
5. In the case of smallpox, there were no long-term carriers, survivors gained lifetime immunity, infections were easily detected, only symptomatic persons could transmit the disease, and vaccination of only 80 percent of the population was necessary to eliminate transmission (Barrett 2007).

REFERENCES

Abeyasinghe, R. R., G. N. Galappaththy, C. Smith Gueye, J. G. Kahn, and R. G. Feachem. 2012. "Malaria Control and Elimination in Sri Lanka: Documenting Progress and Success Factors in a Conflict Setting." *PLoS One* 7 (8): e43162.

Adams, J. S., and R. Victurine. 2011. "Permanent Conservation Trusts: A Study of the Long-Term Benefits of Conservation Endowments." Wildlife Conservation Society, Bronx, NY. http://www.dcnanature.org/wp-content/uploads/fundraising/Permanent-Conservation-Endowments.pdf.

Adjuik, M., T. Smith, S. Clark, J. Todd, A. Garrib, and others. 2006. "Cause-Specific Mortality Rates in Sub-Saharan Africa and Bangladesh." *Bulletin of the World Health Organization* 84 (3): 181–88.

Aksan, A.-M., and S. Chakraborty. 2013. "Childhood Disease and the Precautionary Demand for Children." *Journal of Population Economics* 26 (3): 855–85.

Amaratunga, C., P. Lim, S. Suon, S. Sreng, S. Mao, and others. 2016. "Dihydroartemisinin-Piperaquine Resistance in *Plasmodium falciparum* Malaria in Cambodia: A Multisite Prospective Cohort Study." *The Lancet Infectious Diseases* 16 (3): 357–65.

APLMA (Asia Pacific Leaders Malaria Alliance). 2015. "Asia-Pacific at the Forefront of a Global Movement to Eliminate Malaria." *APLMA Blog*, October 7. http://aplma .org/blog/22/asia-pacific-at-the-forefront-of-a-global -movement-to-eliminate-malaria/.

Ariey, F., B. Witkowski, C. Amaratunga, J. Beghain, A.-C. Langlois, and others. 2014. "A Molecular Marker of Artemisinin-Resistant *Plasmodium falciparum* Malaria." *Nature* 505 (7481): 50–55.

Asante, F. A., and K. Asenso-Okyere. 2003. *Economic Burden of Malaria in Ghana.* Geneva: WHO, African Regional Office.

Ashley, E. A., M. Dhorda, R. M. Fairhurst, C. Amaratunga, P. Lim, and others. 2014. "Spread of Artemisinin Resistance in *Plasmodium falciparum* Malaria." *New England Journal of Medicine* 371: 411–23.

Audibert, M., J. Mathonnat, and M. C. Henry. 2003. "Malaria and Property Accumulation in Rice Production Systems in the Savannah Zone of Côte d'Ivoire." *Tropical Medicine and International Health* 8 (5): 471–83.

Aylward, R. B., A. Acharya, S. England, M. Agocs, and J. Linkins. 2003. "Global Health Goals: Lessons from the Worldwide Effort to Eradicate Poliomyelitis." *The Lancet* 362 (9387): 909–14.

Badiane, O., and J. Ulimwengu. 2013. "Malaria Incidence and Agricultural Efficiency in Uganda." *Agricultural Economics* 44 (1): 15–23.

Baird, J. K. 2009. "Malaria Zoonoses." *Travel Medicine and Infectious Disease* 7 (5): 269–77.

———. 2015. "Point-of-Care G6PD Diagnostics for *Plasmodium vivax* Malaria Is a Clinical and Public Health Urgency." *BMC Medicine* 13 (December): 296.

Baltzell, K. A., D. Shakely, M. Hsiang, J. Kemere, A. S. Ali, and others. 2013. "Short Report: Prevalence of PCR Detectable Malaria Infection among Febrile Patients with a Negative *Plasmodium falciparum* Specific Rapid Diagnostic Test in Zanzibar." *American Journal of Tropical Medicine and Hygiene* 88 (2): 289–91.

Barclay, V., R. Smith, and J. Findeis. 2012. "Surveillance Considerations for Malaria Elimination." *Malaria Journal* 11: 304.

Barlow, R., and L. M. Grobar. 1986. "Costs and Benefits of Controlling Parasitic Diseases." Technical Note PHN 8517, Population, Health, and Nutrition Department, World Bank, Washington, DC.

Barreca, A. I. 2010. "The Long-Term Economic Impact of In Utero and Postnatal Exposure to Malaria." *Journal of Human Resources* 45 (4): 865–92.

Barrett, S. 2004. *Eradication versus Control: The Economics of Global Infectious Disease Policies.* Geneva: WHO.

———. 2007. "The Smallpox Eradication Game." *Public Choice* 130 (1): 179–207.

———. 2013. "Economic Considerations for the Eradication Endgame." *Philosophical Transactions of the Royal Society B: Biological Sciences* 368 (1623): 20120149.

Bart, K. J., J. Foulds, and P. Patriarca. 1996. "Global Eradication of Poliomyelitis: Benefit-Cost Analysis." *Bulletin of the World Health Organization* 74 (1): 35–45.

Bawah, A. A., and F. N. Binka. 2007. "How Many Years of Life Could Be Saved if Malaria Were Eliminated from a Hyperendemic Area of Northern Ghana?" *American Journal of Tropical Medicine & Hygiene* 77 (Suppl 6): 145–52.

Beaver, C. 2011. "Application of a Remoteness Index: Funding Malaria Programs." *International Journal of Geoinformatics* 7 (1).

Bhatt, S., D. J. Weiss, E. Cameron, D. Bisanzio, B. Mappin, and others. 2015. "The Effect of Malaria Control on *Plasmodium falciparum* in Africa between 2000 and 2015." *Nature* 526 (7572): 207–11.

Bhumiratana, A., P. Sorosjinda-Nunthawarasilp, W. Kaewwaen, P. Maneekan, and S. Pimnon. 2013. "Malaria-Associated Rubber Plantations in Thailand." *Travel Medicine and Infectious Disease* 11 (1): 37–50.

Blanford, S., N. E. Jenkins, A. F. Read, and M. B. Thomas. 2012. "Evaluating the Lethal and Pre-Lethal Effects of a Range of Fungi against Adult *Anopheles stephensi* Mosquitoes." *Malaria Journal* 11: 365.

Bleakley, H. 2003. "Disease and Development: Evidence from the American South." *Journal of the European Economic Association* 1 (2–3): 376–86.

———. 2010. "Malaria Eradication in the Americas: A Retrospective Analysis of Childhood Exposure." *American Economic Journal: Applied Economics* 2 (2): 1–45.

Boyd, M. F. 1939. "Malaria: Retrospect and Prospect." *American Journal of Tropical Medicine and Hygiene* 19: 1–6.

Brady, O. 2016. "Vectorial Capacity and Vector Control: Reconsidering Sensitivity to Parameters for Malaria Elimination." *Transactions of the Royal Society of Tropical Medicine and Hygiene* 110 (2): 107–17.

Bruce-Chwatt, L. J. 1959. "Malaria Research and Eradication in the USSR: A Review of Soviet Achievements in the Field of Malariology." *Bulletin of the World Health Organization* 21: 737–72.

Carrara, V., K. Lwin, A. Phyo, E. Ashley, J. Wiladphaingern, and others. 2013. "Malaria Burden and Artemisinin Resistance in the Mobile and Migrant Population on the Thai-Myanmar Border, 1999–2011: An Observational Study." *PLoS One* 10 (3): e1001398.

CEPA (Cambridge Economic and Policy Associates). 2013. "Financing for Malaria Elimination." CEPA and Global Health Group, University of California, San Francisco, CA.

Chen, I., S. E. Clarke, R. Gosling, B. Hamainza, G. Killeen, and others. 2016. "'Asymptomatic' Malaria: A Chronic and Debilitating Infection That Should Be Treated." *PLoS Medicine* 13 (1): e1001942.

Chiyaka, C., A. J. Tatem, J. M. Cohen, P. W. Gething, G. Johnston, and others. 2013. "The Stability of Malaria Elimination." *Science* 339 (6122): 909–10.

Chuma, J. M., M. Thiede, and C. S. Molyneux. 2006. "Rethinking the Economic Costs of Malaria at the Household Level: Evidence from Applying a New Analytical Framework in Rural Kenya." *Malaria Journal* 5: 76.

Chuquiyauri, R., M. Paredes, P. Penataro, S. Torres, S. Marin, and others. 2012. "Socio-Demographics and the Development of Malaria Elimination Strategies in the Low-Transmission Setting." *Acta Tropica* 121 (3): 292–302.

Cohen, J. M., S. Dlamini, J. M. Novotny, D. Kandula, S. Kunene, and others. 2013. "Rapid Case-Based Mapping of Seasonal Malaria Transmission Risk for Strategic Elimination Planning in Swaziland." *Malaria Journal* 12: 61.

Cohen, J. M., B. Moonen, R. W. Snow, and D. L. Smith. 2010. "How Absolute Is Zero? An Evaluation of Historical and Current Definitions of Malaria Elimination." *Malaria Journal* 9: 213.

Cohen, J. M., D. L. Smith, C. Cotter, A. Ward, G. Yamey, and others. 2012. "Malaria Resurgence: A Systematic Review and Assessment of Its Causes." *Malaria Journal* 11: 122.

Corran, P., P. Coleman, E. Riley, and C. Drakeley. 2007. "Serology: A Robust Indicator of Malaria Transmission Intensity?" *Trends in Parasitology* 23 (12): 575–82.

de Zulueta, J., and D. A. Muir. 1972. "Malaria Eradication in the Near East." *Transactions of the Royal Society of Tropical Medicine and Hygiene* 66 (5): 679–96.

Dhingra, N., P. Jha, V. P. Sharma, A. A. Cohen, R. M. Jotkar, and others. 2010. "Adult and Child Malaria Mortality in India: A Nationally Representative Mortality Survey." *The Lancet* 376 (9754): 1768–74.

Dondorp, A. M., F. Nosten, P. Yi, D. Das, A. P. Phyo, and others. 2009. "Artemisinin Resistance in *Plasmodium falciparum* Malaria." *New England Journal of Medicine* 361: 455–67.

Dua, V., S. Sharma, A. Srivastava, and V. Sharma. 1997. "Bioenvironmental Control of Industrial Malaria at Bharat Heavy Electricals Ltd., Hardwar, India: Results of a Nine-Year Study (1987–95)." *Journal of the American Mosquito Control Association* 13 (3): 278–85.

Durnez, L., and M. Coosemans. 2013. "Residual Transmission of Malaria: An Old Issue for New Approaches." In Anopheles Mosquitoes: *New Insights into Malaria Vectors,* edited by S. Manguin, 671–704. Rijeka: InTech.

Duru, V., N. Khim, R. Leang, S. Kim, A. Domergue, and others. 2015. "*Plasmodium falciparum* Dihydroartemisinin-Piperaquine Failures in Cambodia Are Associated with Mutant K13 Parasites Presenting High Survival Rates in Novel Piperaquine In Vitro Assays: Retrospective and Prospective Investigations." *BMC Medicine* 13: 305.

Eckhoff, P., J. Gerardin, and E. Wenger. 2015. "Mass Campaigns with Antimalarial Drugs: A Modelling Comparison of Artemether-Lumefantrine and DHA-Piperaquine with and without Primaquine as Tools for Malaria Control and Elimination." *BMC Infectious Diseases* 15: 144.

El Khyari, T. 2001. *Malaria Elimination Strategy in Morocco: Plan and Elements of Evaluation*. Unpublished report, Morocco Ministry of Health.

Eziefula, A. C., R. Gosling, J. Hwang, M. S. Hsiang, T. Bousema, and others. 2012. "Rationale for Short Course Primaquine in Africa to Interrupt Malaria Transmission." *Malaria Journal* 11 (1): 360.

Feachem, R. G., A. A. Phillips, J. Hwang, C. Cotter, B. Wielgosz, and others. 2010. "Shrinking the Malaria Map: Progress and Prospects." *The Lancet* 376 (9752): 1566–78.

Feachem, R. G., A. A. Phillips, and G. A. T. Targett, eds. 2009. *Shrinking the Malaria Map: A Prospectus on Malaria Elimination.* San Francisco, CA: Global Health Group, University of California San Francisco.

Filler, S. J., J. R. MacArthur, M. Parise, R. Wirtz, M. J. Eliades, and others. 2006. *Locally Acquired Mosquito-Transmitted Malaria: A Guide for Investigations in the United States.* Atlanta, GA: Centers for Disease Control and Prevention.

Floore, T. G. 2006. "Larval Control Practices: Past and Present." *Journal of the American Mosquito Control Association* 22 (3): 527–33.

Gallup, J. L., and J. D. Sachs. 2001. "The Economic Burden of Malaria." *American Journal of Tropical Medicine and Hygiene* 64 (Suppl 1–2): 85–96.

Gates, B., and R. Chambers. 2015. *From Aspiration to Action: What Will It Take to End Malaria?* Seattle, WA: Bill and Melinda Gates Foundation.

GHG (Global Health Group). 2013. "Malaria-Eliminating Country Briefings." GHG, University of California, San Francisco, CA.

———. 2014. "The Impact of the Global Fund's New Funding Model on the 34 Malaria-Eliminating Countries." GHG, University of California, San Francisco, CA.

———. 2016. "Analysing Technical Efficiency in Malaria Elimination Programs: A Self-Help Toolkit." Unpublished.

Girardin, O., D. Dao, B. G. Koudou, C. Esse, G. Cisse, and others. 2004. "Opportunities and Limiting Factors of Intensive Vegetable Farming in Malaria Endemic Côte d'Ivoire." *Acta Tropica* 89 (2): 109–23.

Gosling, J., P. Case, J. Tulloch, D. Chandramohan, C. Smith Gueye, and others. 2014. "Program Management Issues in Implementation of Elimination Strategies." GHG, University of California, San Francisco, CA.

Gosling, J., P. Case, J. Tulloch, D. Chandramohan, J. Wegbreit, and others. 2015. "Effective Program Management: A Cornerstone of Malaria Elimination." *American Journal of Tropical Medicine and Hygiene* 93 (1): 135–38.

Gosling, R. D., L. Okell, J. Mosha, and D. Chandramohan. 2011. "The Role of Antimalarial Treatment in the Elimination of Malaria." *Clinical Microbiology and Infection* 17 (11): 1617–23.

Government of India, Ministry of Health and Family Welfare. 2016. *National Framework for Malaria Elimination in India (2016–2030)*. New Delhi: Directorate of National Vector Borne Disease Control Programme. http://www.searo.who .int/india/publications/national.

Greenwood, B. M. 2008. "Control to Elimination: Implications for Malaria Research." *Trends in Parasitology* 24 (10): 449–54.

Guiguemdé, W. A., and R. K. Guy. 2012. "An All-Purpose Antimalarial Drug Target." *Cell Host and Microbe* 11 (6): 555–57.

Gupta, I., and S. Chowdhury. 2014. "Economic Burden of Malaria in India: The Need for Effective Spending." *South-East Asia Journal of Public Health* 3 (1): 95–102.

Hammond, A., R. Galizi, K. Kyrou, A. Simoni, C. Siniscalchi, and others. 2016. "A CRISPR-Cas9 Gene Drive System

Targeting Female Reproduction in the Malaria Mosquito Vector *Anopheles gambiae*." *Nature Biotechnology* 34 (4): 78–85.

Harris, I., W. W. Sharrock, L. M. Bain, K. A. Gray, A. Bobogare, and others. 2010. "A Large Proportion of Asymptomatic Plasmodium Infections with Low and Sub-Microscopic Parasite Densities in the Low-Transmission Setting of Temotu Province, Solomon Islands: Challenges for Malaria Diagnostics in an Elimination Setting." *Malaria Journal* 9: 254.

Helinski, M., M. Hassan, W. El-Motasim, C. A. Malcolm, B. G. Knols, and B. El-Sayed. 2008. "Towards a Sterile Insect Technique Field Release of *Anopheles arabiensis* Mosquitoes in Sudan: Irradiation, Transportation, and Field Case Experimentation." *Malaria Journal* 7: 65.

Hemingway, J., R. Shretta, T. N. C. Wells, D. Bell, A. A. Djimdé, and others. 2016. "Tools and Strategies for Malaria Control and Elimination: What Do We Need to Achieve a Grand Convergence in Malaria?" *PLoS Biology* 12 (3): e1002380.

Henderson, D. A. 1987. "Principles and Lessons from the Smallpox Eradication Programme." *Bulletin of the World Health Organization* 65 (4): 535–46.

Hien, T. T., N. T. Thuy-Nhien, N. H. Phu, M. F. Boni, N. V. Thanh, and others. 2012. "In Vivo Susceptibility of *Plasmodium falciparum* to Artesunate in Binh Phuoc Province, Vietnam." *Malaria Journal* 11: 355.

Hiwat, H., L. S. Hardjopawiro, W. Takken, and L. Villegas. 2012. "Novel Strategies Lead to Pre-Elimination of Malaria in Previously High-Risk Areas in Suriname, South America." *Malaria Journal* 11: 10.

Hong, S. C. 2011. "Malaria and Economic Productivity: A Longitudinal Analysis of the American Case." *Journal of Economic History* 71 (3): 654–71.

———. 2013. "Malaria: An Early Indicator of Later Disease and Work Level." *Journal of Health Economics* 32 (3): 612–32.

Horton, R. 2015. "Vaccines: A Step Change in Malaria Prevention?" *The Lancet* 385 (9978): 1591.

Hotez, P. J. 2009. "Mass Drug Administration and Integrated Control for the World's High-Prevalence Neglected Tropical Diseases." *Clinical Pharmacology and Therapeutics* 85 (6): 659–64.

Howard, A. F., R. N'Guessan, C. J. Koenraadt, A. Asidi, M. Farenhorst, and others. 2011. "First Report of the Infection of Insecticide-Resistant Malaria Vector Mosquitoes with an Entomopathogenic Fungus under Field Conditions." *Malaria Journal* 10: 24.

Howes, R. E., F. B. Piel, A. P. Patil, O. A. Nyangiri, P. W. Gething, and others. 2012. "G6PD Deficiency Prevalence and Estimates of Affected Populations in Malaria Endemic Countries: A Geostatistical Model-Based Map." *PLoS Medicine* 9 (11): e1001339.

Hoyer, S., S. Nguon, S. Kim, N. Habib, N. Khim, and others. 2012. "Focused Screening and Treatment (FSAT): A PCR-Based Strategy to Detect Malaria Parasite Carriers and Contain Drug-Resistant *P. Falciparum*, Pailin, Cambodia." *PLoS One* 7 (1): e45797.

Hsiang, M. S., B. Greenhouse, and P. J. Rosenthal. 2014. "Point of Care Testing for Malaria Using LAMP, Loop Mediated Isothermal Amplification." *Journal of Infectious Diseases* 210 (8): 1167–69.

Hsiang, M. S., J. Hwang, S. Kunene, C. Drakeley, D. Kandula, and others. 2012. "Surveillance for Malaria Elimination in Swaziland: A National Cross-Sectional Study Using Pooled PCR and Serology." *PLoS One* 7 (1): 329550.

Imwong, M., S. Hanchana, B. Malleret, L. Renia, N. P. Day, and others. 2014. "High-Throughput Ultrasensitive Molecular Techniques for Quantifying Low-Density Malaria Parasitemias." *Journal of Clinical Microbiology* 52 (9): 3303–9.

Jackson, S., A. C. Sleigh, and X. L. Liu. 2002. "Cost of Malaria Control in China: Henan's Consolidation Programme from Community and Government Perspectives." *Bulletin of the World Health Organization* 80 (8): 653–59.

John, G. K., N. M. Douglas, L. von Seidlein, F. Nosten, J. K. Baird, and others. 2012. "Primaquine Radical Cure of *Plasmodium vivax*: A Critical Review of the Literature." *Malaria Journal* 11: 280.

John, R., T. Ephraim, and A. Andrew. 2008. "Reduced Susceptibility to Pyrethroid Insecticide Treated Nets by the Malaria Vector *Anopheles gambiae s. l.* in Western Uganda." *Malaria Journal* 7: 92.

Kahn, J. G., S. Basu, C. Boyle, M. S. Hsiang, D. T. Jamison, and others. 2009. "Financing Elimination." In *Shrinking the Malaria Map: A Prospectus on Malaria Elimination*, edited by R. G. Feachem, A. A. Phillips, and G. A. Targett, 61–80. San Francisco, CA: GHG, University of California.

Kaneko, A., G. Taleo, M. Kalkoa, S. Yamar, T. Kobayakawa, and A. Bjorkman. 2000. "Malaria Eradication on Islands." *The Lancet* 356 (9241): 1560–64.

Katz, T. M., J. H. Miller, and A. A. Hebert. 2008. "Insect Repellents: Historical Perspectives and New Developments." *Journal of the American Academy of Dermatology* 58 (5): 865–71.

Kelly, G. C., M. Tanner, A. Vallely, and A. Clements. 2012. "Malaria Elimination: Moving Forward with Spatial Decision Support Systems." *Trends in Parasitology* 28 (7): 297–304.

Khan, M. J. 1966. "Estimate of Economic Loss due to Malaria in West Pakistan." *Pakistan Journal of Health* 16 (3): 187–93.

Khan, M. M., and J. Ehreth. 2003. "Costs and Benefits of Polio Eradication: A Long-Run Global Perspective." *Vaccine* 21 (7–8): 702–5.

Killeen, G. F. 2014. "Characterizing, Controlling and Eliminating Residual Transmission." *Malaria Journal* 13: 330.

Kimani, E. W., J. M. Vulule, I. W. Kuria, and F. Mugisha. 2006. "Use of Insecticide-Treated Clothes for Personal Protection against Malaria: A Community Trial." *Malaria Journal* 5: 63.

Kondrashin, A. V. 1992. "Malaria in the WHO Southeast Asia Region." *Indian Journal of Malariology* 29 (3): 129–60.

Kühner, A. 1971. "The Impact of Public Health Programs on Economic Development: Report of a Study of Malaria in Thailand." *International Journal of Health Services* 1 (3): 285–92.

Leang, R., A. Barrette, D. M. Bouth, D. Ménard, R. Abdur, and others. 2013. "Efficacy of Dihydroartemisinin-Piperaquine for Treatment of Uncomplicated *Plasmodium falciparum* and *Plasmodium vivax* in Cambodia, 2008 to 2010." *Antimicrobial Agents and Chemotherapy* 57 (2): 818–26.

Leang, R., W. R. Taylor, D. M. Bouth, L. Song, J. Tarning, and others. 2015. "Evidence of *Plasmodium falciparum* Malaria Multidrug Resistance to Artemisinin and Piperaquine in Western Cambodia: Dihydroartemisinin-Piperaquine Open-Label Multicenter Clinical Assessment." Antimicrobial Agents and Chemotherapy 59 (8): 4719–26.

Le Menach, A., A. J. Tatem, J. M. Cohen, S. I. Hay, H. Randell, and others. 2011. "Travel Risk, Malaria Importation, and Malaria Transmission in Zanzibar." *Scientific Reports* 1 (93): 1–7.

Lindblade, K. A., L. Steinhardt, A. Samuels, S. P. Kachur, and L. Slutsker. 2013. "The Silent Threat: Asymptomatic Parasitemia and Malaria Transmission." *Expert Review of Anti-Infective Therapy* 11 (6): 623–39.

Lines, J., C. J. M. Whitty, and K. Hanson. 2007. *Prospects for Eradication and Elimination of Malaria*. London: London School of Hygiene and Tropical Medicine.

Liu, J. X., G. Newby, A. Brackery, C. Smith Gueye, C. J. Candari, and others. 2013. "Determinants of Malaria Program Expenditures during Elimination: Case Study Evidence from Select Provinces in the Philippines." *PLoS One* 8 (9): e73352.

Livadas, G., and D. Athanassatos. 1963. "The Economic Benefits of Malaria Eradication in Greece." *Rivista de Malariologia* 42 (December): 177–87.

Llanos-Cuentas, A., M. V. Lacerda, R. Rueangweerayut, S. Krudsood, S. K. Gupta, and others. 2014. "Tafenoquine Plus Chloroquine for the Treatment and Relapse Prevention of *Plasmodium vivax* Malaria (Detective): A Multicentre, Double-Blind, Randomised, Phase 2b Dose-Selection Study." *The Lancet* 383 (9922): 1049–58.

Lon, C., J. E. Manning, P. Vanachayangkul, M. So, D. Sea, and others. 2014. "Efficacy of Two Versus Three-Day Regimens of Dihydroartemisinin-Piperaquine for Uncomplicated Malaria in Military Personnel in Northern Cambodia: An Open-Label Randomized Trial." *PLoS One* 9 (3): e9313

Lubell, Y., A. Dondorp, P. Guerin, T. Drake, S. Meek, and others. 2014. "Artemisinin Resistance: Modelling the Potential Human and Economic Costs." *Malaria Journal* 13: 452.

Lucas, A. M. 2010. "The Impact of Malaria Eradication on Fertility and Education." Department of Economics, Wellesley College, Wellesley, MA.

Luckhart, S., S. W. Lindsay, A. A. James, and T. W. Scott. 2010. "Reframing Critical Needs in Vector Biology and Management of Vector-Borne Disease." *PLoS Neglected Tropical Diseases* 4 (2): e566.

Maartens, F., B. Sharp, B. Curtis, J. Mthembu, and I. Hatting. 2007. "The Impact of Malaria Control on Perceptions of Tourists and Tourism Operators Concerning Malaria Prevalence in Kwazulu-Natal, 1999/2000 versus 2002/2003." *Journal of Travel Medicine* 14 (2): 96–104.

Magris, M., Y. Rubio-Palis, N. Alexander, B. Ruiz, N. Galván, and others. 2007. "Community-Randomized Trial of Lambdacyhalothrin-Treated Hammock Nets for Malaria Control in Yanomami Communities in the Amazon Region of Venezuela." *Tropical Medicine and International Health* 13 (3): 392–402.

Manguin, S., P. Carnevale, and J. Mouchet. 2008. *Biodiversity of Malaria in the World.* London: John Libbey Eurotext.

Marston, L., G. C. Kelly, E. Hale, A. C. Clements, A. Hodge, and others. 2014. "Cost Analysis of the Development and Implementation of a Spatial Decision Support System for Malaria Elimination in Solomon Islands." *Malaria Journal* 13: 325.

Matowo, N. S., J. Moore, S. Mapua, E. P. Madumla, I. R. Moshi, and others. 2013. "Using a New Odour-Baited Device to Explore Options for Luring and Killing Outdoor-Biting Malaria Vectors: A Report on Design and Field Evaluation of the Mosquito Landing Box." *Parasites and Vectors* 6 (May): 137.

Maude, R., W. Pontavornpinyo, S. Saralamba, R. Aguas, S. Yeung, and others. 2009. "The Last Man Standing Is the Most Resistant: Eliminating Artemisinin-Resistant Malaria in Cambodia." *Malaria Journal* 8: 31.

Maude, R. J., D. Socheat, C. Nguon, P. Saroth, P. Dara, and others. 2012. "Optimising Strategies for *Plasmodium falciparum* Malaria Elimination in Cambodia: Primaquine, Mass Drug Administration and Artemisinin Resistance." *PLoS One* 7 (5): e37166.

McCarthy, F. D., H. Wolf, and Y. Wu. 2000. "The Growth Costs of Malaria." NBER Working Paper, National Bureau of Economic Research, Cambridge, MA.

Ménard, D., N. Khim, J. Beghain, A. A. Adegnika, M. Shafiul Alam, and others. 2016. "A Worldwide Map of *Plasmodium falciparum* K13-Propeller Polymorphisms." *New England Journal of Medicine* 374: 2453–64.

Mendis, K., A. Rietveld, M. Warsame, A. Bosman, G. Greenwood, and others. 2009. "From Malaria Control to Eradication: The WHO Perspective." *Tropical Medicine and International Health* 14 (7): 802–9.

Mills, A., Y. Lubell, and K. Hanson. 2008. "Malaria Eradication: The Economic, Financial, and Institutional Challenge." *Malaria Journal* 7 (Suppl 1): S11.

Modrek, S., J. Liu, R. Gosling, and R. G. Feachem. 2012. "The Economic Benefits of Malaria Elimination: Do They Include Increases in Tourism?" *Malaria Journal* 11: 244.

Moonen, B., S. Barrett, J. Tullock, and D. T. Jamison. 2009. "Making the Decision." In *Shrinking the Malaria Map: A Prospectus on Malaria Elimination,* edited by R. G. Feachem, A. A. Phillips, and G. Targett. San Francisco, CA: GHG, University of California.

Moonen, B., J. M. Cohen, R. W. Snow, L. Slutsker, C. Drakeley, and others. 2010. "Operational Strategies to Achieve and Maintain Malaria Elimination." *The Lancet* 376 (9752): 1592–603.

Moonen, B., J. M. Cohen, A. J. Tatem, J. Cohen, S. I. Hay, and others. 2010. "A Framework for Assessing the Feasibility of Malaria Elimination." *Malaria Journal* 9: 322.

Mosha, J. F., H. J. Sturrock, B. Greenhouse, B. Greenwood, C. J. Sutherland, and others. 2013. "Epidemiology of Subpatent *Plasmodium falciparum* Infection: Implications for Detection of Hotspots with Imperfect Diagnostics." *Malaria Journal* 12: 2221.

Müller, G. C., J. C. Beier, S. F. Traore, M. B. Toure, M. M. Traore, and others. 2010. "Successful Field Trial of Attractive Toxic Sugar Bait (ATSB) Plant-Spraying Methods against Malaria Vectors in the *Anopheles gambiae* Complex in Mali, West Africa." *Malaria Journal* 9: 210.

Nabarro, D. N., and E. M. Taylor. 1998. "The Roll Back Malaria Campaign." *Science* 280 (5372): 2062–68.

Najera, J. A. 1999. "Malaria Control Achievements, Problems, and Strategies." WHO and Roll Back Malaria Partnership, Geneva.

Najera, J. A., M. Gonzalez-Silva, and P. L. Alonso. 2011. "Some Lessons for the Future from the Global Malaria Eradication Programme (1955–1969)." *PLoS Medicine* 8 (1): e1000412. doi:10.1371/journal.pmed.1000412.

Newby, G., A. Bennett, E. Larson, C. Cotter, R. Shretta, and others. 2016. "The Path to Eradication: A Progress Report on the Malaria-Eliminating Countries." *The Lancet* 387 (10029): 177–84.

Newby, G., J. Hwang, K. Koita, I. Chen, B. Greenwood, and others. 2015. "Review of Mass Drug Administration for Malaria and Its Operational Challenges." *American Journal of Tropical Medicine and Hygiene* 93 (1): 125–34.

Ngomane, L., and C. de Jager. 2012. "Changes in Malaria Morbidity and Mortality in Mpumalanga Province, South Africa (2001–2009): A Retrospective Study." *Malaria Journal* 11: 19.

Ngufor, C., M. Chouaïbou, E. Tchicaya, B. Loukou, N. Kesse, and others. 2014. "Combining Organophosphate-Treated Wall Linings and Long-Lasting Insecticidal Nets Fails to Provide Additional Control over Long-Lasting Insecticidal Nets Alone against Multiple Insecticide-Resistant *Anopheles gambiae* in Côte d'Ivoire: An Experimental Hut Trial." *Malaria Journal* 13: 396.

Niazi, A. D. 1969. "Approximate Estimates of the Economic Loss Caused by Malaria with Some Estimates of the Benefits of M.E.P." *Bulletin of Endemic Diseases* 11 (1): 28–39.

Nikolaeva, D., S. J. Draper, and S. Biswas. 2015. "Toward the Development of Effective Transmission-Blocking Vaccines for Malaria." *Expert Review of Vaccines* 14 (5): 653–80.

Ogoma, S. B., S. H. Moore, and M. Maia. 2012. "A Systematic Review of Mosquito Coils and Passive Emanators: Defining Recommendations for Spatial Repellency Testing Methodologies." *Parasites and Vectors* 5 (1): 287.

Oguike, M. C., M. Betson, M. Burke, D. Nolder, J. R. Stothard, and others. 2011. "*Plasmodium ovale curtisi* and *Plasmodium ovale wallikeri* Circulate Simultaneously in African Communities." *International Journal of Parasitology* 41 (6): 677–83.

Ohrt, C., K. W. Roberts, H. J. Sturrock, J. Wegbreit, B. Y. Lee, and others. 2015. "Surveillance Systems for Malaria Elimination." GHG, University of California, San Francisco, CA.

Okell, L. C., T. Bousema, J. T. Griffin, A. L. Ouedraogo, A. C. Ghani, and others. 2012. "Factors Determining the Occurrence of Submicroscopic Malaria Infections and Their Relevance for Control." *Nature Communications* 3: 1237.

Okorosobo, T., F. Okorosobo, G. Mwabu, J. N. Orem, and J. M. Kirigia. 2011. "Economic Burden of Malaria in Six Countries of Africa." *European Journal of Business and Management* 3 (6): 42–62.

Orem, J. N., J. M. Kirigia, R. Azairwe, I. Kasirye, and O. Walker. 2012. "Impact of Malaria Morbidity on Gross Domestic Product in Uganda." *International Archives of Medicine* 5: 12.

Ortiz, J. R. 1968. "Estimación del costo de un programa de erradicación del paludismo." *Boletín de la Oficina Sanitaria Panamericana* 64 (2): 110–15.

Oxborough, R. M., J. Kitau, F. W. Mosha, and M. W. Rowland. 2015. "Modified Veranda-Trap Hut for Improved Evaluation of Vector Control Interventions." *Medical and Veterinary Entomology* 29 (4): 371–79.

Pertakis, R., and W. D. Savedoff. 2014. *An Introduction to Cash on Delivery: Aid for Funders*. Washington, DC: Center for Global Development.

Phyo, A. P., S. Nkhoma, K. Stepniewska, E. A. Ashley, S. Nair, and others. 2012. "Emergence of Artemisinin-Resistant Malaria on the Western Border of Thailand: A Longitudinal Study." *The Lancet* 379 (9830): 1960–66.

Poché, R. M., D. Burruss, L. Polyakova, D. M. Poché, and R. B. Garlapati. 2015. "Treatment of Livestock with Systemic Insecticides for Control of *Anopheles arabiensis* in Western Kenya." *Malaria Journal* 14: 351. doi:10.1186/s12936-015-0883-0.

Poirot, E., J. Skarbinski, D. Sinclair, S. P. Kachur, L. Slutsker, and others. 2013. "Mass Drug Administration for Malaria." *Cochrane Database of Systematic Reviews* 12: CD008846.

Pooda, H. S., J. B. Rayaisse, D. F. de Sale Hien, T. Lefèvre, S. R. Yerbanga, and others. 2015. "Administration of Ivermectin to Peridomestic Cattle: A Promising Approach to Target the Residual Transmission of Human Malaria." *Malaria Journal* 14: 496.

Prakash, A., D. R. Bhattacharyya, P. K. Mohapatra, U. Barua, A. Phukan, and others. 2003. "Malaria Control in a Forest Camp in an Oil Exploration Area of Upper Assam." *National Medical Journal of India* 16 (3): 135–38.

Purdy, M., M. Robinson, K. Wei, and D. Rublin. 2013. "The Economic Case for Combating Malaria." *American Journal of Tropical Medicine and Hygiene* 89 (5): 819–23.

Qualls, W., G. Müller, S. Traore, M. M. Traore, K. L. Arheart, and others. 2015. "Indoor Use of Attractive Toxic Sugar Bait (ATSB) to Effectively Control Malaria Vectors in Mali, West Africa." *Malaria Journal* 14: 301.

Rajahram, G. S., B. E. Barber, T. William, J. Menon, N. M. Anstey, and others. 2012. "Deaths Due to *Plasmodium knowlesi* Malaria in Sabah, Malaysia: Association with Reporting as *Plasmodium malariae* and Delayed Parenteral Artesunate." *Malaria Journal* 11: 284.

Ramaiah, T. 1980. *Cost-Benefit Analysis of Malaria Control and Eradication Programme in India*. Ahmedabad: Public Systems Group, Indian Institute of Management.

Ranson, H., R. N'Guessan, J. Lines, N. Moiroux, Z. Nkuni, and others. 2011. "Pyrethroid Resistance in African Anopheline Mosquitoes: What Are the Implications for Malaria Control?" *Trends in Parasitology* 27 (2): 91–98.

Rezaei-Hemami, M., A. Akbari-Sari, A. Raiesi, H. Vatandoost, and R. Majdzadeh. 2013. "Cost Effectiveness of Malaria

Interventions from Preelimination through Elimination: A Study in Iran." *Journal of Arthropod-Borne Diseases* 8 (1): 43.

RBM (Roll Back Malaria) Partnership. 2008. "The Global Malaria Action Plan: For a Malaria-Free World." WHO, Geneva.

———. 2015. *Action and Investment to Defeat Malaria 2016–2030: For a Malaria-Free World*. Geneva: WHO on behalf of the RBM Partnership Secretariat.

Rowland, M., N. Durrani, S. Hewitt, N. Mohammed, M. Bouma, and others. 1999. "Permethrin-Treated Chaddars and Top-Sheets: Appropriate Technology for Protection against Malaria in Afghanistan and Other Complex Emergencies." *Transactions of the Royal Society of Tropical Medicine and Hygiene* 93 (5): 465–72.

Rowland, M., N. Durrani, M. Kenward, N. Mohammed, H. Urahman, and others. 2001. "Control of Malaria in Pakistan by Applying Deltamethrin Insecticide to Cattle: A Community-Randomised Trial." *The Lancet* 357 (9271): 1837–41.

RTSS Clinical Trials Partnership. 2015. "Efficacy and Safety of RTS,S/AS01 Malaria Vaccine with or without a Booster Dose in Infants and Children in Africa: Final Results of a Phase 3, Individually Randomised, Controlled Trial." *The Lancet* 386 (9988): 31–45.

Sabot, O., J. M. Cohen, M. S. Hsiang, J. G. Kahn, S. Basu, and others. 2010. "Costs and Financial Feasibility of Malaria Elimination." *The Lancet* 376 (9752): 1604–15.

Samaraweera, K. 2015. "Sri Lanka Eligible for WHO Malaria-Free Certification." *The Nation*, October 3.

Saunders, D., and C. Lon. 2016. "Combination Therapies for Malaria Are Failing—What Next?" *The Lancet Infectious Diseases* 16 (3): 274–75.

Shah, N. K. 2010. "Assessing Strategy and Equity in the Elimination of Malaria." *PLoS Medicine* 7 (8): e1000312.

Shamuradova, L., S. Alieva, R. Kurdova-Mintcheva, A. Rietveld, R. Cibulskis, and others. 2012. "Achieving Malaria Elimination and Certification in Turkmenistan." *Malaria Journal* 11: O11.

Sharma, V. P. 1996. "Malaria: Cost to India and Future Trends." *Southeast Asian Journal of Tropical Medicine and Public Health* 27 (1): 4–14.

Shono, Y., V. Jean-Francois, Y. Saint Jean, and T. Itoh. 1991. "Field Evaluation of Ultra-Low Volume Applications with a Mixture of D-Allethrin and D-Phenothrin for Control of *Anopheles albimanus* in Haiti." *Journal of the American Mosquito Control Association* 7 (3): 494–95.

Shretta, R., A. L. V. Avancena, and A. Hatefi. 2016. "The Economics of Malaria Control and Elimination: A Systematic Review." *Malaria Journal* 15: 593.

Shretta, R., R. Baral, A. L. Avancena, K. Fox, A. P. Dannoruwa, and others. 2017. "An Investment Case for Preventing the Re-Introduction of Malaria in Sri Lanka." *American Journal of Tropical Medicine & Hygiene* 96 (3): 602–15.

Sissoko, M. S., L. L. Van Den Hoogen, Y. Samake, A. Tapily, A. Z. Diarra, and others. 2015. "Spatial Patterns of *Plasmodium falciparum* Clinical Incidence, Asymptomatic Parasite Carriage and *Anopheles* Density in Two Villages in Mali." *American Journal of Tropical Medicine and Hygiene* 3 (4): 790–97.

Smith, D. L., J. M. Cohen, C. Chiyaka, G. Johnston, P. W. Gething, and others. 2013. "A Sticky Situation: The Unexpected Stability of Malaria Elimination." *Philosophical Transactions of the Royal Society of London, Series B Biological Sciences* 368 (1623): 20120145.

Smith, D. L., S. I. Hay, A. M. Noor, and R. W. Snow. 2009. "Predicting Changing Malaria Risk after Expanded Insecticide-Treated Net Coverage in Africa." *Trends in Parasitology* 25 (11): 511–16.

Smith Gueye, C., M. Gerigk, G. Newby, C. Lourenco, P. Uusiku, and others. 2014. "Namibia's Path toward Malaria Elimination: A Case Study of Malaria Strategies and Costs along the Northern Border." *BMC Public Health* 14: 1190.

Smith Gueye, C., K. C. Sanders, G. N. Galappaththy, C. Rundi, T. Tobgay, and others. 2013. "Active Case Detection for Malaria Elimination: A Survey among Asia Pacific Countries." *Malaria Journal* 12: 358.

Somi, M. F., J. R. Butler, F. Vahid, J. D. Njau, and S. Abdulla. 2009. "Household Responses to Health Risks and Shocks: A Study from Rural Tanzania Raises Some Methodological Issues." *Journal of International Development* 21 (2): 200–11.

Spring, M. D., J. T. Lin, J. E. Manning, J. P. Vanachayangkul, S. Somethy, and others. 2015. "Dihydroartemisinin-Piperaquine Failure Associated with a Triple Mutant Including Kelch13 C580Y in Cambodia: An Observational Cohort Study." *The Lancet Infectious Diseases* 15 (6): 683–91

Sri Lanka Ministry of Health. 2014. "National Malaria Strategic Plan for Elimination and Prevention of Re-Introduction 2014–2018." Anti-Malaria Campaign, Colombo.

Steenkeste, N., W. O. Rogers, L. Okell, I. Jeanne, S. Incardona, and others. 2010. "Sub-Microscopic Malaria Cases and Mixed Malaria Infection in a Remote Area of High Malaria Endemicity in Rattanakiri Province, Cambodia: Implication for Malaria Elimination." *Malaria Journal* 9: 108.

Straimer, J., N. F. Gnadig, B. Witkowski, C. Amaratunga, V. Duru, and others. 2015. "Drug Resistance: K13-Propeller Mutations Confer Artemisinin Resistance in *Plasmodium falciparum* Clinical Isolates." *Science* 347 (6220): 428–31.

Strode, C., S. Donegan, P. Garner, A. A. Enayati, and J. Hemingway. 2014. "The Impact of Pyrethroid Resistance on the Efficacy of Insecticide-Treated Bed Nets against African Anopheline Mosquitoes: Systematic Review and Meta-Analysis." *PLoS Medicine* 11 (3): e1001619. doi:10.1371/journal.pmed.1001619.

Sturrock, H. J., M. S. Hsiang, J. M. Cohen, D. L. Smith, B. Greenhouse, and others. 2013. "Targeting Asymptomatic Malaria Infections: Active Surveillance in Control and Elimination." *PLoS Medicine* 10 (6): e1001467.

Sturrock, H. J., K. Roberts, J. Wegbreit, C. Ohrt, and R. Gosling. 2014. "Effective Responses to Malaria Importation." GHG, University of California, San Francisco, CA.

Suarez Torres, G. 1970a. "El programa de erradicación del paludismo: Plan de seis años." *Salud Pública Mexicana* 12 (6): 751–73.

———. 1970b. "El programa de erradicación del paludismo: Resumen del plan con incremento regional de operaciones en parte de la vertiente del Golfo de México y en la Península de Yucatán." *Salud Pública Mexicana* 12 (6): 745–50.

Surabattula, R., M. P. Vejandla, P. C. Mallepaddi, K. Faulstich, and R. Polavarapu. 2013. "Simple, Rapid, Inexpensive Platform for the Diagnosis of Malaria by Loop Mediated Isothermal Amplification (LAMP)." *Experimental Parasitology* 134 (3): 333–40.

Tanner, M., and D. de Savigny. 2008. "Malaria Eradication Back on the Table." *Bulletin of the World Health Organization* 86 (2): 82.

Tanner, M., B. Greenwood, C. Whitty, E. K. Ansah, R. N. Price, and others. 2015. "Malaria Eradication and Elimination: Views on How to Translate a Vision into Reality." *BMC Medicine* 13: 167.

Takala-Harrison, S., C. G. Jacob, C. Arze, M. P. Cummings, J. C. Silva, and others. 2015. "Independent Emergence of Artemisinin Resistance Mutations among *Plasmodium falciparum* in Southeast Asia." *Journal of Infectious Diseases* 211 (5): 670–79.

Tao, Z. Y., H. Y. Zhou, H. Xia, S. Xu, H. W. Zhu, and others. 2011. "Adaptation of a Visualized Loop-Mediated Isothermal Amplification Technique for Field Detection of *Plasmodium vivax* Infection." *Parasites and Vectors* 4: 115.

Tatarsky, A., S. Aboobakar, J. M. Cohen, N. Gopee, A. Bheecarry, and others. 2011. "Preventing the Reintroduction of Malaria in Mauritius: A Programmatic and Financial Assessment." *PLoS One* 6 (9): e23832.

Tatem, A. J., Z. Huang, C. Narib, U. Kumar, D. Kandula, and others. 2014. "Integrating Rapid Risk Mapping and Mobile Phone Call Record Data for Strategic Malaria Elimination Planning." *Malaria Journal* 13: 52.

Taylor, C. E., F. Cutts, and M. E. Taylor. 1997. "Ethical Dilemmas in Current Planning for Polio Eradication." *American Journal of Public Health* 87 (6): 922–25.

Thang, N. D., A. Erhart, N. Speybroeck, N. X. Xa, N. N. Thanh, and others. 2009. "Long-Lasting Insecticidal Hammocks for Controlling Forest Malaria: A Community-Based Trial in a Rural Area of Central Vietnam." *PLoS One* 4 (10): e7369.

Tobgay, T., C. E. Torres, and K. Na-Bangchang. 2011. "Malaria Prevention and Control in Bhutan: Successes and Challenges." *Acta Tropica* 117 (3): 225–28.

Tran, T. M., S. Portugal, S. J. Draper, and P. D. Crompton. 2015. "Malaria Vaccines: Moving forward after Encouraging First Steps." *Current Tropical Medicine Reports* 2 (1): 1–3.

Trape, J. F., A. Tall, N. Diagne, O. Ndiath, A. B. Ly, and others. 2011. "Malaria Morbidity and Pyrethroid Resistance after the Introduction of Insecticide-Treated Bednets and Artemisinin-Based Combination Therapies: A Longitudinal Study." *The Lancet Infectious Diseases* 11 (12): 925–32.

Tulloch, J, B. David, R. D. Newman, and S. Meek. 2013. "Artemisinin-Resistant Malaria in the Asia-Pacific Region." *The Lancet* 381 (9881): e16–17.

Turkmenistan Ministry of Health and Medical Industry, WHO (World Health Organization), and the University of California, San Francisco, Global Health Group. 2012. "Eliminating Malaria: Case-Study 1: Achieving Elimination in Turkmenistan." Geneva: WHO.

Tusting, L. S., M. M. Ippolito, B. A. Willey, I. Kleinschmidt, G. Dorsey, and others. 2015. "The Evidence for Improving Housing to Reduce Malaria: A Systematic Review and Meta-Analysis." *Malaria Journal* 14 (1): 209.

United Nations. 2015. "African Leaders Call for Elimination of Malaria by 2030." Office of the UN Secretary-General's Special Envoy for Financing the Health Millennium Development Goals and for Malaria. MDG Health Envoy-News, February 3. http://www.mdghealthenvoy.org/african -leaders-call-for-elimination-of-malaria-by-2030/.

Utzinger, J., Y. Tozan, F. Doumani, and B. H. Singer. 2002. "The Economic Payoffs of Integrated Malaria Control in the Zambian Copperbelt between 1930 and 1950." *Tropical Medicine and International Health* 7 (8): 657–77.

Wells, T. N., and R. Hooft van Huijsduijnen. 2015. "Ferroquine: Welcome to the Next Generation of Antimalarials." *The Lancet Infectious Diseases* 15 (12): 1365–66.

Wells, T. N., R. Hooft van Huijsduijnen, and W. C. Van Voorhis. 2015. "Malaria Medicines: A Glass Half Full?" *Nature Reviews Drug Discovery* 14 (6): 424–42.

Wernsdorfer, W. H., and R. L. Kouznetzov. 1980. "Drug Resistant Malaria: Occurrence, Control and Surveillance." *Bulletin of the World Health Organization* 58 (3): 342–352.

Wesolowski, A., N. Eagle, A. J. Tatem, D. L. Smith, A. M. Noor, and others. 2012. "Quantifying the Impact of Human Mobility on Malaria." *Science* 338 (6104): 267–70.

White, N. J. 2013. "Primaquine to Prevent Transmission of *falciparum* Malaria." *The Lancet Infectious Diseases* 13 (2): 175–81.

WHO (World Health Organization). 1968. "WHO Expert Committee on Malaria: Fourteenth Report." WHO Technical Report Series, Geneva: WHO.

———. 1969. "Re-examination of the Global Strategy of Malaria Eradication." Twenty-Second World Health Assembly, Part I. WHO official records number 176, annex 13, 106–26.

———. 1993. "A Global Malaria Control Strategy." WHO, Geneva.

———. 2005. "The Tashkent Declaration: The Move from Malaria Control to Elimination." WHO Regional Office for Europe, Copenhagen.

———. 2006. *Malaria Vector Control and Personal Protection: Report of a WHO Study Group*. WHO Technical Report Series 936. Geneva: WHO.

———. 2007. *Malaria Elimination: A Field Manual for Low and Moderate Endemic Countries.* Geneva: WHO.

———. 2010. "Turkmenistan Certified Malaria-Free." WHO Regional Office for Europe, Copenhagen.

———. 2012a. "Drug Resistance Threatens Malaria Control." WHO, Geneva.

———. 2012b. *Handbook for Integrated Vector Management.* Geneva: WHO.

———. 2012c. "The Role of Larviciding for Malaria Control in Sub-Saharan Africa." WHO, Geneva.

———. 2012d. *World Malaria Report 2012*. Geneva: WHO.

———. 2013. *World Malaria Report 2013*. Geneva: WHO.

———. 2014a. *From Malaria Control to Malaria Elimination: A Manual for Elimination Scenario Planning.* Geneva: WHO.

———. 2014b. "Policy Brief on Malaria Diagnostics in Low-Transmission Settings." WHO, Geneva. http://www.who

.int/malaria/publications/atoz/malaria-diagnosis-low -transmission-settings-sep2014.pdf.

———. 2015a. *Global Technical Strategy for Malaria 2016–2030*. Geneva: WHO.

———. 2015b. "Q&A on Artemisinin Resistance." WHO, Geneva. http://who.int/malaria/media/artemisinin_resistance_qa/en/.

———. 2015c. "Recommendations on the Role of Mass Drug Administration, Mass Screening and Treatment, and Focal Screening and Treatment for Malaria." WHO, Geneva. http://www.who.int/malaria/publications/atoz/role-of -mda-for-malaria/en/index.html.

———. 2015d. *Strategy for Malaria Elimination in the Greater Mekong Subregion (2015–2030)*. Geneva: WHO.

———. 2015e. *World Malaria Report 2015*. Geneva: WHO.

———. 2016a. "Eliminating Malaria." WHO, Geneva. http:// www.who.int/malaria/publications/atoz/eliminating -malaria/en/.

———. 2016b. "Malaria Vaccine." WHO Position Paper, WHO, Geneva.

———. 2016c. *World Malaria Report 2016*. Geneva: WHO.

——— and GHG (Global Health Group). 2012. *Eliminating Malaria: Case-Study 3; Progress towards Elimination in Sri Lanka*. Geneva: WHO.

Wickremasinghe, R., S. D. Fernando, J. Thillekaratne, P. M. Wijeyaratne, and A. R. Wickremasinghe. 2014. "Importance of Active Case Detection in a Malaria Elimination Programme." *Malaria Journal* 13: 186.

Wilson, A. L., V. Chen-Hussey, J. G. Logan, and S. W. Lindsay. 2014. "Are Topical Insect Repellents Effective against Malaria in Endemic Populations? A Systematic Review and Meta-Analysis." *Malaria Journal* 13: 446.

Yip, K. 2000. "Malaria Eradication: The Taiwan Experience." *Parassitologia* 42 (1–2): 117–26.

Zanzibar Ministry of Health. 2012. "Willingness to Pay for a Tourism Levy on International Arrivals." Unpublished.

Zelman, B., M. Melgar, E. Larson, A. Phillips, and R. Shretta. 2016. "Global Fund Financing to the 34 Malaria-Eliminating Countries under the New Funding Model 2014–2017: An Analysis of National Allocations and Regional Grants." *Malaria Journal* 15: 118.