

STEP
E

STEP
D

STEP
C

STEP
B

STEP
A

PATH MALARIA LEARNING SERIES

A Conceptual Framework for Malaria Elimination



THE PATH MALARIA LEARNING SERIES

The PATH Malaria Learning Series offers concise briefings on the latest evidence in malaria research and science from across our portfolio. Installments will provide an accessible overview of important developments in malaria control and elimination and synthesize results from PATH-supported research.

Making progress against malaria requires collaboration across borders, sectors, and disciplines. PATH engages and connects partners in the public, private, and nonprofit sectors—including country partners such as ministries of health and national malaria programs—to develop, evaluate, and scale tools and strategies to defeat malaria. Our partnership model translates bold ideas into products and strategies, and leverages national capacity and commitment in the fight against malaria.

ACKNOWLEDGMENTS

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IN THIS ISSUE

Much progress has been made in recent years in the fight against malaria—so much so that eliminating the disease from many endemic countries over the next fifteen years is now considered an achievable, if ambitious, goal. In 2015, the World Health Organization (WHO) published the 2016–2030 Global Technical Strategy (GTS) for Malaria that identifies three pillars and two key supporting elements to achieve elimination.¹ This has been accompanied by several documents addressing financial investment and political engagement.^{2,3} WHO recently published a Framework for Malaria Elimination to provide updated guidance on elimination in malaria-endemic countries at all levels of transmission.⁴

This issue of the PATH Malaria Learning Series builds directly upon the WHO Elimination Framework, and further describes the steps to elimination as a practical approach for national malaria programs as they move along the continuum of decreasing malaria transmission intensity. These steps aim to help program managers and team members think about how to best deploy the tools at their disposal according to their country's malaria transmission strata (from high to very low) and varying ecologic, epidemiologic, and societal features.

THE LEARNING AGENDA

In addition to providing a practical action approach, the steps also contribute a program-linked framework to address questions, document progress and impact, and generate lessons that can be applied across different countries, such as:

- What is the best way to stratify geographic areas by transmission intensity and ecologic or epidemiologic features?
- How to best assemble and deliver a package of intervention tools and strategies to use in diverse strata to both manage the malaria burden and further reduce transmission intensity?
- When, where, how, and for how long should different strategies or tools be deployed to accelerate efforts toward elimination?
- What timely and quality information is required to: a) direct changing actions as transmission is reduced; and b) track and document progress at all levels of the health system?
- In the end-game of achieving and then maintaining malaria elimination, what are the final actions required and what activities and information must continue to ensure durable elimination?

KEY TAKEAWAYS

- Every country, including high-burden countries, should consider the full pathway to elimination and assess its current position on that path (e.g., spectrum of transmission intensity; biologic, epidemiologic, and societal contextual factors; and human and financial resources) to determine its next actions.
- Anticipating and planning for the next steps along the path toward elimination as early as possible is key to success.
- No single (currently available) intervention will achieve malaria elimination—thus, a package of interventions must be rolled out as appropriate along the spectrum of malaria transmission intensity.
- Information is a critical aspect of achieving and maintaining malaria elimination; as malaria transmission decreases, surveillance and response systems must become increasingly sensitive and focused to identify, track, and respond to malaria cases and remaining transmission foci.
- While the path may be short for some countries and long for others, progress toward elimination will have many survival and health benefits along the way—these, too, should be celebrated.



Photo: PATH/Gabe Bienczycki

Understanding malaria transmission intensity and patterns

In order to design appropriate elimination strategies, it is essential to understand where the country and its communities lie on the spectrum of malaria transmission. The burden of disease in a given locale, measured as transmission intensity, impacts the feasibility of effective deployment of certain interventions. For example, the number of cases that present to a health facility determines whether the facility can realistically and sustainably test each case and trace it to its geographic origin to find the source of infection and contain its spread.

One way of assessing malaria transmission intensity is to determine the number of confirmed cases per 1,000 population of the health facility catchment area (HFCA). To do this, it is essential to have excellent access to health facilities, strong community outreach, and a robust information system that extends to the

community level. Counts or good estimates of the population served (the denominator) are important for this measure.

Other methods have been used to measure transmission intensity, including the entomological inoculation rate (EIR), which is the estimated number of infective bites received per person in a given unit of time (e.g., one year) in a human population. In turn, the EIR can be extrapolated to a parasite prevalence range and an expected number of malaria cases per HFCA. Table 1 shows the correspondence between parasite prevalence and cases per 1,000 population per week that a health facility might expect to face. This approximative correspondence was defined based on work by Cameron et al., in which the ranges of transmission intensity were labeled from “high” to “very low.”⁵

TABLE 1. Malaria transmission intensity measurements (approximate mid-point of a range for each measure): weekly cases per average health facility and their relationship to annual parasite incidence, parasite prevalence, and entomologic inoculation rate.

MEASURE	HIGH	MODERATE	LOW	VERY LOW	ZERO
<i>P. falciparum</i> prevalence rate (PfPR)	35%+	20%	5%	≤1%	0
Annual parasite incidence (API)	450+	350	175	<100	0
Cases per health facility per week	55+	34	17	10	0

PfPR = the proportion of people currently infected with *P. falciparum*—typically determined by a population-based survey and often timed to a specific interval of the transmission season (e.g., late transmission season when PfPR is likely to be highest).

API = the number of confirmed malaria cases per 1,000 population per year.

Cases per health facility per week = an average number of confirmed malaria cases expected to present on an average week to a health facility serving a population of 5,000 people. Because many infections can be asymptomatic at any point in time (and thus not present to the health services), the proportion of asymptomatic individuals varies with transmission intensity; because most transmission is seasonal, these average estimates may vary substantially by location and season.

Zero = refers to no locally transmitted cases of malaria infection; imported infections may be identified. Of note, these categories and measures coincide with the previously used entomologic inoculation rate (EIR) where the corresponding average EIRs for high, moderate, low, and very low would be 10+, 1, 0.1, and 0.01, respectively.

Many endemic areas also show seasonal patterns of transmission, with high transmission only part of the year. Figure 1 shows the seasonal pattern of confirmed malaria cases in the Ranérou District of Senegal between 2008 and 2016. The population experiences very few malaria cases for half of the year, but during the rainy season, malaria incidence rises considerably.

Patterns such as these suggest that efforts to reduce transmission may be best applied at certain times of the year; thus, specific work may be episodic (e.g., seasonal malaria chemoprevention, as described below).

Both transmission intensity and transmission timing are important considerations for developing elimination strategies.

FIGURE 1. Seasonal pattern of malaria transmission in Ranérou District, Senegal 2008–2016.

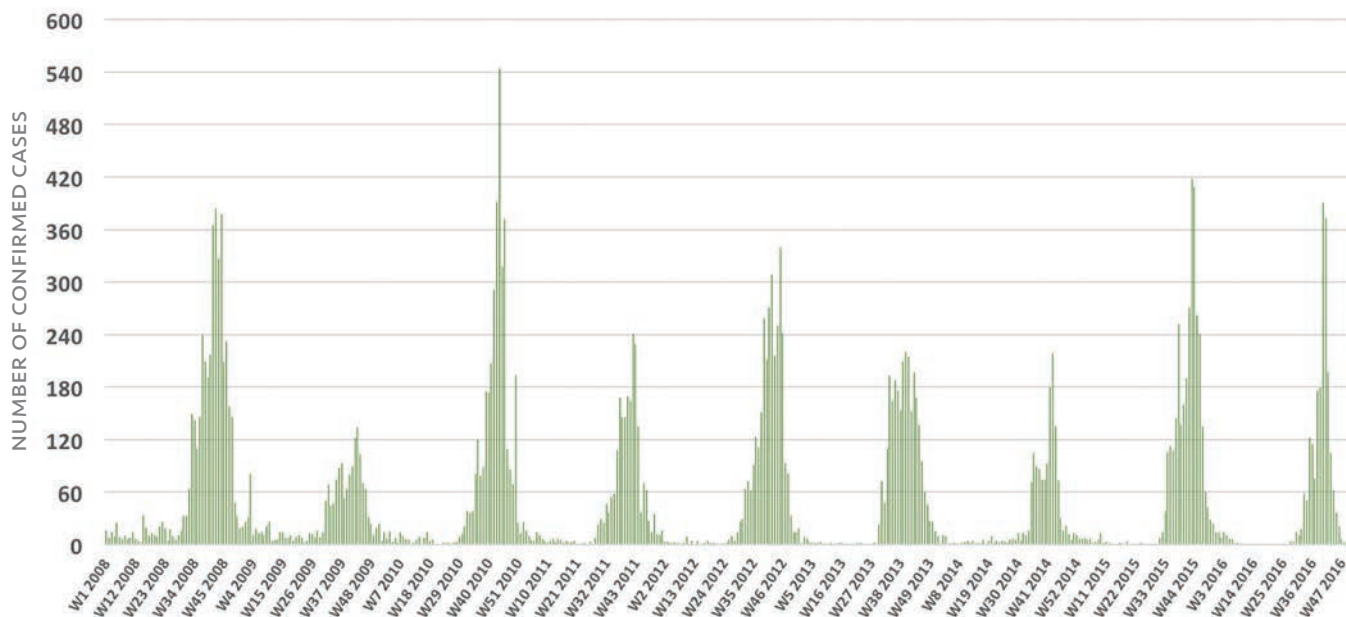


Photo: PATH/Paul Libiszowski

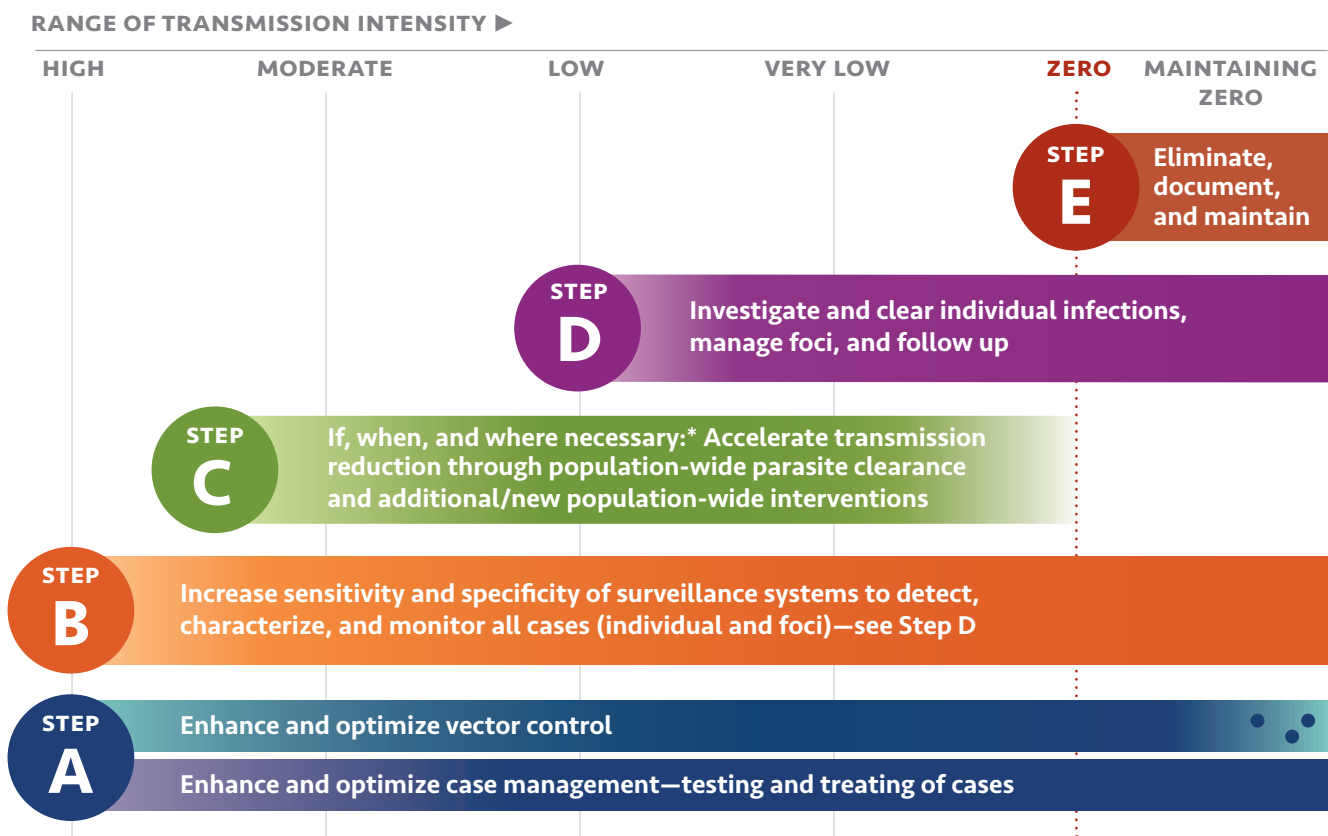
A stepwise approach to malaria elimination

Direct in-country experience suggests that a stepwise approach facilitates a number of program responsibilities (Figure 2):

- The consideration of the current situation (existing geographic spectrum of infection and disease burden, and coverage with core interventions).
- Developing near-term and longer-term objectives and targets.
- The planning, deployment, and optimization of the appropriate package of tools and strategies.
- Measuring change and progress, and tracking continued challenges. This approach includes:

- A** Enhancing and optimizing both vector control and case management tools and strategies.
- B** Strengthening surveillance systems to be able to optimally deploy interventions and track progress.
- C** Using “accelerator tools and strategies” to rapidly reduce transmission where appropriate.
- D** Developing information and action systems to identify and clear infections in low-transmission settings to achieve elimination.
- E** Documenting elimination and maintaining zero local transmission.

FIGURE 2. Illustrative intervention package for elimination of malaria (adapted from *A framework for malaria elimination*, WHO, 2017).



* Depending on local context

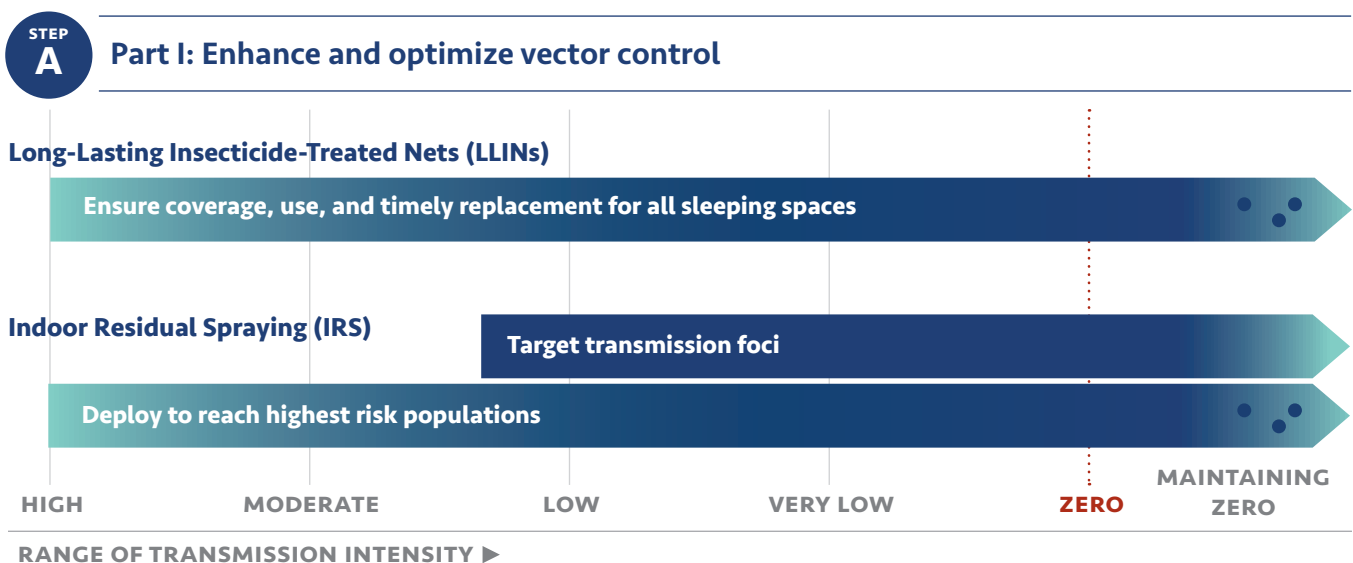
STEP A: Optimize vector control and case management

The path toward elimination begins with Scale-Up for Impact (SUFII). The scale-up of current proven interventions, such as long-lasting insecticide-treated nets (LLINs), targeted indoor residual spraying (IRS), and improved case management through the use of rapid diagnostic tests (RDTs) and artemisinin-based combination therapy (ACT), has in many places led to substantial reduction in infection prevalence and case incidence since being adopted as global policy in 2000.⁶ Continued efforts are required to offer these preventive and curative interventions to at-risk populations until elimination is achieved. While it is essential to accelerate scale-up in countries or areas where transmission remains high or moderate, access to prevention and case management should also remain a mainstay of the intervention package in low-transmission settings in order to preserve gains.

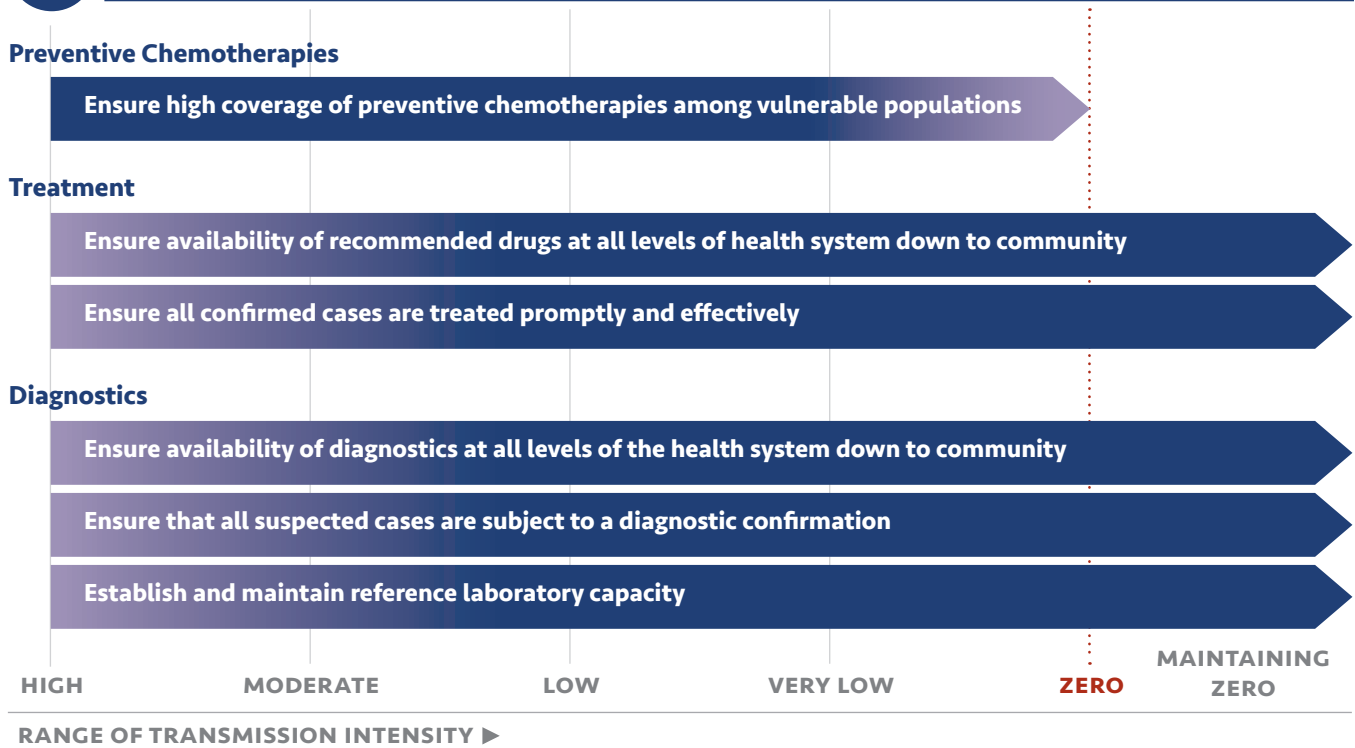
The main interventions implemented under Step A are vector control and case management. In areas with high transmission, additional proven interventions include the use of preventive chemotherapies such as intermittent preventive treatment in pregnancy (IPTp) and in infants (IPTi), and seasonal malaria chemoprevention (SMC); each of these is oriented specifically to reduce disease burden, and may have limited impact on infection transmission. The following Step A graphics describe when these different interventions should be deployed across the range of transmission settings.

VECTOR CONTROL

Increasing the coverage and use of LLINs in at-risk populations and/or spraying houses with insecticide (IRS) are core vector control interventions that reduce the biting rate and/or survival of vector populations. Additional vector control interventions such as larval source management or new tools to address remaining or outdoor biting and resting mosquitoes may be considered if they meet existing recommendations, or as new findings indicate their value. Vector control interventions can greatly contribute to reductions in transmission intensity, and should be maintained even when zero transmission has been achieved. Indeed, even in areas where there have been substantial reductions in malaria transmission, discontinuing vector control confers a high risk of malaria resurgence. Therefore, the scale-back of vector control should be based on a detailed analysis that includes assessment of receptivity (the ability of an ecosystem to allow malaria transmission) and vulnerability (which depends on the risk of malaria being reintroduced from elsewhere), information on case incidence from a robust surveillance system, and capacity for case management and vector control response.⁷



Note: gradient indicates intensity of effort and degree of target population coverage, and dots indicate focality of intervention after zero transmission has been achieved.



Note: gradient indicates intensity of effort and degree of target population coverage

CASE MANAGEMENT

Case management refers to the prompt diagnosis and treatment of malaria infections to reduce the likelihood of progression to severe disease and death. Additionally, timely case management may reduce transmission by markedly shortening the duration of infection and the likelihood of parasite transmission onto mosquitoes. Following the standardization of information and quality control, and the large-scale deployment of RDTs in 2010, WHO recommended that—where possible—all cases should be confirmed by parasitological diagnosis before treatment with artemisinin-based combination therapy (ACT). Case management should also include tracking and reporting of cases through a system that enables national programs to know where and when cases occur (see Step B). Like vector control, improved case management contributed substantially to the decline in malaria prevalence and incidence between 2000 and 2015, especially in areas of high coverage.⁶

In high-transmission settings, programs focus on scaling up diagnostic testing and the timely provision of effective treatment to all confirmed malaria

patients. Diagnosis can be provided at all levels of health care—from the community to hospitals—by RDT or microscopy. Because of their ease of use (especially for point-of-care diagnosis) and their comparable sensitivity, RDTs should be considered a standard diagnostic in all settings. As microscopy requires specially trained staff, it is usually reserved for hospitals and malaria laboratories at health facilities. In areas of lower transmission, case management interventions should include both active and passive case detection to find and treat all symptomatic cases (including in hard-to-reach populations, such as migrants, refugees, and internally displaced persons) and as many asymptomatic cases as possible. Treatment should be provided through all available channels, including public and private health facilities and community outreach programs. As the overall number of cases declines, it is important to strengthen reference laboratory strategies to ensure accuracy of malaria diagnosis, which might include the speciation of parasites and detection of false-positive RDT results. It is also essential that all confirmed cases be reported by all levels of the health care system, including community and private-sector facilities.

PREVENTIVE CHEMOTHERAPIES

In addition to case management, antimalarial drugs can be used in high-transmission settings as preventive chemotherapy to reduce disease burden, even if this does not directly contribute to transmission reduction. Examples of preventive chemotherapy with proven morbidity reduction include intermittent preventive treatment in pregnancy (IPTp), intermittent preventive treatment in infants (IPTi), and seasonal malaria chemoprevention (SMC).

In order to prevent malaria in pregnancy, WHO recommends that pregnant women in high- to moderate-transmission areas be given IPTp with sulfadoxine-pyrimethamine (SP) at each scheduled antenatal care visit in addition to using LLINs.⁸ Given

the lack of evidence on when to stop implementing this measure, areas where transmission has been reduced through successful strategies should not stop giving IPTp.

In some geographic areas, intermittent preventive therapy with SP is also recommended in infancy (IPTi); in areas of high to moderate transmission, infants should receive three doses of SP through the expanded program on immunization (EPI).⁹

In specified areas with highly seasonal malaria, children between 3 and 59 months of age should be given a maximum of four doses of amodiaquine-SP at monthly intervals.¹⁰ Recent data showed that SMC given to older children contributed to reducing overall malaria transmission, but it is currently not recommended as a transmission reduction strategy.¹¹

STEP
A

FROM THE FIELD

Scaling up proven interventions

Continued efforts to scale up proven interventions—such as vector control through LLINs, IRS, and improved case management—are required to reach elimination, but also to maintain zero malaria transmission.

Through national support systems, PATH's MACEPA program has provided support to the Zambia Ministry of Health to support LLIN distributions and a targeted IRS program, financed by the Global Fund and the US President's Malaria Initiative (PMI). As documented in the national Malaria Indicator Survey (MIS) of 2015, LLIN coverage reached 76% of homes with at least one net, and 58% of children less than 5 years of age had used an LLIN the previous night. IRS coverage exceeded 90% of homes in targeted areas and reached almost 30% of homes overall. Nationwide, over 80% of homes were protected, either with LLINs or with IRS.

Improved case management means better diagnosis—both in terms of timing and quality—and effective treatment of positive cases. In order to improve diagnosis, the PATH-led MalariaCare project is supporting national programs to expand parasitological testing through quality-assured malaria RDTs and/or microscopy. In the Zambezia region of Mozambique, MalariaCare worked with the national program and rural hospitals to strengthen quality assurance systems by training selected clinical and laboratory supervisors from both provincial and district levels to provide supervision and mentorship to local health facility staff. The project also facilitated the establishment of facility-led malaria committee meetings to regularly review data and address trouble spots. These activities led to an increase in adherence to malaria test results, which is essential for effective treatment and efficient use of resources.

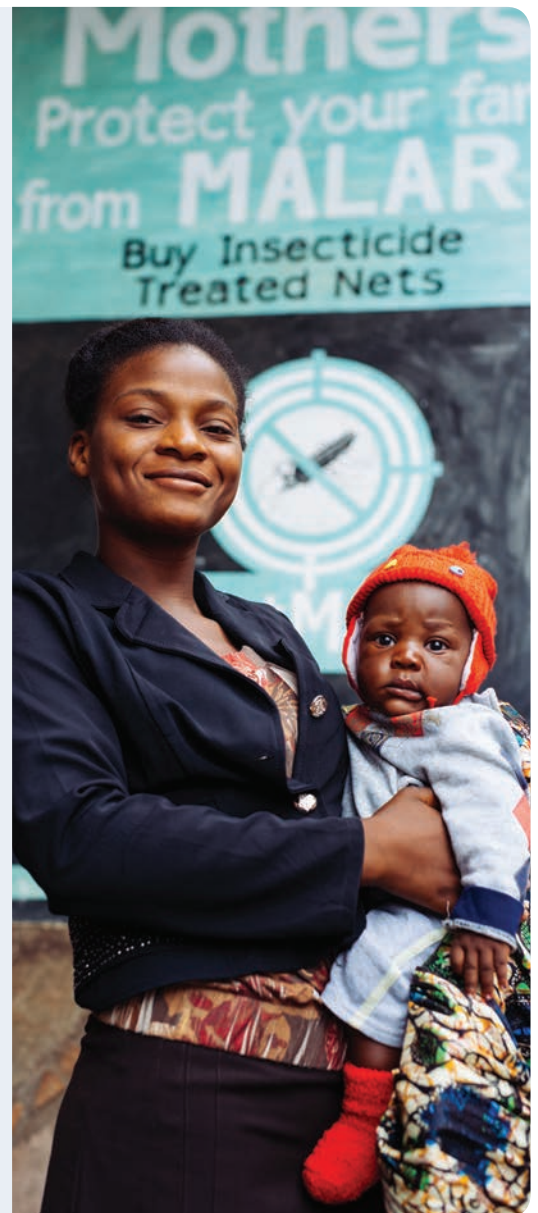


Photo: PATH/Gabe Biencyzcki

STEP B: Increase sensitivity and specificity of surveillance systems to detect, characterize, and monitor all cases (individual and foci)

As countries progress toward elimination, their surveillance systems must become the cornerstone of the framework—all successful disease elimination programs have relied on solid information systems that initially track transmission and subsequently guide prevention and containment of disease reintroduction. All countries have health management information systems that record health facility data, and most countries use population-based survey data and specific studies to estimate intervention coverage and parasite prevalence. As countries (or regions) move down the transmission spectrum toward elimination, they require increasingly detailed information to:

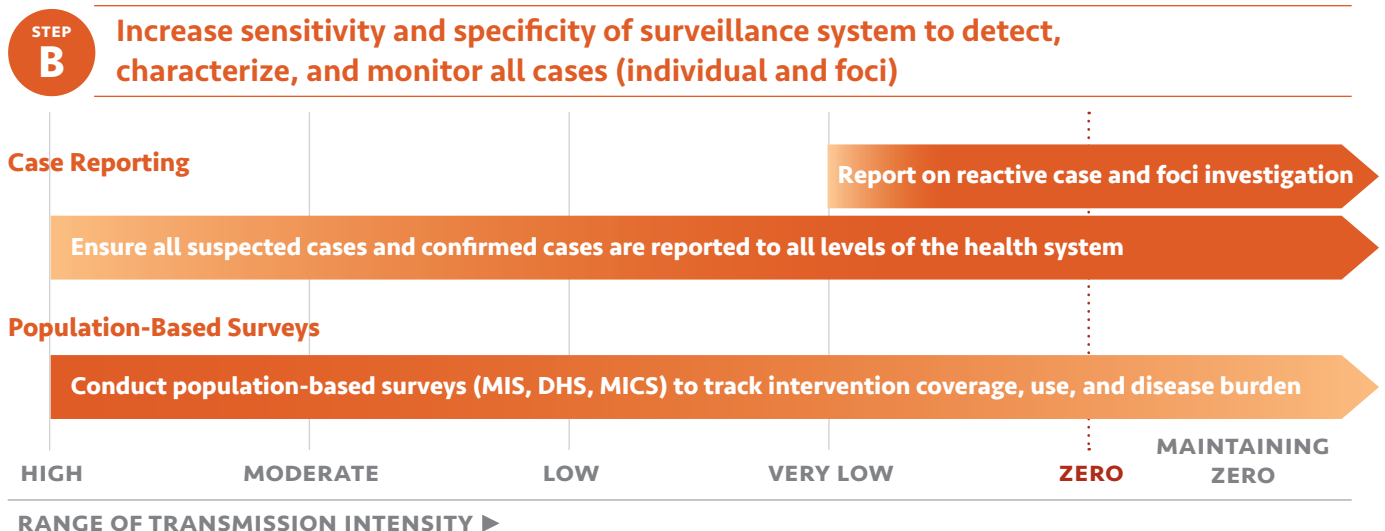
1. Understand the heterogeneity of transmission within a country.
2. Rapidly identify and eliminate individual cases and foci.
3. Prevent re-establishment by continuously identifying and containing new cases.

Surveillance (defined as the ongoing systematic collection, analysis, and interpretation of health data) becomes an intervention in itself (in line with the WHO Global Technical Strategy), whereby surveillance activities lead directly to an effective and timely public health response.^{12,13} In fact, the global information and communication technology revolution supporting surveillance systems is the “new tool” enabling the current progress toward malaria elimination.

An effective malaria surveillance system enables program managers to:

- Identify the areas or population groups most affected by malaria.
- Identify trends in cases and deaths that require additional interventions.
- Assess the impact of implemented interventions.
- Target resources most efficiently.

Data that feed into surveillance systems come from various sources, including reports of test-confirmed malaria cases, malaria inpatient visits, and malaria deaths (obtained from all or selected health facilities). Additional sources include the results of nationally representative household surveys—such as demographic and health surveys (DHS), multiple indicator cluster surveys (MICS), or malaria indicator surveys (MIS)—that indicate the extent to which people with fever can access case management services, and which type of provider they choose. Household and health facility surveys can also provide information on the extent to which interventions are implemented equitably (by wealth quintile or urban/rural area). The quality of data should be monitored regularly, and data should be analyzed carefully to assess completeness and accuracy. Efforts should focus on gathering high-quality data from communities and extending reporting to community-based health workers.



Note: gradient indicates intensity of effort and degree of target population coverage

Building robust reporting systems

Surveillance systems that provide data to stratify malarious areas in a country, identify pockets of transmission, and characterize each case are essential to malaria elimination programs. In recent years, technology has evolved rapidly, and now provides programs with cost-effective, easy-to-use tools that enable all levels of the health system—from community health workers and private providers to district-, provincial-, and national-level staff—to track cases and monitor responses, giving programs the opportunity to target interventions and resources.

Starting in 2013, the PATH MACEPA program deployed a reporting system based on the DHIS2 platform to 213 villages within 8 districts in the Amhara region of Ethiopia. Each village was assigned a surveillance assistant trained to report weekly morbidity and commodity data using mobile phones into the web-based DHIS2 platform. The reporting system tracked seven morbidity data elements (disaggregated by age: under and over five years of age) and six commodity data elements. Weekly reporting of data enabled health workers to visualize accurate data, follow morbidity and trends in commodity availability, and trigger local response decisions accordingly. Data have been regularly audited by an external team and compared with data uploaded to DHIS2 from health facility reports. The results of the data quality audit have been shared with health facility staff, and an action plan to address any identified recording or reporting issues has been created. MACEPA is working in a similar manner with national programs in Senegal and Zambia to scale up their rapid reporting systems.



Photo: PATH/Gabe Biencycki

Making the most of data

As malaria rates decline, cases become increasingly clustered. It is essential to know when and where the remaining cases are occurring in order to treat them rapidly. Data on the number of cases and how they were treated are usually collected at the community level (either in paper form or via mobile phones) and are aggregated at the central level. As such, it can often be difficult to visualize the data in a “big picture” way to draw trends, target interventions, and/or redirect resources more effectively. The Visualize No Malaria campaign (visualizenomalaria.org), a partnership between Zambia’s Ministry of Health, PATH, Tableau Foundation, and engaging many private-sector partners, provides powerful analysis and data visualization capabilities to track cases in real time and overlay data onto maps to show movement and travel patterns. User-friendly dashboards are generated that enable staff at all levels of the health system to see emerging patterns and optimize resource distribution to respond to every last case. The partnership is a powerful example of how innovation and public-private partnerships can support countries as they eliminate malaria.

The first application of data collected through the surveillance system is to help national programs stratify their country according to malaria risk, which enables them to determine the most appropriate intervention package for specific areas. Risk stratification should occur at the smallest possible level—typically the district level—highlighting the need for granular information. As a country approaches elimination, stratification should be done at the health facility level, in order to refine and further stratify the

“very low” column described in Table 1. These data also enable national programs to assess the impact of deployed interventions, with the opportunity to adjust and reorient activities if needed.

As surveillance systems become increasingly sensitive, they provide essential information that enables interventions to detect, investigate, and clear individual cases and foci in areas of low to very low transmission (see Step D).

STEP C: Population-wide parasite clearance and introducing additional/new interventions (where applicable and as they become available)

Once prevention measures and case management are optimal, and robust surveillance systems are in place, Step C can be considered and implemented as appropriate. The purpose of Step C is to accelerate transmission reduction in populations and enable the rapid transition to individual case and foci investigation (see Step D). While the scale-up of case management focuses on prompt, effective diagnosis and treatment of passively detected cases, it misses sub-clinical or asymptomatic cases, and is insufficient to clear all human infections and subsequently stop them from being transmitted back to mosquitoes. This step relies on finding and clearing all or nearly all parasites from the population, regardless of symptoms.

There are a number of ways to tackle the parasite clearance challenge—depending on the context, Step C may include a combination of the following approaches:

- Detecting all parasites—this requires an effective, highly sensitive test that can be used at the point of care.
- Treating all people with a safe and effective antimalarial drug that will clear all stages of parasites (mass drug administration [MDA]).¹⁴

Additional tools—beyond or in conjunction with drug use for parasite clearance—may become available to aid in the process of accelerating transmission reduction. For example, vaccines that help the human immune system stop or clear infections, or those that

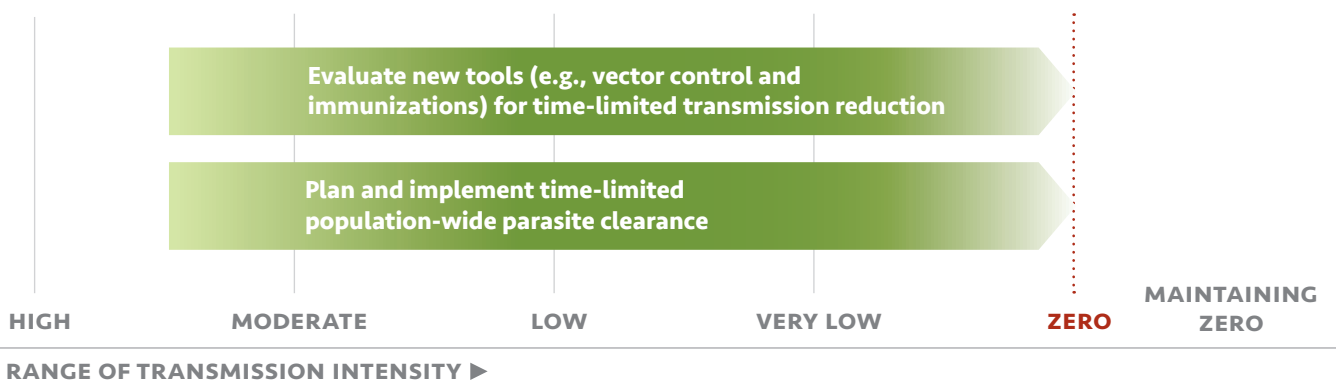
help reduce transmission to or from mosquitoes, could become available. Similarly, additional vector control measures that directly address the remaining biting/transmitting mosquitoes may become available and could be deployed across populations or targeted to certain areas to accelerate transmission reduction.

Interventions to reduce transmission at a population level cannot be considered an end in themselves. Rather, they are meant to be time-limited measures—possibly used during several transmission seasons, but not suggested for long-term use—that aim to bring transmission to sufficiently low levels so that each of the few remaining infections can be found and treated immediately.



Photo: PATH/Laura Newman

STEP C Reduce transmission through population-wide parasite clearance strategies (when and where applicable)



Note: gradient indicates intensity of effort and degree of target population coverage

Accelerating malaria elimination

In Zambia, from 2014–2016, a study supported by PATH-MACEPA evaluated mass drug administration (MDA) provided as two rounds per year for two years in a population of approximately 300,000 people. The trial showed that MDA targeting the whole population with dihydroartemisinin-piperaquine, when added to the standard of care (enhanced case management, insecticide-treated bednets, indoor residual spraying with pirimiphos-methyl [Actellic-CSR], and robust surveillance including rapid reporting and case investigation), resulted in rapid, substantial, and durable reductions in infection incidence and prevalence in areas with either high or low malaria transmission. The study underlined the importance of achieving high coverage with such an intervention package, as well as the need for a strong surveillance system to direct the work and continue to identify and treat any infected individuals in these communities, regardless of whether the infection is imported or locally acquired.¹⁵ More information can be found at <http://www.path.org/publications/detail.php?i=2629>.



Photo: PATH/Stacey Naggiar

STEP D: Investigate and clear individual cases, manage foci, and follow up

After achieving a community-wide transmission reduction, the next step is to proactively and aggressively find and treat new infections as soon as they arise. This requires rapid and intense investigation and is feasible only when the number of cases per HFCA is low enough for health workers to identify index cases, track and investigate them at the household level, and clear all infection foci. Although this will depend on each country's human and financial resources, this intervention should be considered when three or fewer cases present to the health facility each week (corresponding to health facility catchment areas with an API of 30 or less).

It is important that planning for this step start as early as possible, to ensure that all systems are fully operational once the acceleration phase is implemented. Indeed, as noted above, interventions to accelerate transmission reduction are time-limited in nature and must be part of a sustainable strategy to keep transmission levels down.

Interventions under Step D include:

- Characterizing, classifying, and registering each index case and determining the likelihood of local acquisition of the infection (as opposed to acquisition during travel).
- Visiting each affected household and neighborhood.
- Screening all residents of each household and neighbors for fever, travel history, or other risk factors.
- Testing everyone in the household and some, or all, in the neighborhood.
- Treating any confirmed infections and possibly providing treatment/chemoprophylaxis for a wider group if indicated.



Photo: PATH/Gabe Bienczycki

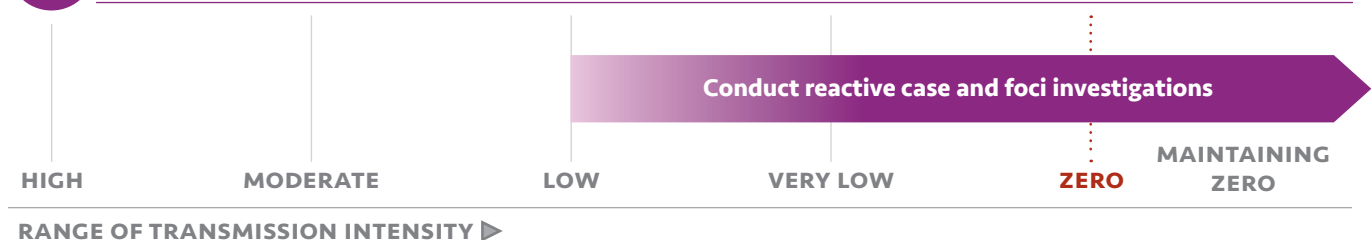
- Enhancing other malaria prevention strategies including LLIN ownership and use, IRS, or other interventions.

If the number of cases uncovered through case investigations exceeds the capacity of the health system, reinforced control measures and, potentially, additional Step C interventions to clear infections in the community may be needed before being able to implement Step D.

It is also possible that case investigations will establish that infections are likely due to importation from another endemic area. This should be documented to become part of the evidence base supporting a future declaration that elimination has been achieved (see Step E).

STEP D

Investigate and clear individual cases, manage foci, and follow up



Note: gradient indicates intensity of effort and degree of target population coverage

Finding new infections quickly

In areas of Ethiopia, Senegal, and Zambia with low or very low malaria transmission levels, PATH has tested a number of reactive case detection (RCD) protocols to aggressively find and treat new infections as soon as they arise. Data collected through these activities can help national programs design at-scale implementation of Step D. In Ethiopia, for example, through spatial analysis of RCD data, the Amhara Regional Health Bureau was able to determine the most cost-effective investigation radius around the index case household. The use of mobile technology permitted transmission of data to higher levels of the health system to inform decisions in a timely manner. In Zambia, patient-level information has been collected through Open Data Kit (ODK) and uploaded to the DHIS2 platform. Data from RCD activities helped identify case foci. In the Richard-Toll region of Senegal, results from RCD activities showed that most cases were due to travel and originated from specific areas in the southern part of the country; in Ethiopia, data showed that a large proportion of index cases were seasonal migrant workers who left home to work in higher transmission areas. These data can enable programs to design interventions that target a specific geographical area or population group to help create malaria-free areas within a country.

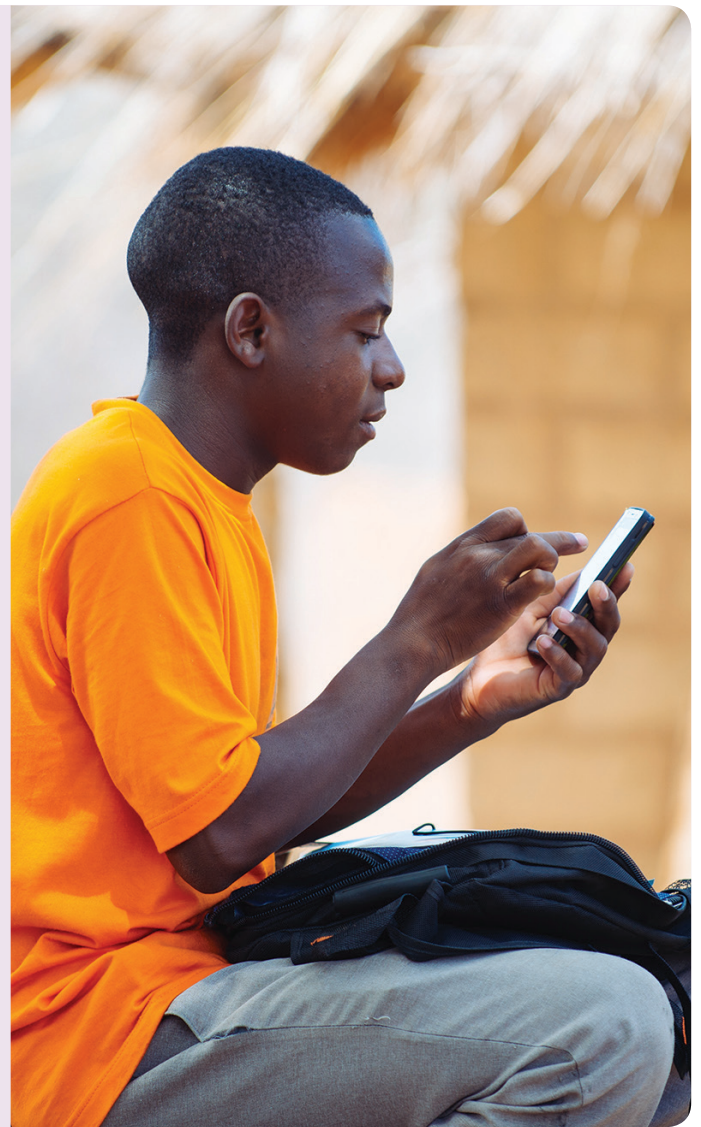


Photo: PATH/Gabe Biencycki



Photo: PATH/Gabe Biencycki

STEP E: Eliminate, document, and maintain

Achievement of national malaria elimination in a specific country is officially recognized through the process of WHO verification and certification. In order to obtain WHO certification, countries must prove beyond a reasonable doubt that:

1. Malaria transmission has ended in the country at a given time.
2. A surveillance and response system that would rapidly detect and respond to any malaria case and local transmission has been established and can be sustained.¹⁶

Step E is the final step of achieving zero local malaria transmission; the responsibility includes both documenting the achievement and maintaining zero transmission despite the potential for reintroduction by importation.

Every case or infection focus should be characterized, investigated, and classified in order to document the absence of local transmission, which is critical in verifying (in the local HFCAs, districts, or provinces) and ultimately certifying (at the national level) that elimination has been achieved.¹⁷ Countries should be fully aware of the necessary documentation required to apply for elimination certification, and should have systems in place early in the program to allow for malaria-free certification. Countries can apply for certification after reporting zero indigenous cases for at least the past three years.

Large countries can choose to document sub-national malaria elimination—termed “sub-national

verification”—as a way to celebrate success, as well as to prepare for WHO certification. Such sub-national verification is solely the responsibility of the country (not of WHO), but can use the WHO certification methodology.⁴

Once elimination has been achieved, surveillance (identifying and responding to cases or foci) becomes the mainstay for the future health system work to maintain elimination. This is now the case in every country where malaria has been eliminated and where surveillance, information systems, and the ability to detect any introduced/imported cases (and assure no local transmission) are maintained over time.

Components include:

- Maintaining an information system that can detect and characterize cases to determine if local transmission has or has not occurred.
- Maintaining a system that can assess the risk of reintroduction of infections (e.g., via residents or visitors traveling to endemic areas and bringing infections back into the malaria-free area).
- Maintaining a system that continues to reduce/stop the risk of local transmission from an introduced case. This may require the maintenance of existing vector control programs to limit any potential local vector-borne spread of malaria. Thus, the elimination program actions should only be withdrawn after careful examination of ongoing risks of reintroduction and possible spread.

STEP
E

FROM THE FIELD

Making malaria history

The PATH-MACEPA program has collaborated with the London School of Hygiene and Tropical Medicine and national programs in Ethiopia, Senegal, and Zambia to evaluate methods and measures to document the absence of local malaria transmission. With a common approach using both random selection and convenience sampling methods, young children, adolescents, and adults were assessed for current infection (using RDTs, microscopy, and polymerase chain reaction [PCR] testing) and evidence of past infection (through malaria-antibody serology). In selected settings with no reported malaria cases over the previous three years, infections were identified in either zero or one per thousand population. Serology results were consistent with dramatic reduction in infections prior to these past three years. These testing tools and sampling methods may be helpful to programs as they begin to interrupt malaria transmission and must document and understand these achievements.

Photo: PATH/Gabe Bienczycki



The Zambia malaria elimination strategy

Over the past decade, Zambia has made considerable progress in the fight against malaria. However, there is still work to be done. In 2015, there were over 5 million malaria cases reported across the country (HMIS 2015).¹⁷ In that same year, with nationwide enhanced diagnosis and treatment policies, and local procedures, there were over nine million LLINs made available through mass distribution, including to pregnant mothers and young children. Together with improvements in providing IRS to rural areas of Zambia, these activities are the primary control tools that have led to marked reductions in current levels of malaria seen across the country. The country's last two National Malaria Strategic Plans aimed to reduce transmission through multiple strategies, including vector control and improved case management using RDTs and treatment with ACT. Zambia is now committed to continuing to scale up malaria interventions in pursuit of a malaria-free Zambia by 2021, as described in the recently launched Strategy to Move from Accelerated Burden Reduction to Malaria Elimination in Zambia 2017–2021. The strategy aims to:

- Clear infections and interrupt malaria transmission.
- Document the reduction of infection, illness, severe disease, and mortality in districts, provinces, and nationally, and to assess progress toward elimination.
- Develop, strengthen, and maintain national political support, technical and operational capacity, and financial resources for malaria elimination.
- Prevent the reemergence of malaria transmission through importation in districts where it had been eliminated.

In order to achieve these objectives, Zambia has developed a phased approach based on the framework described here. Districts are classified according to their malaria levels, based on information from the national HMIS, as well as from the rapid reporting system being introduced across the country. Districts are then targeted with specific intervention packages that represent a combination of Steps A to E.

Conclusion

A growing number of countries in sub-Saharan Africa are setting goals to eliminate malaria by 2030 or earlier. The conceptual framework presented in this issue of the PATH Malaria Learning Series is intended to assist national programs working to eliminate malaria by describing a dynamic, evidence-based approach to elimination. At the core of this approach is the principle that interventions and program actions can be tailored to transmission intensity in a stepwise progression. Sustained impact will require proactive and data-informed planning to ensure that intervention packages are implemented at high coverage levels and in a timely manner. In particular, attention should be paid to:

- 1 Building quality information systems that can inform action and track progress.
- 2 Clearing parasite reservoirs from communities and individuals, achieving high population coverage, and addressing local epidemiology and environmental characteristics.
- 3 Strengthening all levels of the health system so that every case can be identified, treated, and reported. Together with political commitment, engagement with other sectors (e.g., education, agriculture, and the private sector), financial investment, and a capable health system, this conceptual framework for malaria elimination may help national programs as they work toward documentable and maintainable elimination across the African continent.

REFERENCES

- 1 WHO. *Global Technical Strategy for Malaria 2016–2030*. http://www.who.int/malaria/areas/global_technical_strategy/en/
- 2 Roll Back Malaria Partnership. *Action and Investment to Defeat Malaria 2016-2030*. <http://www.rollbackmalaria.org/about/about-rbm/aim-2016-2030>
- 3 *From Aspiration to Action – What Will it Take to End Malaria?* <http://endmalaria2040.org/>
- 4 WHO. *A Framework for Malaria Elimination*, 2017. <http://apps.who.int/iris/bitstream/10665/254761/1/9789241511988-eng.pdf?ua=1>
- 5 Cameron E, Battle KE, Bhatt S, Weiss DJ, Bisanzio D, Mappin B, Dalrymple U, Hay SI, Smith DL, Griffin JT, Wenger EA, Eckhoff PA, Smith TA, Penny MA, Gething PW. Defining the relationship between infection prevalence and clinical incidence of *Plasmodium falciparum* malaria. *Nat Commun*. 2015 Sep 8;6:8170.
- 6 Bhatt, S. et al. The effect of malaria control on *Plasmodium falciparum* in Africa between 2000 and 2015, *Nature*, 2015/10/08/print, 10.1038/nature15535
- 7 Information note on the risks associated with the scale back of vector control in areas where transmission has been reduced, November 2015, WHO/HTM/GMP/2015.7
- 8 WHO. *Intermittent preventive treatment in pregnancy (IPTp)*. 20 March 2016. http://www.who.int/malaria/areas/preventive_therapies/pregnancy/en/
- 9 WHO. *Intermittent preventive treatment in infants (IPTi)*. 20 April 2016. http://www.who.int/malaria/areas/preventive_therapies/infants/en/
- 10 WHO. *WHO Policy Recommendation: Seasonal Malaria Chemoprevention (SMC) for Plasmodium falciparum malaria control in highly seasonal transmission areas of the Sahel sub-region in Africa*. March 2012. http://www.who.int/malaria/mpac/feb2012/smc_policy_recommendation.pdf
- 11 Cissé, B. et al. Effectiveness of Seasonal Malaria Chemoprevention in Children under Ten Years of Age in Senegal: A Stepped-Wedge Cluster-Randomised Trial. *PLoS Med*. 2016 Nov 22; 13(11):e1002175. <http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002175>
- 12 A research agenda for malaria eradication: monitoring, evaluation, and surveillance. malERA Consultative Group on Monitoring, Evaluation, and Surveillance. *PLoS Med*. 2011 Jan 25; 8(1):e1000400
- 13 Zhou X-N, Bergquist R, Tanner M. Elimination of tropical disease through surveillance and response. *Infectious Diseases of Poverty*. 2013;2:1. doi:10.1186/2049-9957-2-1.
- 14 See, for example, PATH. *Malaria Learning Series: Population-Wide Drug-Based Strategies for Malaria Elimination*, 2016. http://www.makingmalariahistory.org/wp-content/uploads/2016/10/PATH-MalariaLearningSeries_Drug-based-web.pdf
- 15 Eisele TP, Bennett A, Silumbe K, et al. Short-term Impact of Mass Drug Administration with Dihydroartemisinin Plus Piperaquine on Malaria in Southern Province Zambia: A Cluster-Randomized Controlled Trial. *The Journal of Infectious Diseases*. 2016;214(12):1831-1839. doi:10.1093/infdis/jiw416.
- 16 WHO Weekly epidemiological record 18 JULY 2014, 89th year No. 29, 2014, 89, 321-336 <http://www.who.int/wer>
- 17 Zambia Ministry of Health (MOH). *Zambia National Malaria Elimination Centre (NMEC) Health Management Information System (HMIS)* [database]. Lusaka: Zambia MOH; 2015.

PATH is a leader in the battle to control and eliminate malaria nationally and regionally, and ultimately to eradicate it worldwide. PATH is partnering with national programs to optimize the delivery of current solutions and approaches, while developing new strategies to eliminate malaria in local and regional settings. With an unparalleled portfolio of malaria projects, PATH is developing the next generation of tools to accelerate efforts to detect, prevent, and treat malaria.

Diagnostics. In collaboration with public- and private-sector partners, PATH is pioneering the use of diagnostics for malaria elimination. We are improving access to available tests while advancing the development of new ones that support improved case management.

Vaccines. PATH's pipeline of vaccine candidates and approaches, under development with partners from across the globe, is one of the most robust in the world. It includes candidates that would prevent infection and those that attempt to block transmission of the malaria parasite from humans to mosquitoes and back again.

Drugs. PATH is working to improve malaria treatment so that no one who contracts the disease dies from it. We are ensuring a stable supply of malaria drugs and strengthening the existing supply. We are also strengthening health systems and improving the quality of malaria case management in Africa and the Mekong Region.

System and Service Innovations. To develop the science behind how to eliminate malaria in Africa, we are piloting new strategies with the goal of developing a package of approaches that are adoptable and adaptable across the region. These include strategies to stop the transmission of the malaria parasite from humans to mosquitoes and back again through community-wide treatment. We are collaborating closely with endemic countries to create malaria-free zones, the first step on the path to elimination.

Better Data for Decision-Making and Improved Surveillance. PATH is working with partners to use data in new and better ways to track emerging transmission patterns, optimize the way resources are deployed, and eventually track down the last malaria parasite.



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