Malaria control in Malawi: Current status and directions for the future


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ABSTRACT

The last decade has seen an increase in investment and concerted efforts by the Malawi Ministry of Health and partners to control malaria disease. This report summarizes what is known about the burden of malaria and the strategies being implemented to control it in Malawi. Over the past 5 years, roll out of treatment and prevention efforts have been successful in the country, as demonstrated by increased use of insecticide treated nets, improved access to prompt and effective treatment and the initiation of pilot studies of indoor residual spraying. However, unlike other countries in the region, the recent data have not suggested a decrease in the burden of disease. We describe the environment in which the activities of Malawi’s International Center for Excellence in Malaria Research (ICEMR) will be carried out and provide the rationale for the clinical, entomological and molecular studies. Our approach is to establish consistent, sustainable data collection systems that are embedded within the public health sector. Through standardized and long-term studies of hosts, parasites and vectors, we hope to contribute to assessment of malaria disease burden, the appropriate application of interventions and policies and provide both the data collection and the health care infrastructure to ultimately eliminate the disease.

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1. Introduction

As one of the poorest countries in the world, Malawi suffers from a disproportionate burden of infectious diseases, particularly malaria. Every Malawian resident lives in a region of high malaria transmission, defined as greater than one case per 1000 residents. In 2008, in a country with a population just under 14 million, the World Health Organization reported there were an estimated 5 million cases of malaria illness. Illnesses classified as malaria represent one half of all outpatient consultations that occur in the country (World Health Organization, 2010). Since the adoption of the recent strategic plan in 2005, Malawi dramatically scaled up malaria control measures focusing on vector control, case management and protection of vulnerable groups including pregnant women and infants. Uptake of these interventions has generally been successful, although they have been implemented heterogeneously throughout the country. To date, there has not been a systematic evaluation of their impact on malaria disease burden and transmission intensity.

The goal of this review is to summarize what is known about the burden of malaria and the strategies being implemented to control malaria in Malawi. We aim to describe the context in which the activities of Malawi’s International Center for Excellence in Malaria Research (ICEMR) will be carried out, provide the rationale for the studies being proposed and highlight how the ICEMR research activities will enhance our understanding of the disease and improve the effectiveness of interventions.

1.1. Risk and burden of malaria in Malawi

1.1.1. Environmental factors

Recent surveys suggest that malaria infection risk exists throughout Malawi, with the highest risk being along hotter, wetter and more humid low-lying regions (lakeshore, Shire River valley and central plain areas), and the lowest in the highland
areas of Rumphi, Mzimba, Chitipa and the Kirk range (Kazembe et al., 2006). Although the disease is widely endemic and stable in Malawi, transmission patterns show substantial seasonal variation, determined largely by the annual rains that typically begin in November–December and last through March–April in most parts of the country.

1.1.2. Vector ecology

Few studies on the malaria vectors of Malawi and dynamics of transmission have been published. The two most comprehensive studies occurred 10–15 years ago although published several years later, by Hawley (Hawley, 2002) and Spiers (Spiers et al., 2002). The principal vectors identified were An. arabiensis, An. funestus, An. gambiae s.s. and An. quadriannulatus (a member of the An. gambiae s.l. species complex but not a malaria vector). Spillings et al. (2009) documented a new and as yet un-named member of the Anopheles funestus species group from the Karonga area of northern Malawi. The significance of this finding to human malaria is uncertain as none of the 63 females collected were positive for sporozoite infection. The malaria sporozoite infection rates ranged from 2 to 5% and most blood meals were identified as emanating from the human host. The number of infective bites per person per year ranged from 16 to 27 infective bites/person/year in Mangochi (Hawley, 2002). Since Hawley conducted the study during a drought (rainfall was approximately 60% of normal), it is possible that estimates of transmission intensity in years of normal precipitation would be higher.

Studies on insecticide resistance status of anopheline vectors of malaria in Malawi are few but highly relevant to the implementation of anti-vector measures such as insecticide treated bed nets and indoor residual spraying. In 2002, Mzilahowa and colleagues conducted bioassays which demonstrated that An. arabiensis and An. Quadriannulatus were susceptible to pyrethroids and organophosphate but exhibited reduced susceptibility to DDT (Mzilahowa et al., 2008).

1.2. Disease epidemiology

Reliable estimates of the incidence of malaria is not available through the standard national surveillance system in Malawi. The available data are based on the Health Management Information System (HMIS), a passive surveillance of outpatient and inpatient malaria cases reporting to any government or mission health facility in Malawi. Cases of malaria include those diagnosed either with or without parasitological confirmation. According to the HMIS, the number of reported cases of malaria increased from 3.7 million in 2005 to about 6.1 million in 2009. Why this number increased during a period when anti-malaria interventions were being scaled up is unclear. Part of the increase is due to population growth (National Statistics Office of Malawi, 2008). The rise in reported cases could be due to improved surveillance and reporting and increased use of health services. Since 2007, the recommended first-line therapy for malaria, artemisinin-based combination therapy (ACT), has been available without cost only from health facilities, and this may have changed the health seeking behavior of the population. It is unlikely to be due to increased true incidence of disease as there is no evidence of increasing burden of malaria in Malawi, as described below.

As in most of sub-Saharan Africa (SSA), children under the age of 5 years bear the highest burden of malaria. Nearly 50% of the new cases recorded between 2005 and 2009 occurred among this age group with annual incidence rates as high as 1160 episodes per 1000 children (World Health Organization, 2010), a finding that has been corroborated by other local studies (Kazembe, 2007). Although infants (under 6 months of age) have been considered to be relatively protected against malaria, there is a substantial burden of the disease in Malawian infants during the first 6 months of life, with 10% of children under 5 years of age hospitalized with malaria being under 6 months of age (Lunn et al., 2009).

The most recent cross sectional data were collected by the National Malaria Control Program in a nationally representative malaria indicator survey (MIS) in March and April 2010. Overall, 43% of children ages 6 months to 5 years in the community were infected with malaria parasites. Parasitemia was more common among rural compared to urban children (47% vs. 15%, respectively) and was more prevalent in the central region (50%) than in the southern (42%) or northern (23%) regions (National Malaria Control Program, 2010).

2. Malaria control in Malawi

2.1. Malaria strategic plan

The Malawi government has responded to the challenges of treating and preventing this disease by developing a comprehensive strategic plan, a monitoring and evaluation plan, and enhancing the national malaria control program to coordinate the implementation of these plans. The 2005–2010 Malaria Strategic Plan (Ministry of Health, 2005), which all partners committed to reaching a goal of 85% coverage among groups at risk of malaria with four key interventions: prompt access to ACTs, intermittent preventive treatment during pregnancy (IPTp), long lasting insecticide treated nets (LLINs), and indoor spraying with residual insecticides. This partnership approach has resulted in increased funding for malaria control within the last 5 years, primarily from the health sector-wide approach (SWAP). The health SWAP is a common funding mechanism that pools resources from partners to coordinate efforts and achieve sustained improvements in peoples’ health according to nationally defined goals and strategies. The main source of malaria funding in the SWAP has come from Global Fund Rounds 2 and 7, which were consolidated in 2008. Outside the SWAP, President’s Malaria Initiative has increased funding from US$ 18.5 million in 2007 to US$ 27 million in 2010. Although this strategic plan started in 2005, malaria prevention activities underwent rapid expansion from 2007 through 2010 (see Table 1).

2.2. Current strategies and extent of coverage

2.2.1. Long lasting insecticidal treated nets (LLIN)

A new LLIN policy has been recently developed to include free distribution of LLINs to children born in health facilities, children attending their first visit under the Expanded Program on Immunization (EPI) and pregnant women at their first visit to an antenatal care clinic (ANC). The policy supports national distribution campaigns every 2–3 years and targets pregnant women and children under five, considered the most vulnerable populations in Malawi. Since 2008, the country has distributed 3.7 million LLINs through ANC and EPI clinics. Overall, approximately 57% and 50% of children and pregnant women sleep under a treated net the previous night (National Malaria Control Program, 2010). Although the women were not asked if the bed net was a standard ITN or LLIN, among the children almost all of the nets were LLINs.

2.2.2. Indoor residual spraying (IRS)

The MOH launched a pilot IRS program in Nkhata Bay District in 2007. Nationally, IRS activities have been limited to the pilot district, certain sugar plantations, and private spraying in the urban centers. A recent survey showed that 83% of houses in the pilot district, but <2% of the households throughout the country, had been sprayed within the last 12 months (National
Table 1

Key indicators of malaria and child health intervention coverage in Malawi between 2000 and 2010, in percentages.

<table>
<thead>
<tr>
<th>Indicators</th>
<th>DHS 2000</th>
<th>DHS 2004</th>
<th>MICS 2006</th>
<th>MIS 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coverage of key malaria interventions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Households with at least 1 bed net</td>
<td>13.1</td>
<td>41.9</td>
<td>49.5</td>
<td>63.4</td>
</tr>
<tr>
<td>Households with at least one bed net</td>
<td>5.4</td>
<td>11.6</td>
<td>35.0</td>
<td>59.8</td>
</tr>
<tr>
<td>Children sleeping under bed nets</td>
<td>7.6</td>
<td>20.2</td>
<td>29.0</td>
<td>59.6</td>
</tr>
<tr>
<td>Children sleeping under ITN</td>
<td>n/a</td>
<td>14.8</td>
<td>23.0</td>
<td>53.6</td>
</tr>
<tr>
<td>PW slept under ITN last night</td>
<td>n/a</td>
<td>14.7</td>
<td>26.0</td>
<td>49.9</td>
</tr>
<tr>
<td>PW took 2 or more doses IPT</td>
<td>25.3</td>
<td>46.5</td>
<td>47.0</td>
<td>60.3</td>
</tr>
<tr>
<td>Coverage of other key interventions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exclusive breastfeeding (6 months)</td>
<td>n/a</td>
<td>27.5</td>
<td>56.4</td>
<td>n/a</td>
</tr>
<tr>
<td>Vitamin A supplementation</td>
<td>n/a</td>
<td>n/a</td>
<td>69</td>
<td>n/a</td>
</tr>
<tr>
<td>Fully immunized</td>
<td>70.4</td>
<td>64</td>
<td>71.4</td>
<td>n/a</td>
</tr>
<tr>
<td>ANC attendance (once or more)</td>
<td>94.4</td>
<td>94.8</td>
<td>91.8</td>
<td>n/a</td>
</tr>
<tr>
<td>Mortality per 1000 live births</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infant</td>
<td>103.8</td>
<td>76</td>
<td>72</td>
<td>n/a</td>
</tr>
<tr>
<td>Neonatal</td>
<td>41.8</td>
<td>27</td>
<td>33</td>
<td>n/a</td>
</tr>
<tr>
<td>Under 5 years</td>
<td>188.6</td>
<td>133</td>
<td>122</td>
<td>n/a</td>
</tr>
</tbody>
</table>

DHS = demographic health survey; MICS = multiple cluster indicator survey; MIS = malaria indicator survey; ITN = insecticide treated net; PW = pregnant women; ANC = antenatal care; IPTp = intermittent preventive treatment in pregnancy; and n/a = not available.


Malaria Control Program, 2010). Lessons learned from this pilot are being used to scale-up IRS interventions; as December 2010, the Ministry of Health has expanded the IRS program to spray a total of seven high-prevalence districts along the lakeshore and in the Shire Valley, covering a population of 2.7 million people.

2.2.3. Intermittent preventive treatment during pregnancy (IPTp)

The IPTp strategy has been recommended in Malawi since 1993. The guidelines for IPTp are that all pregnant women take at least two treatment doses of sulfadoxine–pyrimethamine (SP) during routine antenatal care visits. The last 2 years have seen alternative distribution channels, including community-based mechanisms. National surveys of IPTp have shown that although attendance is high at the ANC clinics, the proportion of women who took ≥2 doses of IPT during an ANC visit increased from 47% to only 60% in the last 6 years (National Statistical Office [NSO] [Malawi] and ORC Macro, 2005; National Malaria Control Program, 2010).

2.2.4. Prompt and effective treatment with ACTs

The Malawi government changed its drug policy from a monotherapy with chloroquine to sulfadoxine–pyrimethamine (SP) in 1993 and from monotherapy with SP to ACT with artemether–lumefantrine (AL) in 2007. Under this new treatment policy, children under 5 years of age with fever continue to be treated presumptively based on clinical symptoms until laboratory diagnosis that allows for universal diagnosis in all age groups is scaled up. With international donor funding, AL has been provided for free since 2007 to all fever patients presenting at health facilities across the country. Efforts are also underway to scale-up community management of malaria through the provision of AL at village clinics. Although prompt administration of antimalarial treatment is a key objective in the Malawi malaria treatment policy, the scale-up of this intervention has proven difficult. Between 2004 and 2010, the proportion of under-five children with fever who used an anti-malarial drug the day of or day after diagnosis remained at approximately 25% (National Statistical Office [NSO] [Malawi] and ORC Macro, 2005; National Malaria Control Program, 2010). Once patient are given the appropriate therapy, their adherence to the ACTs is high with 75% of all patients taking all doses within the recommended 72-h of the initial health center visit (Mathanga, unpublished data).

3. Impact of control measures

3.1. All-cause mortality

Overall, Malawi has seen a substantial and steady decline of all-cause under-five mortality, from 218 per 1000 live births in 1990 to 110 per 1000 by 2009 (The World Bank, 2011). These national estimates from routine surveys have been validated with data from a demographic surveillance system (Jahn et al., 2010). Although other child health programs involving immunizations, access to safe drinking water, and exclusive breastfeeding certainly contributed to this enormous reduction in mortality, a review of data from recent nationally representative surveys showed rapid increase in access to malaria interventions whilst there was little or no change in coverage of other child health program interventions, suggesting that the change in mortality could be as result of scaling up of malaria interventions. An overview of the changes in access to key malaria and other child survival interventions are shown in Table 1.

In contrast, according to HMIS data, malaria mortality rates have risen from 2004 through 2008. As discussed previously, HMIS data are subject to many biases. However, they do support the persistence of intense malaria transmission and a significant impact on the health and survival of children.

3.2. Malaria morbidity

There are no systematic studies of patterns in malaria-specific mortality throughout Malawi. However, community surveys support the continued existence of a high burden of malaria infection and disease. Between 2005 and 2009, the prevalence of anemia (Hb < 8 g/dl) and parasitemia showed no change among children aged 6–30 months (Mathanga et al., 2010). Thus, the prevalence of anemia and parasitemia did not reflect the scale up of access to interventions that was initiated in 2005–2007. The only exception was the significant reduction in the prevalence of anemia and parasitemia in Nkhobotako, a district where a pilot IRS program is being implemented. In 2008, the prevalence of anemia and parasitemia were significantly reduced from 27 to 12% (p < 0.00001) and from 52% to 27% (p < 0.00001), respectively, within 6 months of the first round of spraying (Mathanga, unpublished data).

One population that has benefited from new efforts of malaria control has been pregnant women. Malaria prevalence in pregnant
women and their birth outcomes were recorded continuously from 1997 to 2006 at a referral hospital in southern Malawi. The prevalence of peripheral parasitemia and placental malaria dropped from 23.5% and 25.2%, respectively, to 5.0% and 6.8%. Over the same period, the prevalence of maternal anemia decreased from 37.0% to 24.5%, while prevalence of low birth weight also decreased from 14.1% to 8.9% (Feng et al., 2010). These improvements were attributed to LLIN use, not IPTp.

4. The Malawi ICEMR

For malaria control and ultimately elimination to succeed in Malawi and other countries in the region, further research is required to assess the impact of the current strategies and to help prioritize the implementation of established and new interventions in the face of changing transmission patterns. The distribution of malaria, the vectors and intensity of transmission and the burden of disease and infection in Malawi have not been well characterized, as is the case in many malaria-endemic countries. Poor public health infrastructure and record keeping, the absence of diagnostic capacity and a national treatment policy that advocates treatment of all children with fever with an anti-malarial drug have led to the inability to capture the full extent of the disease. In addition, large-scale coordinated efforts have been difficult to establish due to limited funding and the restricted focus of individual studies. Surveillance is also critical to detect any rebound effects during and after interventions. A better understanding of whether and how control efforts affect Plasmodium population genetics and drug resistance is needed. The environmental determinants of Anopheles vector abundance and behavior, as well as risk of insecticide resistance, are also critical issues to study.

The Malawi ICEMR was designed to address these key gaps in knowledge and to support the rational and sustainable development implementation of anti-malarial control and, in the future, elimination policies. The clinical studies include multi-faceted surveillance in three eco-geographic regions. The three districts we have selected to study are Blantyre, Thyolo and Chikwawa. The city of Blantyre is the second largest city in Malawi and the commercial and cultural center of the country. The surrounding district is rural. Thyolo and Chikhwawa are both rural districts. Most of Thyolo is in the mountains, with a relatively modest (but presently poorly characterized) burden of malaria. In contrast, Chikhwawa is located in the Shire Valley, where P. falciparum and Anopheles thrive, with an estimated entomological inoculation rate (EIR) for P. falciparum of 172 infective bites per year (Mzilahowa, unpublished). Activities will include facility based surveillance, cross-sectional studies and cohort studies. An in-depth assessment of urban malaria will also take place in Blantyre district. This is a case–control study to evaluate the vectors of malaria transmission in Blantyre District and the effect of spatial and environmental factors on transmission. The projects will be supported by an administrative, data management and administrative core and are expected to form the basis for further epidemiological, entomological and molecular investigations in the near future through existing and new partnerships.

The studies will be embedded within the current government public health system and have been developed to be aligned with national malaria control priorities. The surveillance systems will be established as expansions of laboratory capacity within the district health clinics and hospitals. The application of rapid diagnostic testing and microscopic diagnosis will be piloted through the proposed surveillance system. Laboratory and clinical support, training and quality improvement are essential goals of our collaborative efforts.

4.1. Determining the optimal surveillance methods

Gauging the impact of any intervention requires ongoing surveillance with the capacity to generate meaningful information and to address gaps in our knowledge and understanding. One fundamental challenge to measuring the burden of disease is capturing the relevant data. The overwhelming majority of Malawians do not seek care for febrile illnesses through the formal health care sector. Approximately 30% of children with fever are taken to a government or missionary hospital or health center (National Statistical Office (NSO) [Malawi] and ORC Macro, 2005), meaning that 70% of patients who seek care elsewhere are not captured in the national HMS.

Most health centers in Malawi do not have access to accurate malaria diagnosis. As a result, national treatment guidelines recommend treating all febrile children with the first-line therapy for malaria. In a recent study of four health centers in rural and urban health centers in Malawi, only 25% of children over five years old with fever had malaria parasitemia based on expert microscopy and among the study sites the range was 3–40%. Even rapid diagnostic tests, promoted because of their ease of interpretation in the field, provide poor specificity in these settings (Chinkhumba et al., 2010). The inability to distinguish malarial fevers from other causes of fever will lead to the dilution of the measured effect of interventions. If only 25% of fevers are attributable to malaria, and an intervention is able to decrease true malaria incidence by half, the efficacy of the intervention will appear to be only 12.5% because 75% of fevers with not be affected by the intervention. Accurate measures of malaria disease are essential to assessing the efficacy of new programs.

The Malawi ICEMR is designed to conduct surveillance on a variety of levels and using a range of epidemiological and molecular techniques. Surveillance will occur in a standardized manner in the three eco-geographic areas and will encompass facility based surveillance for passive case detection, cross-sectional studies to capture asymptomatic infections and sources of transmission and cohort studies to evaluate the dynamics of infection within a single host. Cohort studies will use active and passive surveillance so as to detect episodes of disease that might otherwise not be detected through facility-based surveillance. These strategies will not only shed light on the burden and ecology of disease in different populations, but, through the conduct of coordinated and consistent protocols, we will be able to draw inferences about the sensitivity of each method to measure impact.

We will also implement funduscopic evaluation of comatose patients with evidence of peripheral parasitemia to detect the ophthalmological changes that characterize cerebral malaria (Beare et al., 2006, 2011; White et al., 2009). This screening tool allows a clinician with basic training to distinguish of true cases of cerebral malaria from neurological disease of another etiology with concomitant malaria infection. Like many aspects of the ICEMR project, the element will improve the accuracy of our surveillance and also provide training to a cadre of government staff who will be able to use this technique to improve patient care and improve diagnostic accuracy throughout the country.

4.2. Shifting burden of disease and rebound effects

Another concern is that as transmission decreases, the disease burden will shift to older age groups. Reyburn and colleagues have shown that with increasing altitude in Tanzania, representing decreasing malaria transmission intensity, malaria hospitalization and cerebral malaria become more prominent in older children (Reyburn et al., 2005). If only children under 5 years of age are under surveillance, the disease may seem to decrease in severity when, in fact, severity is increasing, but in a different population.
The recent MIS calls into question the current strategy of limiting surveillance to children under 5 years of age. The highest prevalence of parasitemia was found in the oldest cohort evaluated: 48.5% in children 48–59 months of age (National Malaria Control Program, 2010). It likely that this represents frequent asymptomatic infection, as this age cohort is the least likely to receive antimarial medication. This suggests that a infection in children may extend well beyond 5 years of age.

The rebound effect is an increase in the incidence or severity of disease after the period of an intervention ceases. The concern for rebound illness among infants who received intermittent preventive therapy (IPTi) was raised in an Institute of Medicine report in 2008 (Committee on the Perspectives on the Role of Intermittent Preventive Treatment for Malaria in Infants, 2008). Almost all studies of IPTi and the only study to follow up children after an ITN study showed no rebound effect, it has been noted in children who received continuous chemoprophylaxis and in one IPTi study (Greenwood, 1984; Mockenhaupt et al., 2007). For large scale interventions, such as active distribution programs of LLIN or IRS, a level of accuracy and longitudinal follow up are needed in detecting true malaria incidence so that changes in the rate and severity of cases can be detected.

The facility based surveillance and cross-sectional studies conducted within the context of the Malawi ICEMR will capture the burden of disease and infection, respectively, in all age groups. The cohort studies will be stratified to include teenagers, as well as the younger children typically targeted for malaria incidence studies. The studies will include typically under-monitored groups from the beginning, so that changes that occur over the course of the ICEMR study period will be detectable when comparing to a well-established baseline.

### 4.3 Human sources of malaria transmission

The prevention and treatment of asexual stage infection will protect against disease, but gametocytes are the agents of malaria transmission. The epidemiology of gametocytemia probably differs from the epidemiology of blood-stage disease. Interventions that target gametocytes, such as transmission-blocking vaccines and mass treatment with primaquine to eradicate gametocytemia, will need to target all humans carrying gametocytes, even in the absence of the typical asexual ring-stage infection or symptomatic disease. Very little is known about gametocyte reservoirs in malaria-endemic areas in general and in Malawi, in particular.

New methods are being developed to detect gametocytes in the field so that they can be used in cross-sectional studies to accurately identify the reservoirs of transmission. The density of gametocytemia is low compared to asexual stage parasites, making microscopy an insensitive measure. Because gametocytes are a different life stage as the asexual parasites, but still the same parasite, techniques based on DNA will fail to distinguish gametocytes. Expression-based methods are under development in Malawi, and once they have been adopted for field-use, the epidemiology of gametocytes in Malawi (seasonality, age-specific prevalence, response to antimalarial drugs) will be explored, using the sampling infrastructure established by the Malawi ICEMR.

### 4.4 Benefits of interventions in different settings and in combination

In the last 10 years, there has been a dramatic increase in investment in malaria control in Malawi from the Global Fund and the Presidents Malaria Initiative. As a result of the increase in resources, the NMCP is deploying all proven intervention in the same malaria risk areas. However, the cost effectiveness of interventions, such as LLIN distribution and IRS, vary according to setting (rural vs. urban) and intensity of malaria transmission. Against a background of increased investment in malaria control and growing national demand for sustained scaling up of proven interventions, there is urgent need to inform the Malawi NMCP on how best to use or combine these interventions to reduce and thereby sustain reductions in the level of malaria transmission (Table 2).

One example in Malawi that highlights the need to evaluate the role of interventions in combination is the recent decline in the prevalence of placental malaria in the large referral hospital. The trend was associated with improved uptake of LLINs among pregnant women and also a significant increase in the administration of IPTp although on careful analysis the impact was attributed only to LLIN use, not IPTp (Feng et al., 2010).

Through the two clinical studies that are the central components of the ICEMR, both rural and urban populations will be evaluated consistently. The close link between the National Malaria Control Program and the ICEMR leadership will allow the evaluation of each intervention accurately, with the goal of determining the impact at every level of surveillance.

### 4.5 Effect of control efforts on malaria population genetics and drug resistance

We have recently demonstrated that chloroquine-susceptible malaria regained prominence after the cessation of chloroquine use in Malawi in 1993 (Kublin et al., 2003; Lauffer et al., 2006). This is in contrast to the observations in Southeast Asia and South America, where chloroquine resistance has remained fixed in the population (Nash et al., 2005). This difference is thought to be due to reduced genetic diversity in the low transmission settings, leading to infrequent recombination and fixation of the drug resistant genotype in the population. If malaria control in sub-Saharan Africa leads to a drastic reduction in effective population size, then undesirable traits, such as resistance to old and new drugs may, become fixed in the population. Also, if the genetic diversity changes, trait mapping, through genome-wide association studies and single-nucleotide polymorphism genotyping may lead to false associations. Monitoring of the effect of reduced transmission will help us continue to tailor interventions and maintain genomic analysis at the highest standard.

### 4.6 From policy to implementation to impact

The Malawi ICEMR is an effort to bring together an integrated approach to understanding how to control and prevent malaria. Through basic yet standardized and rigorous collection of data from human hosts, parasites and vectors, we will be able to assess the impact of interventions, guide research towards new and improved strategies and provide policy makers with evidence-based recommendations to tackle this age-old infection.

The implementation of policies is a challenge in any context, but the Malawi Ministry of Health and the National Malaria Control Program have a long history of generated data-driven, evidence-based policies. There is a reciprocal exchange of

**Table 2**

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Urban</th>
<th>Rural</th>
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</thead>
<tbody>
<tr>
<td>Households with at least one bed net</td>
<td>68.9</td>
<td>62.5</td>
</tr>
<tr>
<td>Children who slept under a bed net</td>
<td>61.6</td>
<td>59.3</td>
</tr>
<tr>
<td>Pregnant women who slept under a net last night</td>
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<td>55.3</td>
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<tr>
<td>Mothers who took 2+ doses of IPT</td>
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</tr>
<tr>
<td>Children with fever who took any antimalarial drug</td>
<td>39.1</td>
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</tr>
<tr>
<td>Children with malaria parasites on blood smear</td>
<td>14.7</td>
<td>46.9</td>
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</table>
information between the Malawi ICMR team and their counterparts in the Malawi policy-making community. The Malawi ICMR priorities and activities have been developed on the basis of input from policy makers and the data generated will be reviewed in “real time” with these bodies. The close collaboration will facilitate changes in policy and expedite the transition to implementation. An important early step was the recognition that the sustainability of improved diagnosis and surveillance depends on embedding those activities within the ongoing activities of healthcare personnel (as opposed to vesting them in project-specific teams). Establishing this *modus operandi* requires more time and effort initially, but the grassroots capacity building will pay dividends in the future, as the systems will be sustainable beyond the single grant period.

5. Conclusion

Malaria continues to be one of the leading causes of morbidity and mortality in Malawi. Interventions to decrease the burden of disease, LLIN, IPTp and improved access to prompt and effective treatment, are reaching larger populations than in the past. However, the absence of standardized collection of measures of the burden of disease impedes our ability to determine their impact. In addition, determining the distribution of asymptomatic infection and reservoirs of transmission will be essential to developing a plan to eliminate malaria in the foreseeable future. This review points to the need for an interdisciplinary approach to malaria control and elimination. The Malawi ICMR brings together epidemiologists, entomologists, clinicians, biostatisticians, genomic specialists, implementation scientists and policy makers to find the most effective way to save the lives of children, improve the health of the whole population and ultimately eliminate the disease.

References


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