Evaluation of the Impact of Malaria Control Interventions on All-Cause Mortality in Children under Five Years of Age in Malawi

Malawi Malaria Impact Evaluation Group

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Executive Summary

BACKGROUND AND OBJECTIVE

In Malawi, malaria is highly endemic with 95% of the country's population at risk of infection. Malaria is estimated to be responsible for 34% of all outpatient visits and for 40% of hospital deaths. It is the major cause for hospital admissions in children under five years of age. During the decade from 2000–2010, the Government of Malawi (GoM) and other international donors invested heavily in malaria control activities such as insecticide-treated nets (ITNs), indoor residual spraying (IRS) in selected areas, intermittent preventive treatment in pregnancy (IPTp), and prompt and effective malaria case management. This report was co-commissioned by the US President's Malaria Initiative (PMI) and Malawi's Ministry of Health (MoH) to report on the impact of these investments during the period 2000–2010.

EVALUATION DESIGN

The evaluation was based on a before-and-after assessment, which used a plausibility evaluation design that measured changes in malaria intervention coverage, malaria-related morbidity, and all-cause mortality in children under five years of age (ACCM), while accounting for other contextual determinants of child survival during the evaluation period. ACCM was used as the primary measure of impact. Several multivariable analyses were included to investigate links between household ITN ownership and impact measures including parasitemia, severe anemia, and ACCM.

DATA SOURCES

Data used in the report mainly come from four large population-based household surveys: three Demographic and Health Surveys (DHS) conducted during 2000, 2004, and 2010; and one UNICEF Multiple Indicator Cluster Survey (MICS) conducted in 2006. Other nationally-representative data sources, used to examine trends in parasitemia and severe anemia, include a Malaria Indicator Survey (MIS) in 2010, and national micronutrient surveys (NMS) conducted in 2001 and again in 2009. These national survey data are supplemented, where relevant, by programmatic data from the Health Management Information System (HMIS) and Integrated Disease Surveillance and Response (IDSR) data, sub-national data such as the Karonga Health and Demographic Surveillance System (HDSS) data and data from the anemia and parasitemia (A&P) surveys and a rolling MIS in Chikwawa District. Data sources are clearly cited throughout the report.

SCALE-UP

During the evaluation period, Malawi dramatically increased malaria control efforts at the national level. ITNs were incorporated into antenatal care (ANC) and Expanded Program on Immunization (EPI) clinic visits for free national distribution in 2008. Although originally adopted as national policy in the 1990s, IPTp programs were scaled-up during the evaluation period. Efforts to improve case management included implementation of community-based care provided by health surveillance assistants (HSAs), adoption of artemisinin-based combination therapy (ACT) as the first-line

antimalarial treatment, and provision for national distribution of ACTs. Additional interventions, including IRS, were implemented at a sub-national level.

IMPLEMENTATION RESULTS

Household ITN ownership increased from about 13% in 2004 to 57% in 2010. ITNs were used by 39% of children under-five, 35% of pregnant women, and 29% of the entire surveyed population in 2010.

In Malawi, the use of at least two doses of sulfadoxine-pyrimethamine (SP) for the prevention of malaria during pregnancy was first instituted as national policy in 1993, well before the World Health Organization recommended this IPTp policy in 2002. Thus, even as early as 2000, 28% of women who gave birth in the preceding two years had received at least two doses of SP during their last pregnancy. IPTp coverage increased from 43% in 2004 to 54% in 2010.

Case management of children with fever also improved over this period. The percentage of children under five years of age with fever for whom advice or treatment was sought from a health facility, health care professional or a pharmacy increased from 35% in 2000 to 65% in 2010. Similarly, the proportion of children under five years of age with recent fever who received antimalarials increased from 19% in 2000 to 24% in 2010. However, the proportion of treated children who received the recommended first-line antimalarial did not change significantly over this time period but remained high (86% in 2000 compared to 84% in 2010). During this period, the national treatment guidelines changed the first-line antimalarial in 2007 from a drug with declining efficacy, SP, to highly efficacious ACTs.

IMPACT RESULTS

Morbidity

In Malawi, national parasitemia estimates were only available for two survey years (NMS) during low transmission seasons and for one survey year (MIS) during the high transmission season. Repeat cross-sectional data from national NMS indicate that a significant decrease in malaria parasite prevalence occurred between 2001 and 2009 in children 6–35 months of age. Sub-national anemia and parasitemia surveys in eight districts (out of 28) did not reveal a uniform temporal trend in parasitemia, as parasitemia prevalence decreased in some districts but not all between 2005 and 2009.

Available evidence from the 2004 and 2010 DHS, from the 2001 and 2009 NMS and from the sub-national A&P surveys suggest that the prevalence of severe anemia declined over the period of malaria control intervention scale-up in young children most at risk of malaria (6–23 months of age). The decline was significant among young children living in areas of medium to high risk of malaria transmission but not in those living in low risk areas, consistent with expectations in areas with multifactorial causes of childhood anemia.

Trends in suspected malaria cases in children under five years of age reported by health facilities have increased between 2005 and 2010. HMIS data show a rise in suspected malaria cases per 1,000 children per year from 817 to 1,363 over this period; however,

the number of out-patient visits and the number of health facilities reporting have also increased during this period. Similarly, IDSR data show increases in the numbers of suspected malaria cases in children under five years of age from 2005 to 2010, although trends varied by season and region. Thus, available facility-based data in Malawi suggest a trend of increasing malaria cases, at least between 2005–2010, which may be confounded by other secular trends in care seeking for childhood illness, facility reporting, and lack of laboratory confirmation.

Mortality

According to estimates from national household surveys, ACCM has been steadily decreasing in Malawi since 1990, from 189 deaths per 1,000 live births in 1996–2000 to 112 deaths per 1,000 live births in 2006–2010, a decrease of 41%. Significant reductions in ACCM occurred in all age groups (neonates, infants, children 6–23 months, 24–59 months, 0–59 months, etc.) between 1996–2000 and 2006–2010. However, ACCM declines were greater in higher and medium malaria risk areas than those with lower malaria risk (41%, 44%, and 32% relative declines in higher, medium, and lower risk areas, respectively). Many aspects of mortality analysis presented in this section (timing, residence differentials, and relationship to malaria risk) are consistent with the results that would be expected if malaria were a major factor underlying the mortality change in Malawi.

Contextual Factors

This report includes a comprehensive review of contextual determinants of child survival, which offer alternate explanations for the observed changes in mortality during the evaluation period. Several non-malaria related child health interventions likely contributed to reductions in ACCM, including increased literacy of women, improved care seeking and treatment for diarrhea and suspected acute respiratory illness (ARI), increased proportion of children less than six months exclusively breastfed, improved child nutrition, increased coverage of Hib immunizations, and increased use of health facilities for child birth. In addition, the GDP increased between 2000 and 2010, which could have contributed to the decline in ACCM. Rainfall and temperature patterns do not suggest that any climate differences existed over the period of malaria control scale-up that would have led to a substantially different pattern of malaria morbidity and mortality at the end of the evaluation period versus the start.

Multivariable models & Lives Saved Tool (LiST)

Multivariable analyses examined the effects of malaria control interventions on parasitemia prevalence, anemia prevalence, and suspected malaria cases. Results of multivariable analyses support the hypothesis that ITN ownership is associated with decreased risk of parasitemia and severe anemia, controlling for climate and other relevant factors. In anemia and parasitemia surveys, the odds of parasitemia were 19% lower in children living in households owning at least one ITN compared to those in households without ITNs. Similarly, ITN ownership was protective against severe anemia; the odds of severe anemia were 23% lower in children living in households owning at least one ITN compared to those in households without ITNs.

Multivariable analyses also support the hypothesis that ITN ownership is associated with decreased risk of mortality in children under five years of age, controlling for other

predictors of child mortality. At an individual level, children living in households with at least one ITN were less likely to die than children in households without ITNs (Hazard Ratio = 0.75; 95% Confidence Interval = 0.62–0.90). In addition, districts with greater proportions of children living in households owning ITNs had significantly fewer deaths among children under five years of age (Incident Rate Ratio = 0.55; 95% Confidence Interval = 0.21–0.99).

Calculations using the LiST model conservatively estimate that the scale-up of malaria control interventions during 2000–2010 could have prevented at least 21,600 deaths among children under five years of age in Malawi. This is not used as evidence to support the plausibility argument, but is instead used to show what the impact could have been given the malaria control intervention scale-up.

CONCLUSION

In summary, results from successive nationwide household surveys spanning the decade 2000–2010 show that ACCM in Malawi fell by 41% while malaria control interventions were being dramatically scaled-up. Household ownership of ITNs doubled between 2004 and 2010, reaching 57% of households (a level at which we would expect impact on morbidity and mortality); use of ITNs by children under five years of age increased 13-fold from 2000 to 2010 with 39% using ITNs in 2010; use of IPTp doubled from 28% in 2000 to 55% in 2010. Case management of malaria has also improved over this period: care seeking for children with fever has almost doubled from 35% in 2000 to 65% in 2010 and the proportion of children receiving the recommended first-line treatment among those who received any antimalarial, remained high at over 80%. Part of the decline in ACCM is likely due to the improvements in GDP and in the coverage of non-malaria control interventions including increased women's literacy, women giving birth in a health facility, exclusive breast feeding, care seeking for suspected ARI and diarrhea, improvements in nutrition, and the introduction of the Hib vaccine. However, not all of the decline in ACCM can be accounted for by the improvements in non-malaria control interventions. It is likely that the decline in all-cause mortality among children under five years of age was in part due to a reduction in malaria-specific mortality. Multivariable models support this claim; districts with more ITNs were shown to have fewer deaths in children under five years of age, controlling for other predictors of child mortality. Similarly, ITN ownership was found to be protective against severe anemia and parasitemia in children 6–30 months of age in multivariable models. Given all of the evidence, it is plausible that the scale-up of malaria interventions contributed to reductions in ACCM from 2000–2010.

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Acronyms

$_1q_0$	Infant mortality rate (per 1,000 live births)
$_4q_1$	Child mortality rate between exact age 1 and exact age 5
$_5q_0$	Under-five mortality rate (per 1,000 live births)
ACCM	All-cause childhood mortality
ACT	Artemisinin-based combination therapy
AL	Artemether-lumefantrine
ALMA	African Leaders Malaria Alliance
ANC	Antenatal care
ARV	Anti-retroviral therapy
ASWAp	Agricultural Sector Wide Approach
BASICS	Basic support for institutionalizing child survival
BCC	Behavior change communication
BMI	Body mass index
CCM	Community Case Management
CDC	(United States) Centers for Disease Control and Prevention
CHAM	Christian Hospitals Association of Malawi
CHERG	Child Health Epidemiology Reference Group
CI	Confidence interval (95%, unless otherwise stated)
CQ	Chloroquine
DH	District hospital
DDT	Dichlorodiphenyltrichloroethane
DFID	(United Kingdom) Department for International Development
DHS	Demographic and Health Survey
DPT-HBV	Diphtheria, Tetanus, Pertussis, Hepatitis B virus (vaccine)
DOTS	Directly-observed therapy (short-course)
EANMAT	East African network for monitoring antimalarial treatment
EHP	Essential Healthcare Package
EIR	Entomological Inoculation Rate
EPI	Expanded Program on Immunization
FEWS	Famine Early Warning System
GDP	Gross domestic product
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
GNI	Gross national income
GoM	Government of Malawi
Hb	Hemoglobin
Hib	*Haemophilus influenzae* type b
HDI	Human development index
HDSS	Health and demographic surveillance system
HIV	Human Immunodeficiency Virus
HMIS	Health management information system
HRP2	Histidine-rich protein II
HSA	Health surveillance assistant
IDSR	Integrated disease surveillance and response
IEC	Information, education, and communication
IGME	Inter-agency group for mortality estimation
IMCI	Integrated management of childhood illness
IPTi	Intermittent preventive treatment in infants

IPTp	Intermittent preventive treatment in pregnancy
IRS	Indoor residual spraying
ITN	Insecticide-treated mosquito net
IUGR	Intrauterine growth retardation
KAP	Knowledge, attitudes, and practices
LBW	Low birth weight
LiST	Lives Saved Tool
LLIN	Long-lasting insecticide-treated net
LMIS	Logistics management information system
M&E	Monitoring and evaluation
MAC	Malaria Alert Centre
MACEPA	Malaria Control and Evaluation Partnership in Africa
MDG	Millennium development goals
MERG	Monitoring and Evaluation Reference Group
MICS	Multiple Indicator Cluster Survey
MIS	Malaria Indicator Survey
MoH	Ministry of Health
MoLG	Ministry of local government
MSD	Medical Stores Department
NGO	Non-governmental organization
NMCP	National Malaria Control Program
NMS	National micronutrient surveys
NN	Neonatal (mortality)
OPD	Outpatient department
ORS	Oral rehydration salts
ORT	Oral rehydration therapy
*Pf*PR$_{2-10}$	*Plasmodium falciparum* parasite rate in children 2-10 years
PMI	(United States) President's Malaria Initiative
PMTCT	Prevention of mother-to-child (HIV) transmission
PNN	Postneonatal (mortality)
PSI	Population Services International
RBM	Roll Back Malaria partnership
RDT	Rapid diagnostic test
SP	Sulfadoxine-pyrimethamine
StC	Save the Children
SWAp	Sector Wide Approach
TT	Tetanus toxoid
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
USGS	United States Geological Survey
VitA	Vitamin A (supplementation)
WHA	World Health Assembly
WHO	World Health Organization

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INTRODUCTION AND BACKGROUND

Introduction

Purpose and Scope

In Malawi, malaria is highly endemic with 95% of the country's population at risk of infection. Malaria is estimated to be responsible for 34% of all outpatient visits and for 40% of hospital deaths [1]. It is the major cause for hospital admissions in children under five years of age. Due to the serious disease burden caused by malaria, and the extensive funding, both internal and external, which has been devoted to malaria control, there is a growing demand from policy-makers, program managers, donors and researchers to measure the extent to which malaria control interventions have made an impact on malaria. The objective of this report is thus to assess progress in Malawi's malaria control efforts over the past decade, in particular the progress towards the malaria control goals set forth in the 2008 Global Malaria Action Plan, and updated in 2011 [2, 3], and the Millennium Development Goals [4] and the Abuja Declaration.

The report is co-commissioned by the US President's Malaria Initiative (PMI) and Malawi's Ministry of Health (MoH) in support of the monitoring and evaluation activities conducted by the Roll Back Malaria Partnership (RBM) and Malawi's MoH. The main objective of the evaluation is to assess the impact of malaria control interventions, such as insecticide-treated bednets (ITNs), indoor residual spraying of insecticide (IRS), intermittent preventive treatment in pregnant women (IPTp) and malaria case management, on malaria morbidity and all-cause mortality in children under five years of age, during 2000–2010. This report provides detailed descriptions of intervention scale-up and sub-national variations in intervention coverage. The evaluation also considers other factors that might have contributed to the mortality decline over the period.

The evaluation focuses on the 2000–2010 period during which most malaria control interventions were introduced. Prior to 2000, ITN scale-up had not yet begun on a national scale, IRS was not used, and artemisinin combination therapy (ACT) antimalarial drugs had not yet been introduced. Mortality data and background information on relevant malaria control policies from the 1990s are included where this helps to put recent changes into perspective.

This time period is also relevant as it has been a decade of rapid changes in malaria control. Enabled by over $125 million in external funding for scale-up of Malawi's standard malaria control interventions, Malawi's capacity to control malaria was strengthened during the evaluation period.

Evaluation Design

The evaluation is based on a before-and-after assessment, which uses a plausibility evaluation design that measures changes in malaria control intervention coverage, malaria-related morbidity, and all-cause mortality in children under five years of age (ACCM) while accounting for other known contextual determinants of child survival during the evaluation period [5, 6].

This report, therefore seeks to describe in detail the improvements in malaria control interventions, as well as changes in malaria morbidity and mortality. The plausibility of a cause and effect relationship is further bolstered if:

- the magnitude of impact is consistent with intervention efficacy;
- the age-pattern of change is consistent with malaria-mediated morbidity and mortality;
- the timing of intervention scale-up matches trend change in impact, and if there is an ecological association between malaria risk and the observed impact.

Where data permit, each of these conditions is explored in the evaluation. Plausibility of causal association is also examined through a number of sub-national studies, where richer data sets permit:

- close examination of the temporal association between intervention scale-up and reduction of malaria-related morbidity, malaria cases and/or malaria-associated deaths;
- statistical tests of association between interventions, morbidity and mortality; and
- more detailed analysis of contextual factors that could have contributed to morbidity and mortality change.

At the national level, the report examines changes in other factors that have the potential to influence changes in malaria-related morbidity and/or ACCM. These contextual factors include climate, socio-economic factors such as gross domestic product (GDP), education, access to improved water and sanitation, and proximate determinants including access to health services, and other predictors of maternal and child health such as nutrition, immunization and comorbidities.

Where data permit, regression analysis is performed to assess impact of malaria control interventions on malaria morbidity (malaria parasitemia and anemia) and ACCM. Several sub-national case studies are examined in this way. Results of an individual level multivariable Cox Proportional Hazards analysis and a district-level multivariable Poisson analysis using national data from the 2010 Demographic and Health Survey (DHS) are also presented.

After determining if there has been a plausible impact on ACCM, the Lives Saved Tool (LiST), created by the Child Health Epidemiology Reference Group (CHERG), is then used to model the potential contribution of various health interventions (including, but not limited to malaria control interventions) to changes in mortality of children under five years of age between 2000 and 2010. This tool has been used by the malaria community to estimate the number of deaths prevented due to ITN and IPTp scale-up in multiple countries in sub-Saharan Africa [7, 8].

Evaluation Indicators

The selection and definition of indicators used in this evaluation for national-level analysis was guided by the recommendations of RBM's Monitoring & Evaluation Reference Group (MERG) shown in Table 1.

Table 1: Roll Back Malaria core population-based indicators used in this report

Intervention	Indicator Description
Prevention	
Vector Control via Insecticide-treated nets (ITNs) and Indoor Residual Spraying (IRS)	1. Proportion of households with at least one ITN
	2. Proportion of households with at least one ITN for every two people
	3. Proportion of population with access to an ITN within their household
	4. Proportion of population who slept under an ITN the previous night
	5. Proportion of children under 5 years old who slept under an ITN the previous night
	6. Proportion of households with at least one ITN and/or sprayed by IRS in the last 12 months
Prevention and control of malaria in pregnant women	7. Proportion of pregnant women who slept under an ITN the previous night
	8. Proportion of women who received intermittent preventive treatment for malaria during ANC visits during their last pregnancy
Case Management	
Diagnosis	9. Proportion of children under 5 years old with fever in the last 2 weeks who had a finger or heel stick
Treatment	10. Proportion of children under 5 years old with fever in the last 2 weeks for whom advice or treatment was sought
	11. Proportion receiving first line treatment, among children under five years old with fever in the last two weeks who received any antimalarial drugs
	12. Proportion of children under five years old with fever in last two weeks who received any antimalarial treatment.*
	13. Proportion of children under five years old with fever in last two weeks who received first-line treatment according to national policy within 24 hours from onset of fever.*
Impact Measure	**Indicator Description**
Mortality Indicator	14. All-cause under 5 mortality rate (ACCM).
Morbidity Indicators	15. Parasitemia Prevalence: proportion of children aged 6–59 months with malaria infection.
	16. Severe Anemia Prevalence: proportion of children aged 6–59 months with a hemoglobin measurement of <8 g/dL

Source: Household Survey Indicators for Malaria Control, June 2013 [9].
*These indicators are no longer recommended by the RBM MERG but are included here as they are still used to track NMCP targets and/or MDG.

ITNs are one of the principal tools in the arsenal of malaria control. The RBM ITN indicators report on both ownership and use of ITNs. ITN ownership is a household-level indicator, whereas use is measured for the individual. Use at the population level is

measured, as is use by the target populations historically at greatest risk of malaria morbidity and mortality: children under five years of age and pregnant women. IRS is another vector control tool used to control malaria by killing the mosquitoes resting on the walls of the house. The combined household ITN ownership or household sprayed by IRS indicator is used in this evaluation. Because IRS is conducted on a limited geographic scale, it is not expected to have a national level impact, but could have sub-national effects.

Intermittent preventive treatment for malaria in pregnancy (IPTp) is another key tool of malaria control programs which is measured by RBM indicators. The World Health Organization (WHO) recommends IPTp in highly endemic countries. IPTp was defined as at least two doses of SP after quickening and at least one month apart during the period under evaluation; however the WHO recommendations have since changed [10].

Proper diagnosis and treatment of malaria cases that were not prevented is also essential to malaria control. RBM population-based indicators also measure some elements of diagnosis and treatment of malaria; however, facility-based data are often better suited to monitoring trends in malaria case management and are included in this report where relevant. Population-based surveys do not typically contain data on outcomes from visits to health facilities; thus, the proportion of children with fever receiving diagnostic tests for malaria is measured via a proxy indicator in which receipt of a finger or heel stick is considered an indicator for having had a diagnostic test. Questions on care seeking behavior for fever in children under five years of age, and of the type and timing of treatment with antimalarial drugs are also included.

The prevalence of severe anemia and parasitemia in children 6–59 months of age are two outcomes examined in this evaluation. Severe anemia, defined as blood hemoglobin levels less than 8 grams per deciliter, is an impact measure for total malaria-related disease burden as it is associated with malaria-related mortality and it is measurable at the population level with less seasonality than parasitemia [11-13]. Parasitemia prevalence is perhaps the most direct measure of malaria burden but there are challenges to using national estimates to measure success of programs given the focal nature of malaria transmission. For this reason, morbidity analyses are supplemented by longitudinal facility-based data on malaria cases where possible.

In line with RBM-MERG guidance, the principal measure of impact used in this evaluation is ACCM, because malaria-specific mortality cannot be reliably measured in most parts of sub-Saharan Africa with the current sources of data. This measure is preferable to malaria-attributable mortality for a number of reasons, including: the non-availability of national-level malaria-specific mortality data; concerns about the sensitivity and specificity of the verbal autopsy method for distinguishing malaria deaths from deaths from other febrile illnesses [14] and the fact that malaria has an "indirect" contribution to under-five mortality (due to non-malaria deaths) that is equivalent to 50%–100% of the mortality that can be directly attributed to malaria [15].

Data Sources

This evaluation relied on existing data sources. The data source for mortality in children under five years of age, malaria control intervention coverage indicators and many contextual factors, is the series of DHS surveys conducted in 2000, 2004 and 2010 as well as a Multiple Indicator Cluster Survey (MICS) conducted in 2006. Additional data sources are referred to where relevant – particularly where these shed light on variables that were not measured in the main national surveys. The 2010 national Malaria Indicator Survey was not used as a primary source for analyses of trends in coverage indicators due to differences in timing of data collection between DHS/MICS and MIS surveys; DHS/MICS are typically conducted during dry seasons and MIS are designed to collect data during high transmission seasons, during or directly following rainy seasons. Supplementary data sources include: the 2010 Malaria Indicator Survey (MIS), national micronutrient surveys (NMS) from 2001 and 2009; and a series of anemia and parasitemia (A&P) surveys conducted in several districts from 2005–2009. Integrated Disease Surveillance and Response (IDSR) and Health Management Information System (HMIS) health facility-based morbidity data are also included. Additional data were obtained on antimalarial stockouts from Malawi's Logistics Management Information System (LMIS) and on financing information from the National Health Accounts. Data on climate variables included satellite temperature data from the Moderate Resolution Imaging Spectroradiometer (MODIS) (NASA Processes Distributed Active Archive Center data pool from the U.S. Geological Survey (USGS)/Earth Resources Observation and Science Center) and rainfall data from the USGS Famine Early Warning Systems Network (FEWS NET). Data sources used for analyses are summarized on a timeline in Figure 1. Finally, this evaluation makes reference to numerous published studies on the relationship between malaria control interventions and their impact. Throughout the report, the sources of data are clearly cited. A more detailed description of the data sets,

HIV bias in Mortality Measurement

Mortality estimates presented here have not been adjusted for HIV. In high prevalence countries, deaths of mothers due to AIDS will result in an omission of birth histories that include children with elevated mortality risk. The UN Inter-agency Group for Child Mortality Estimation has developed methods of HIV-adjustment of child mortality estimates and recommends this adjustment in countries where >5% of adult women are infected with HIV. However, other analyses of potential HIV bias by Rajaratnam and colleagues* using DHS data from 21 countries shows substantial variation in effect on child mortality estimates in both directions, even in countries where HIV prevalence exceeds 20%.

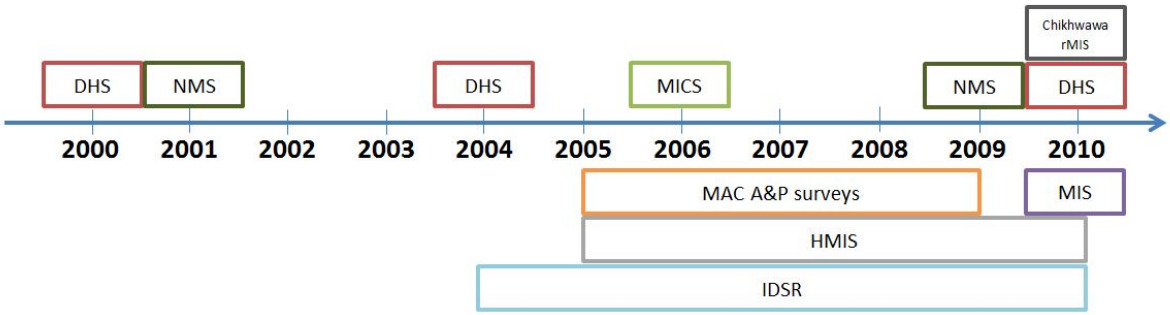
Data from the Malawi DHS indicate that HIV prevalence among women age 15–49 has not changed significantly from 2004 to 2010 (13.3% vs. 12.9%), indicating that any bias introduced in child mortality estimates by HIV has likely not changed over the study period. Finally, improvement in coverage of ARV and PMTCT over the evaluation period should reduce any favorable bias (exaggeration of mortality decline) because birth histories of HIV positive mothers are progressively more likely to be included over time due to improved survival of HIV infected women. Therefore, in this evaluation report, the mortality estimation methods do not take into account potential selection bias arising from high HIV prevalence, and this could be considered a limitation of the report.

**Rajaratnam et al. Lancet. 2010 Jun 5;375(9730):1988-2008.*

survey methods, sample sizes and other statistical parameters can be found in the annexes.

This report includes both DHS mortality estimates and those from the inter-agency group for mortality estimation (IGME). IGME was established in 2004 to produce harmonized estimates of child mortality and to improve mortality estimation methods. IGME mortality estimates are based on available survey, vital registration and census data weighted according to data quality. These data are then fitted to a regression curve and smoothed. The models are used to extrapolate data to target years. Some additional adjustments are made in high HIV prevalence countries (see box: HIV bias in Mortality Measurement). DHS estimates were used in regression analyses for this evaluation because IGME estimates lag behind DHS direct estimates of mortality and do not permit stratification needed to inform the plausibility argument [16-18].

Figure 1: Data sources timeline



Country Context

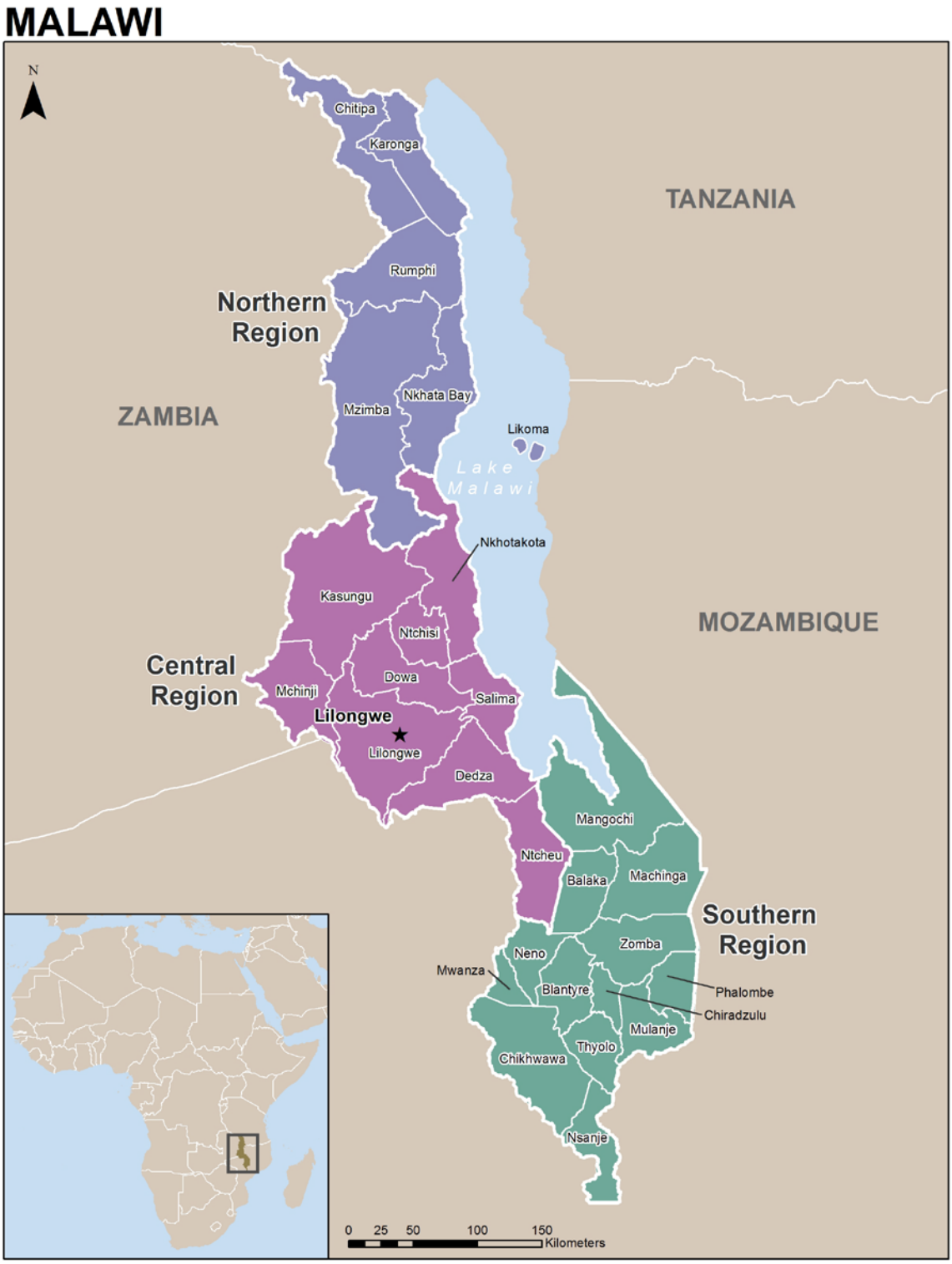
Background

Malawi covers an area of approximately 119,310 square kilometers and is landlocked between Zambia to the northwest, Tanzania to the north, and Mozambique to the east and southwest (Figure 2). Physically, Malawi is part of the Great Rift Valley of East and Central Africa. Three great lakes (Lake Malawi, Lake Malombe, and Lake Chirwa) make up approximately 21% of its surface land cover. Rising from Lake Malawi, the majority of the country sits on a plateau between 900–1,200 meters above sea level, with the elevation increasing to >2,500 meters in parts of the northern and southern highlands. Malawi's climate is tropical with three distinct seasons: rainy (November to April), cold and dry (May to mid-August) with nighttime temperatures sometimes as low as 10–14 ° C and hot (mid-August to November) with temperatures reaching 40–42°C. Areas along the lakeshore have an extended hot season and higher humidity, while the rains are more prolonged in the North.

The country is divided administratively into three regions which are further divided into 28 districts (Figure 2). In 2008, Malawi's population was estimated to be 13.1 million and predominantly rural (84%), with 46% under 15 years old and 18% under five years old [19].

Malawi's economy is based on agriculture, which employs 80% of the workforce, contributes over 80% to foreign exchange earnings and accounts for over a third of GDP [20]. Two agricultural sub-sectors are: the smallholder sub-sector and the estate sub-sector. Although the smallholder subsector contributes 70% to agricultural GDP and the estate subsector only 30%, crop yields have been insufficient for national food needs.

Figure 2: Map of Malawi showing the international, regional, and district boundaries [21]



Some basic development indicators for Malawi are presented in Table 2. According to the United Nations Development Program, Malawi ranked 171 out of 187 countries in 2011 in the Human Development Index (HDI), a composite measure of health, education and income. Malawi's HDI score of 0.400 was below the 2011 regional average of 0.463 for sub-Saharan Africa and far below the global average of 0.682 [22]. GDP per capita in 2009 in current US$ was 318.4 [23]. In 2010/11, 51% of the population was

characterized as poor[1] and 25% were ultra-poor, and the poorest 10% of the population had a median income of US$101.60 per year[2] [24]. As of 2010, the end of the evaluation period, life expectancy at birth was 54.2 years. Child and maternal mortality was high (under-five mortality = 112 deaths per 1,000 live births; maternal mortality ratio = 675 deaths per 100,000 births), despite recent declines (see
Table 2 below). In 2010, the HIV/AIDS prevalence among adult women (age 15–49) was 12.9% with a very uneven distribution of HIV positive women by location of residence; HIV prevalence in women in urban areas was 22.7% compared to 10.5% in women from rural areas (DHS, 2010). Stunting among children under five years was high in 2010 at 47% and 13% of children under five years were underweight.

Table 2: Basic development indicators for Malawi, 2010

Socioeconomic Indicators	
GDP per capita in current US$†	318.4
Rural population*	84%
Unemployment (% of total labor force)*	6%
Net primary school attendance rate (attended at least some primary school)** Male Female	 93.4% 84.8%
Literacy** Male Female	81.0% 67.6%
Use of improved drinking water sources**	79.3%
Maternal Health Indicators	
Total fertility rate (no. of children per woman)**	5.7
% Births assisted by a skilled provider**	71.4%
% HIV prevalence (women 15-49 yrs)**	10.6%
Maternal mortality ratio (deaths per 100,000 live births)**	675
Child Health Indicators	
% Children under five years who are underweight**	12.8%
% Children 12–23 months fully vaccinated**	81.0%
% Children under five years who are stunted**	47.0%

†2009 UN data accessed July 3, 2012 http://data.un.org/CountryProfile.aspx?crName=MALAWI
*Data are from the Malawi National Statistical Office (CountrySTAT Malawi) derived from 2008 census data (http://www.countrystat.org/mwi/cont/pages/page/indicators/en)

[1] Poor is defined as the population having a total consumption per person per year less than 37,002 Malawi Kwacha and ultra-poor is consumption less than 22,956 MK.
[2] The average conversion rate for March 2010-March 2011 (the dates of the Integrated Household Survey 3 field work) was US$ 0.0065 per 1 Malawi kwacha. http://www.oanda.com/currency/historical-rates/

**Data are derived from the Malawi DHS 2010

Health Services

The country's health service delivery system is pyramidal, consisting of community, primary, secondary and tertiary care levels [25]. At the community level, service is provided through Health Surveillance Assistants (HSAs)—community-based government-employed health extension workers—with a focus on preventive interventions and community case management. Primary care is delivered through clinics and health centers where curative, maternity child health and preventive services are offered. District and central hospitals provide secondary and tertiary care services respectively. The major providers of health services are public entities including the Ministry of Health, which manages 380 (62.9%) facilities, and the Ministry of Local Government (MoLG) which manages 32 (5.3%) facilities (Table 3). The private not-for-profit sector also plays a significant role in service provision. For example, religious organizations, under the umbrella of the Christian Hospitals Association of Malawi (CHAM), manage 160 (26.5%) facilities and NGOs own 5.3% of the health facilities. The public and private not-for-profit facilities all follow the MoH guidelines. The remaining facilities, not represented in Table 3, are owned by the for-profit private sector, which is mostly concentrated in urban settings.

Table 3: List of health facilities by ownership [1]

Type of facility	Private, not-for-profit		Public		Total	Level of Service
	NGO	CHAM	MoLG	MoH		
Central hospital	0	0	0	4	4	Tertiary
Mental hospital	0	1	0	1	2	Tertiary
District hospital	0	0	0	22	22	Secondary
Rural hospital	0	27	0	19	46	Secondary
Health center	1	115	12	288	416	Primary
Clinic	28	8	4	2	42	Primary
Maternity center	3	1	12	2	18	Primary
Dispensary	0	8	4	42	54	Primary
Village clinics	0	0	0	4000	4000	Primary
Total	**32**	**160**	**32**	**4380**	**4604**	

NGO – Non Governmental Organization; CHAM – Christian Hospitals Association of Malawi; MoLG – Ministry of Local Government; MoH – Ministry of Health

In order to respond to the enormous health problems with very limited resources, the Government of Malawi has developed a Sector Wide Approach (SWAp) program. One of the activities implemented within this framework is the provision of an essential healthcare package (EHP). The EHP addresses the most common causes of morbidity and mortality [26], including pneumonia, diarrhea, malaria, HIV/AIDS and malnutrition, and focuses mainly on health problems that disproportionately affect the poor. The EHP is delivered at the community, primary and secondary levels of the healthcare delivery system and is provided free of charge. Currently, uncomplicated malaria is treated at community level by HSAs in hard to reach areas and in the outpatient departments of

health facilities. However, all cases of severe malaria are referred to the district and central hospitals for management.

The distribution of health care workers by specialization and location are summarized in Table 4.

Table 4: Health worker population ratios at national level and distribution

Occupational categories/Cadres	2008		Distributions %	
	National	HW/1000 population	Urban	Rural
Generalist medical practitioners	190	0.01	77%	23%
Nursing professionals	2,928	0.2	71%	29%
Nursing associate professionals	968	0.07	60%	40%
Pharmaceuticals technicians and assistants	293	0.02	58%	42%
Medical and pathology laboratory technicians	473	0.03	63%	37%
Health Surveillance Assistants (HSAs)	10,055	0.77	21%	79%

Source: Health Worker Census 2008

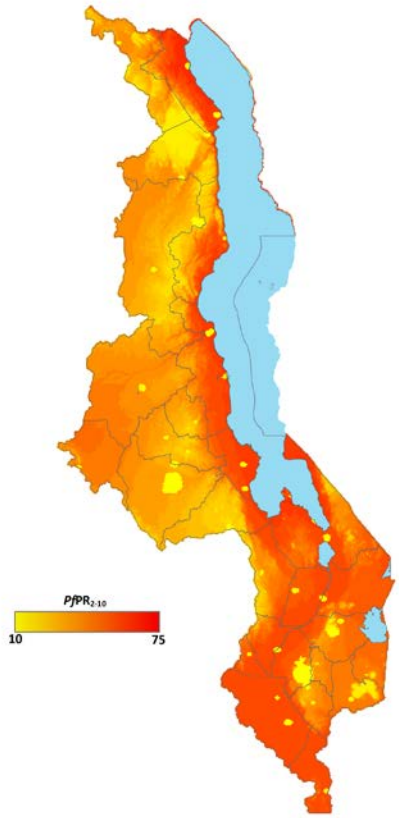
HW = Health worker

Malaria in Malawi

In Malawi, malaria is endemic in more than 95% of the country. Non-endemic regions include the mountainous areas in the north and south of the country. Malaria transmission increases with the annual rains that typically begin in November-December and last through March-April in most parts of the country. The highest transmission areas are along the hotter, wetter and more humid low-lying areas (lakeshore, Shire River valley and central plain), while the lowest risk areas are along the highland areas of Rumphi, Mzimba, Chitipa and Kirk range as shown in Figure 3 [27]. Figure 3 shows the malaria risk (*Plasmodium falciparum* parasite rate ($Pf\text{Pr}_{2\text{-}10}$) for 2010. *P. falciparum* is the most commonly transmitted species, accounting for 98% of the infections and almost all cases of severe disease and deaths. *P. malariae* and *P. ovale* are responsible for approximately 2% of cases. *P. vivax* is very rare in Malawi [28].

As in most of sub-Saharan Africa, children under five years of age and pregnant women in Malawi bear the highest burden of malaria. Approximately one-third of all outpatient visits and 40% of hospitalizations of children under five years of age are reported to be due to malaria according to the 2010 HMIS report. Further analysis of trends in malaria cases during the evaluation period are presented later in this report.

Figure 3: Predicted *Plasmodium falciparum* parasite prevalence (*Pf*Pr) in children 2–10 years of age ($PfPr_{2-10}$), Malawi 2010[3]



Source: Map from Bennett *et al.*, 2013 [29]

Malaria Vectors in Malawi

Some regional entomologic studies have been conducted in Malawi. Data from the Lower Shire Valley (Chikwawa District) in Southern Malawi from January 2002 to January 2003 [30], demonstrate that in the Lower Shire valley, malaria transmission is perennial and in certain months, intense. In 2003, the entomological inoculation rate (EIR) was calculated as 183 infective bites per person per year. The EIR measures the intensity of malaria parasite transmission by anopheline vectors. *Anopheles gambiae s.s.*, *An. arabiensis,* and *An. funestus* were responsible for 48%, 36%, and 15% of the malaria transmission, respectively. Most transmission took place during the rainy season (between January and April).

[3] Cross-sectional community *P. falciparum* parasite rate (*Pf*PR) data for the period 2000-2011 for Malawi were assembled by year from a combination of published and unpublished sources. The $PfPR_{2-10}$ samples were then used to generate a continuous map of the annual mean for the year 2010. The spatial distribution of malaria risk remained largely consistent throughout the period 2000-2011, with the highest predicted prevalence (40 to 50%) along the shore of Lake Malawi, along the Shire River Valley, and portions of the central plains. Across the entire period prevalence was lowest in urban areas (notably urban areas within Lilongwe, Blantyre, and Mzuzu districts, where prevalence was between 10 and 20%) and along the northern and central highlands. Provided by Adam Bennett (Tulane University).

Vector densities were also measured in in Southern Malawi [30]. *An. arabiensis* was found to be abundant throughout the year, *An. gambiae* s.s. was most common during the wet season, and *An. funestus* was found in all samples but was most common during the dry season. Both *An. Gambiae* s.s. and *An. funestus* were highly anthropophilic, preferring human blood meals, with human indices of 99.2% and 96.3%. *An. arabiensis* fed primarily on humans (85.0%) but a significant number fed on cattle (10.9%). Sporozoite rates were significantly higher ($p<0.01$) in *An. gambiae* s.s. (10.6%) than in *An. arabiensis* (3.2%) or *An. funestus* (4.5%) [30].

The emergence of insecticide resistance is highly relevant to the implementation and effectiveness of vector control measures such as ITNs and IRS. Emerging insecticide resistance of anopheline vectors has recently been documented in Malawi. In 2002, Spiers and colleagues demonstrated that *An. arabiensis* was susceptible to pyrethroids and organophosphate but exhibited reduced susceptibility to DDT [31]. In 2009, resistance of *An. funestus* to pyrethroids and bendiocarb (carbamate) was reported in Nkhotakota District in central Malawi, a site where a pilot IRS program was being implemented [32] and on Likoma Island, situated in Lake Malawi [33]. Of note, pyrethroid resistance was also detected in non-IRS areas, which could be a result of different selection pressures other than IRS such as wide-spread use of pyrethroids for agricultural use on cotton or vegetables. *An. gambiae* complex populations, collected from Karonga District in the northern region, were completely susceptible to all three pyrethroids tested [34]. This indicates the use of pyrethroids, both in IRS and ITNs, are still effective at reducing the *An. gambiae* vector population in Malawi.

Malaria Control Strategy

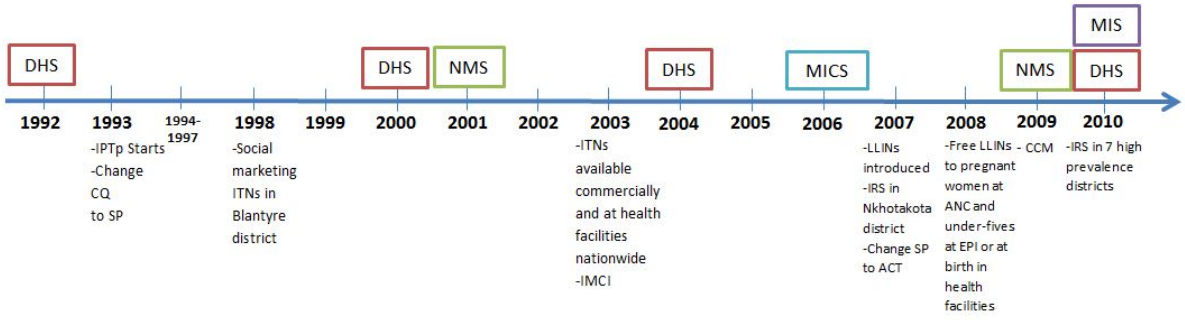
The first attempt at establishing a national malaria control policy was in 1970. The policy consisted of three main strategies [28]:

1. Chloroquine prophylaxis for children under five years of age through under-five clinics
2. Presumptive treatment of symptomatic malaria among children and adults with chloroquine
3. Vector control with indoor residual spraying and larvicides in certain urban areas.

In 1984, recognizing that malaria was a major public health problem, the Government of Malawi established the National Malaria Control Committee to investigate suspicions of *P. falciparum* resistance to chloroquine. In 1987 a manager was appointed and the NMCP was formally established within the Directorate of Preventive Services. The formation of this government body marked the start of a coordinated and organized effort for malaria prevention, control and treatment with an emphasis at that time on case management and the investigation of antimalarial drug efficacy. Malawi was a pioneer among African countries, initiating important changes in malaria policies. In 1993, Malawi was the first country to officially recommend use of SP for IPTp, and Malawi was the first to change their first-line antimalarial drug from chloroquine to SP following evidence of chloroquine resistance. In addition, Malawi was the first country in sub-Saharan Africa to have a national ITN program [1].

From 2001 to date, the response to the malaria problem in Malawi has been captured through three consecutive five-year Malaria Strategic Plans. The first strategic plan of 2001–2005 was aimed at renewing efforts to reduce malaria morbidity and mortality through effective case management in the context of multi-sectoral implementation of malaria control involving the government, NGOs, private sector, civil society, research institutions and communities [35]. This first strategic plan was based on the following pillars: (1) building and strengthening partnership among all stakeholders; (2) promoting ownership of malaria activities at all levels of health care delivery; (3) contributing to health sector reforms; (4) integrating malaria control activities into primary health care and other social economic development programs; (5) strengthening the health information system and research; (6) increasing coverage of cost-effective interventions such as ITNs; and (7) strengthening community participation such as home management of uncomplicated malaria. The 2005–2010 Malaria Strategic Plan was focused on rapidly scaling up interventions to reduce malaria morbidity and mortality. Three strategic areas were identified for scale-up, including (1) case management, (2) intermittent preventive treatment of pregnant women (IPTp) and, (3) use of ITNs [26]. The 2011–2015 Malaria Strategic Plan was the third plan released by the MoH [1]. Intervention implementation efforts to date are depicted in Figure 4.

Figure 4: Milestones in Malaria Strategy in Malawi



At a global level, Malawi is a signatory to the Abuja Declaration and the Roll Back Malaria (RBM) partnership. The RBM targets therefore form the basis for the Malawi national malaria policy, which is captured in a series of policy documents and guidelines. In addition, the Malawi national malaria goals align with the Millennium Development Goals to reduce child mortality (Goal 4) and to halt and begin to reverse the incidence of malaria (Goal 6) [4]. Malawi is also a member of the African Leaders Malaria Alliance (ALMA), an organization of African Heads of State working in unison to end malaria-related deaths.

Operational Research in Malawi

Since 1984 when the National Malaria Control Committee and later the NMCP of Malawi were first established, locally-collected data have been used to shape policies on malaria control. Topics of operational research studies used to shape the original national malaria policy and subsequent strategic plans include assessments of malaria burden, drug efficacy studies, socio-behavioral studies and analysis of the economic cost

of malaria. Malawi's extensive malaria research has led to advancements in regional and international understanding of malaria control and prevention.

Malawi was on the forefront of drug efficacy studies in the early 1990s. Results of these studies led to recommendations for changing first-line antimalarial drugs from chloroquine (CQ) to SP. Malawi was the first country to implement this change in drug policy. In addition, seminal research showing that the use of SP for IPTp could reduce low birth weight in first or second pregnancies was conducted in Malawi [36]. These results helped WHO develop its IPTp recommendations and established IPTp as one of the key malaria prevention interventions in highly endemic sub-Saharan African countries. Other research topics investigated in Malawi by organizations such as the Blantyre Malaria Project, Michigan State University, and Wellcome Trust include the pathogenesis and management of severe malaria, the spread of drug resistance, and the interaction between HIV and malaria.

The Malaria Alert Centre (MAC) is a local organization contributing to important malaria research in Malawi. MAC was founded in 1989 to fulfill the malaria research component of the agenda of the University of Malawi College of Medicine. MAC is also tasked with supporting the NMCP with training, operational research, and monitoring and evaluation of malaria interventions. MAC receives funding from various agencies, including the Bill and Melinda Gates Foundation, USAID, CDC, and WHO. MAC has carried out research in alternative distribution methods for malaria control interventions, pioneered work on the collection of routine malaria data at the community level, conducted drug efficacy trials, and evaluated the effectiveness and cost-effectiveness of intermittent preventive treatment in infants (IPTi).

Financial Resources & Inputs

Malawi's major sources of external funding for malaria, the Global Fund and PMI, have distinct mechanisms and timeframes for planning, disbursement and procurement that make analysis on a calendar basis difficult. Commitments and disbursements appear when they were made and appear in official documents. Amounts for commodities were counted in the calendar year in which they actually occurred. It is possible that commitments and procurements may have occurred in different years for the same procurement.

The capital costs of malaria control—initial costs of scaling up interventions—are significant for any country to assume on its own. According to some estimates, ideally, a median per capita per annum amount of US$2.43 is necessary to scale up and maintain the necessary levels of coverage for the different interventions in African countries [37]. Since this can amount to as much as 1.2% of the total GDP per annum (2005 data) in a country such as Malawi, external funding from global partners is critical.

In Malawi, total health expenditures for malaria control came mainly from three sources; Government of Malawi (GoM), external donors—Global Fund and PMI; and, households. Table 5 shows annual totals and percentages for key financial indicators for malaria (2006 – 2009). On average, $75 million were spent annually in Malawi from all sources on malaria prevention and case management, accounting for 17% of all

expenditures on health in the country. Of the $75 million, an average of 54% of expenditures for malaria came from external donors—mainly the Global Fund and PMI; household out of pocket expenses, at an annual average of 27%, were the second largest source of funding. GoM resources constituted around 12%–18% of total malaria funding in 2006 – 2009. An average of 17% of all malaria expenditures, including out of pocket expenses, was spent on preventive services, including ITNs and IRS, whereas curative services, including purchase of ACTs and inpatient care consumed 76% of the total. Most donor funding was for procurement of commodities for malaria prevention.

Table 5: Malaria health expenditures, 2006/07–2008/09*

Indicator	2006–07	2007–08	2008–09	Average 2006–09
Total expenditure on health for Malaria (USD)	$61,193,771	$66,884,554	$97,340,917	$75,139,747
Total expenditure on malaria as % of total health expenditure	16.6%	14.6%	18.9%	16.7%
Total government expenditure on health for malaria (USD)	$7,332,636	$15,825,904	$17,672,399	$13,610,313
Per capita total expenditure on health for malaria	$4.72	$5.09	$7.31	$5.70
Total expenditure on health for malaria as a % of GDP	1.86%	1.78%	2.21%	1.95%
Government spending on health for malaria as % of GDP	0.22%	0.42%	0.40%	0.35%
Government expenditure on health for malaria as a % of the total health expenditure for malaria	11.98%	23.66%	18.16%	17.93%
Government per capita total health expenditure	$0.57	$1.20	$1.33	$1.03
Government total expenditure on health as a % of total government expenditure	0.56%	1.13%	0.99%	0.90%

*Dates are based on the Malawi fiscal year (July 1-June 30)

In common with other countries in the region, the sharp rise in funding for malaria control has enabled an accelerated scale-up of key malaria control interventions in Malawi. The significant boost in funding for malaria that started around 2006 came mainly from the Global Fund and PMI. In 2006, under Round 2, Malawi received a $17.9 million Global Fund grant to fight malaria, and a further $68.9 million was granted under Round 7 in 2011. PMI has contributed $83 million between 2006 and 2010. Table 6 shows the increases in funding commitments and actual expenditures Malawi has received between 2006 and 2010 (in some cases amounts cited may be less than the commitment for a specific year). 2008 was the year with the highest per capita funding— US$2.2. In 2006 and 2009, funding was just US$0.66 and US$1.48 per capita respectively.

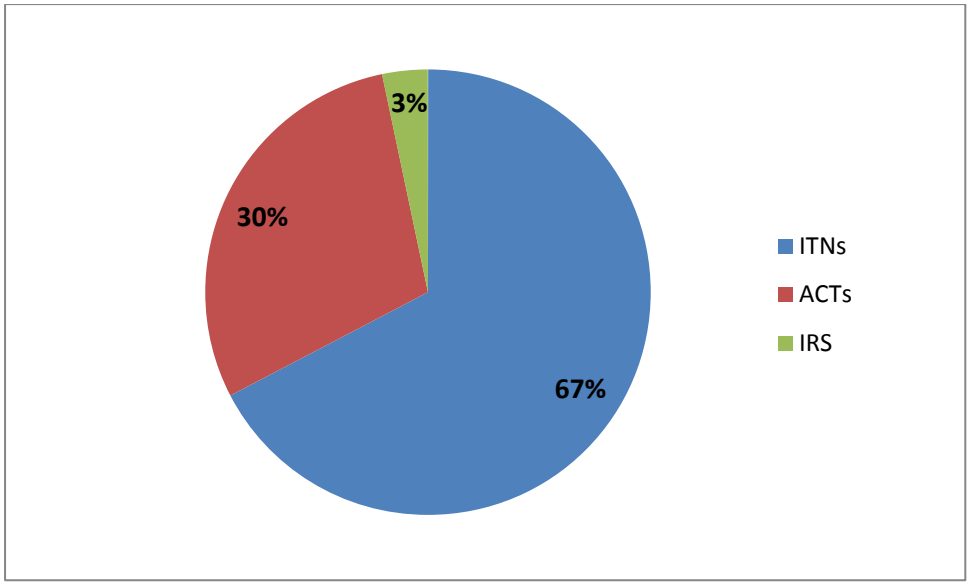
Table 6: Disbursements and commitments from PMI and Global Fund in US$ millions, 2006–2010

Source	2006	2007	2008	2009	2010	Total
PMI*	2.0	18.5	17.9	17.7	27.0	83.1
Global Fund (Rounds 2 & 7)**	6.4	11.6	15.0	3.7	5.5	42.2
Total	2014.4	2037.1	2040.9	2030.4	2042.5	125.2

*Commitments ** Disbursements

Figure 5 shows Global Fund and PMI expenditures by commodity type for the period between 2004 and 2010. The largest percentage of Global Fund and PMI procurements were expenditures for ITNs—a total of more than 9 million ITNs. Accounting for nets that need to be replaced and assuming homogeneous distribution in 3.4 million households across the country, a coverage of almost 100% with at least one ITN could have been achieved during some years of the period under study. Since 2007, more than 21 million ACTs were procured. Accounting for the number of malaria cases expected to be seen in facilities on an annual basis, the amounts of ACTs procured filled most needs for the country. RDTs were not purchased during the evaluation timeframe. Indoor residual spraying was very limited in Malawi and did not reach a sufficiently large population to have a major impact on morbidity and mortality.

Figure 5: Malaria commodity expenditures by type of commodity for the period 2004–2010, from Global Fund and PMI sources. Total: $61,746,858.



Note: ACTs were costed at an average of $.91 and $.82 per treatment for procurements by the US- PMI and Global Fund, respectively. ITNs were costed at $4.47 per ITN for procurements by the US-PMI and Global Fund. ACT procurements began in 2007. ITN procurements began in 2004. RDTs were not procured before 2010.
Source: ITNs –Global Fund; DELIVER Project; ACTs – DELIVER Project; IRS – RTI International

SCALE UP OF MALARIA CONTROL INTERVENTIONS

Insecticide-Treated Nets (ITNs)

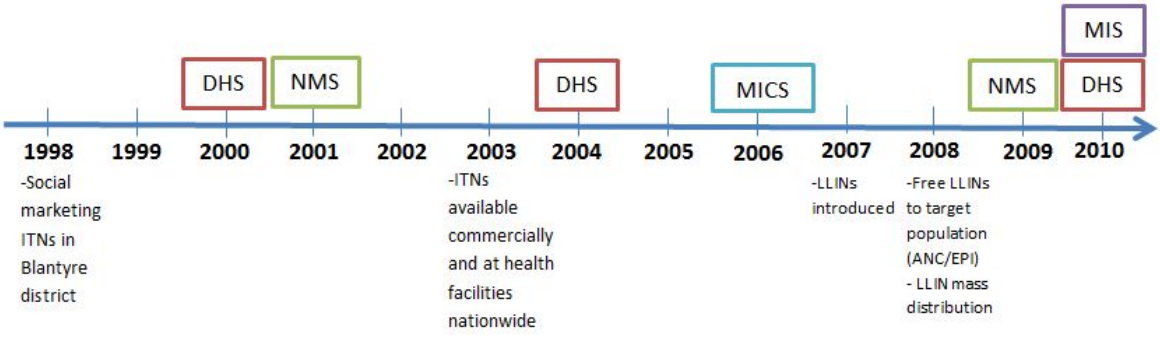
Background

ITNs are a highly effective tool for prevention of malaria both through direct insecticidal effects, and by reducing contact between vectors and humans, therefore lowering parasite loads at the community level [38-40]. Use of ITNs has been found to reduce child mortality [41], lower the risk of clinical malaria illness, reduce parasite prevalence and reduce the risk of high-density parasitemia [42]. ITN use also reduces the risk of severe anemia and splenomegaly and may improve anthropometric outcomes in children [43]. ITN use by pregnant women has been shown to reduce placental parasitemia, improve birth weight and reduce fetal loss and stillbirth [44, 45]. The protective effects of ITNs are most pronounced in high transmission settings in children under two years of age and in pregnant women, both of whom have limited immunity to malaria [46, 47]. In Malawi, ITNs have been shown to be effective in protecting pregnant women from parasitemia and low birth weight [48], and in protecting children under five years of age from malaria infection [49].

ITN Implementation

The history of ITN implementation in Malawi is summarized in Figure 6. In 1998, Malawi started a pilot social marketing ITN program in Blantyre District. Through this program, subsidized nets (with a treatment kit) were sold to pregnant women and children under five years of age for US$0.60, through public health facilities. At the same time, a more expensive conical net (with insecticide treatment kit) was made available to consumers for $5–6 through private sector outlets, targeting those who could afford a commercially priced net. The nets were branded and heavily promoted to the public through a range of mass media and interpersonal communication channels. By January 2003, subsidized ITNs were being delivered via social marketing to pregnant women and children under five years of age through commercial outlets and public health facilities in all 28 districts of the country. Thus, Malawi had the first national ITN program in sub-Saharan Africa [1]. Long-lasting insecticidal nets (LLINs) were introduced in 2007, followed by a mass distribution campaign in 2008 [28].

Figure 6: Milestones in ITN strategy and interventions in Malawi*



*DHS = Demographic and Health Survey; NMS = National Micronutrient Survey; MIS = Malaria Indicator Survey.

In 2008, a new LLIN policy was launched supporting national distribution campaigns every two to three years, together with new programs for free distribution of LLINs to target populations. Pregnant women were eligible to receive one free LLIN during the first antenatal care (ANC) visit, and children were eligible to receive one free LLIN either at birth if born in a health facility, or at the first visit under the Expanded Program on Immunization (EPI). Since 2008, the country has distributed 4.8 million LLINs through ANC, EPI clinics, and a time-limited mass distribution campaign targeting the poor and vulnerable groups (i.e. the 2008 LLIN campaign). Annual data on national ITN distribution from 2005–2010 are shown in Table 7.

Table 7: National ITN Distribution in Malawi, 2005–2009 [28]

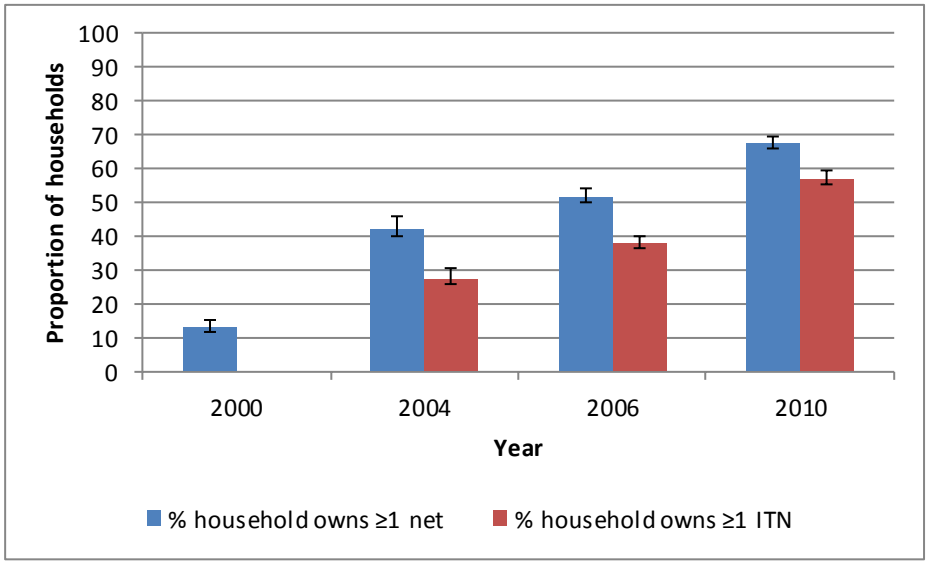
Year	ITN Distribution	Mid-year Population
1998	13,500	9,933,868
1999	3,530	10,152,753
2000	41,835	10,475,257
2001	46,062	10,816,294
2002	185,968	11,174,648
2003	1,029,884	11,548,841
2004	1,295,498	11,937,934
2005	815,620	11,999,585
2006	1,508,735	12,345,253
2007	673,348	12,700,877
2008	2,520,044	13,066,746
2009	957,000	13,432,615
2010	1,258,001	13,808,728
Total	**7,732,748**	

Source: Mid-year population from NMCP, based on 1998 and 2008 Censuses.

ITN Coverage Trends

The proportion of households that owned at least one net (treated or untreated) increased from 13.1% in 2000 to 67.3% in 2010 (Figure 7). Ownership of ITNs rose from 27.4% in 2004 to 56.8% in 2010 (Figure 7). These trends indicate a dramatic increase in net ownership over the past decade.

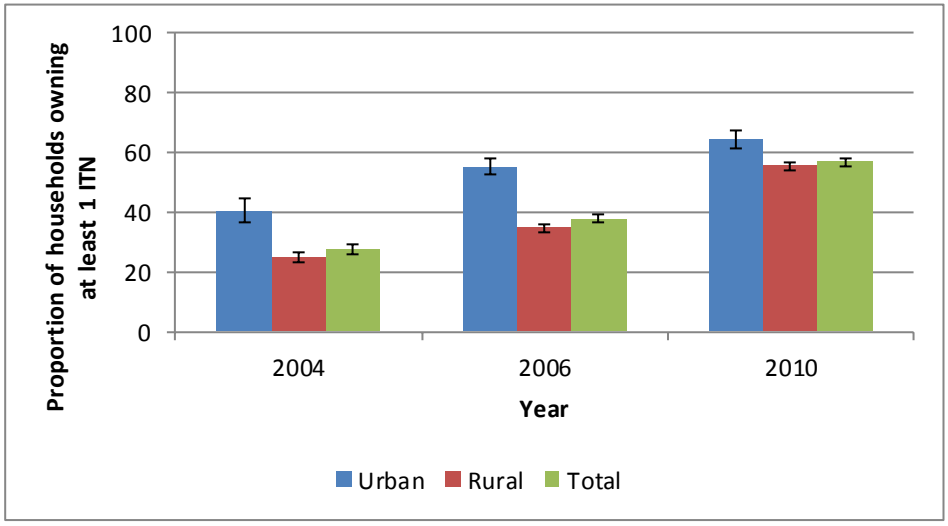
Figure 7: Household ownership of any nets and ITNs, 2000–2010



Note: questions on brand of net and on treatment of nets with insecticide were not included in the 2000 DHS thus ITN ownership cannot be estimated for this survey.

As seen in Figure 8, household ownership of ITNs varies greatly by location of household residence with urban households being significantly more likely to own at least one ITN compared to rural households in all survey years, although this disparity appears to be narrowing.

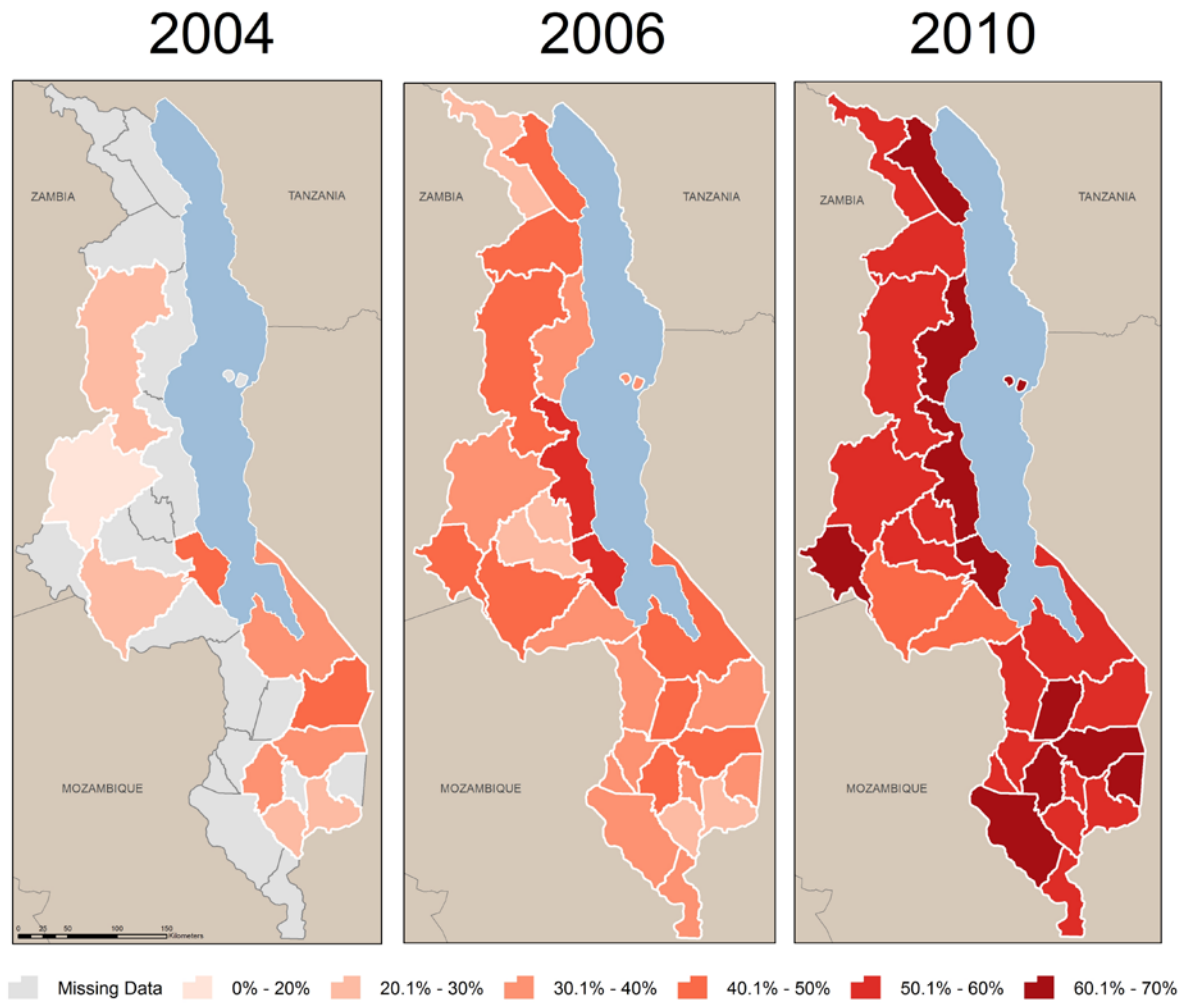
Figure 8: Household ownership of ITNs by residence, 2004–2010



Note: questions on brand of net and on treatment of nets with insecticide were not included in the 2000 DHS thus ITN ownership cannot be estimated for this survey.

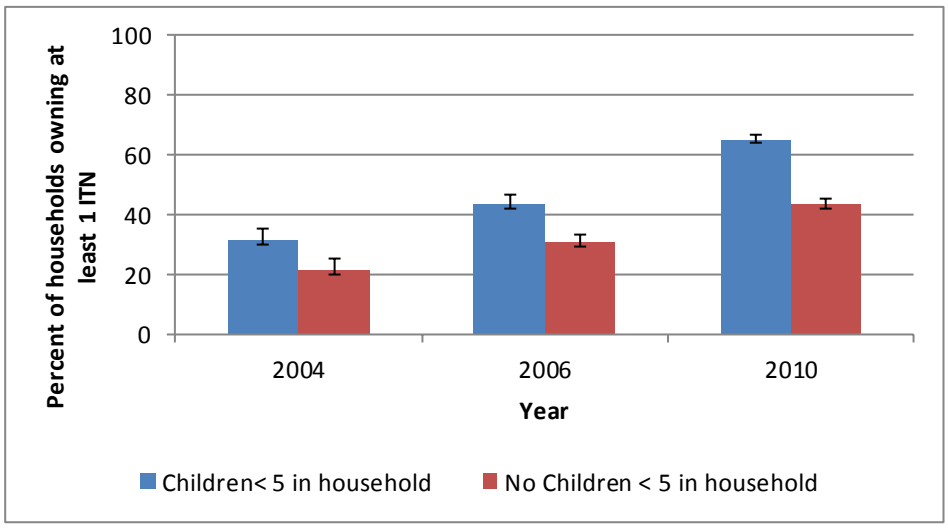
Although some variation in household ownership of ITNs exists at the district-level, improvements have been made nationwide (Figure 9).

Figure 9: Household ownership of ITNs by district, 2004–2010



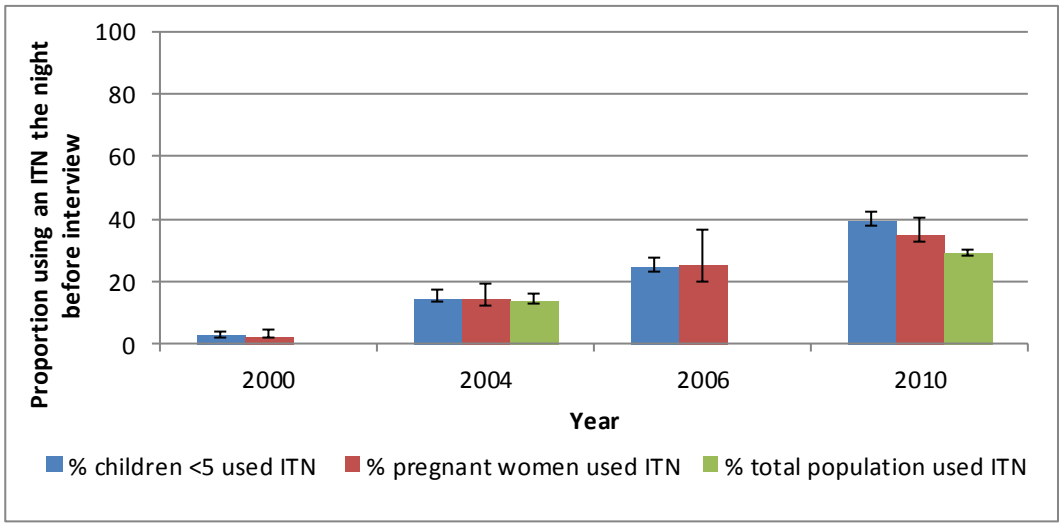
Household ownership of ITNs is significantly higher in households with children under five than in those without (Figure 10). In 2010, 65.3% of households with children under five owned at least one ITN whereas only 45.7% of households without children under five owned an ITN. These findings are not surprising, given that malaria control interventions were targeted to pregnant women and children under five.

Figure 10: ITN ownership in households with/without children under five years, 2004–2010



Similar to household ownership, use of ITNs has increased dramatically during 2000–2010 (Figure 11). ITN use is highest in children under five and pregnant women who have traditionally been targeted by net distribution campaigns; however, increases in ITN use have occurred among all subgroups.

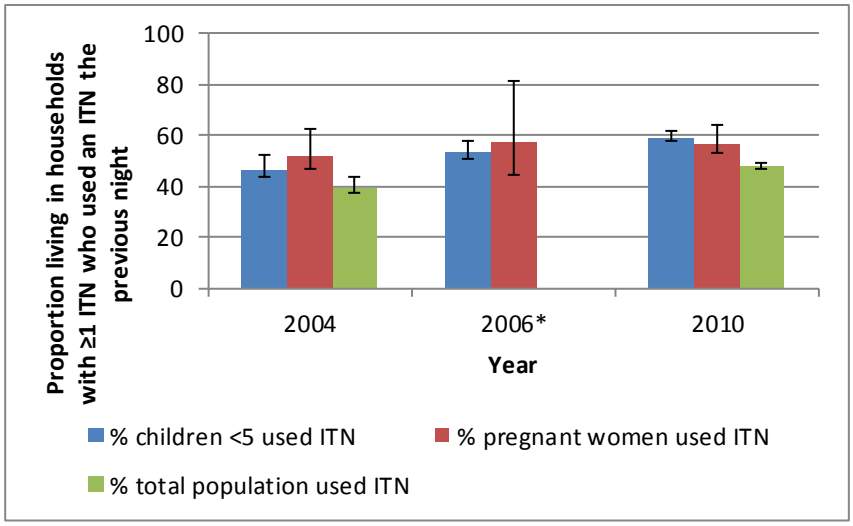
Figure 11: ITN use among children under five, pregnant women and the total population, 2000–2010



*Note: questions on net use by the total population were not included in the 2000 DHS nor the 2006 MICS. The 2006 MICS is only representative for pregnant women who have had a birth in the past 2 years.

As shown in Figure 12, in households owning at least one ITN, ITN use has increased from 47% in 2004 to 59% in 2010 in children under five years, and from 39% to 48% in the total population (all persons who slept in the house the previous night). In pregnant women living in households owning at least one ITN, ITN use did not change significantly between 2004 and 2010, remaining between 52% and 57%.

Figure 12: In households owning at least one ITN, the proportion of children under five, pregnant women and total population who slept under an ITN the previous night, 2004–2010



*The 2006 MICS is only representative for pregnant women who have had a birth in the past 2 years.

Equity in ITN Use

Table 8 presents data on ITN use by children under five and pregnant women stratified by residence, wealth quintiles and mother's education. Clear improvements in ITN use over time are evident across all strata, both for children under five years of age and for pregnant women. In 2010, ITN use was similar in males and females but inequities in ITN use were still evident between urban and rural residents, between children from different wealth quintiles and by level of mother's education. ITN use by pregnant women also differed by residence, household wealth quintile and woman's education. 95% confidence intervals around each stratified ITN use estimate can be found in Annex A.3.1 (Tables A.3.1.2 and A.3.1.4).

Table 8: ITN use by children under-five and pregnant women by background characteristics, 2004–2010

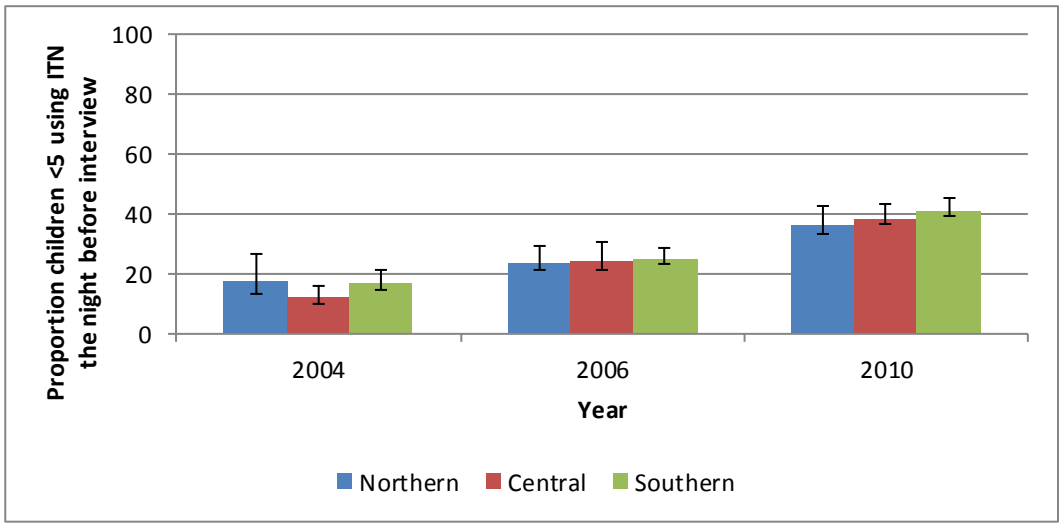
	Children under five years of age					Pregnant women				
	2000	2004	2006	2010	Absolute Change	2000	2004	2006	2010	Absolute Change
Sex										
Male	2.8	14.3	25.1	38.6	35.8					
Female	2.7	15.2	24.2	40.2	37.5					
Residence										
Urban	11.5	30.2	42.3	48.4	36.9	9.6	29.8	(40.3)	43.6	34.0
Rural	1.5	12.4	21.6	38.0	36.5	1.6	12.4	22.2	34.1	32.5
Wealth										
Lowest	0.6	6.4	14.6	28.8	28.2	0.7	6.0	14.3	22.5	21.8
Second	0.9	9.2	19.9	35.1	34.2	0.3	9.6	16.7	28.6	28.3
Middle	2.2	12.1	24.1	41.5	39.3	2.7	12.6	16.8	38.1	35.4
Fourth	2.4	16.7	25.5	42.1	39.7	2.5	17.0	47.9	42.2	39.7
Highest	8.2	33.8	41.8	54.0	45.8	7.4	32.6	32.7	48.5	41.1
Mother's/Women's education*										
None	0.8	7.3	18.1	32.4	31.6	0.7	8.6	19.4	31.7	31
Primary Incomplete	2.0	15.3	23.6	39.7	37.7	2.0	14.5	26.3	33.0	31
Secondary or Higher	18.4	33.8	46.2	56.6	38.2	15.9	26.7	28.9	49.3	33.4
Missing		10.1	23.6	21.1						

* Mother's education for children under-five and woman's education for pregnant women.
() unweighted cases were between 25–49

Geographic Variation in ITN Use

No significant regional variation exists in ITN use by children under five from 2004–2010 (Figure 13).

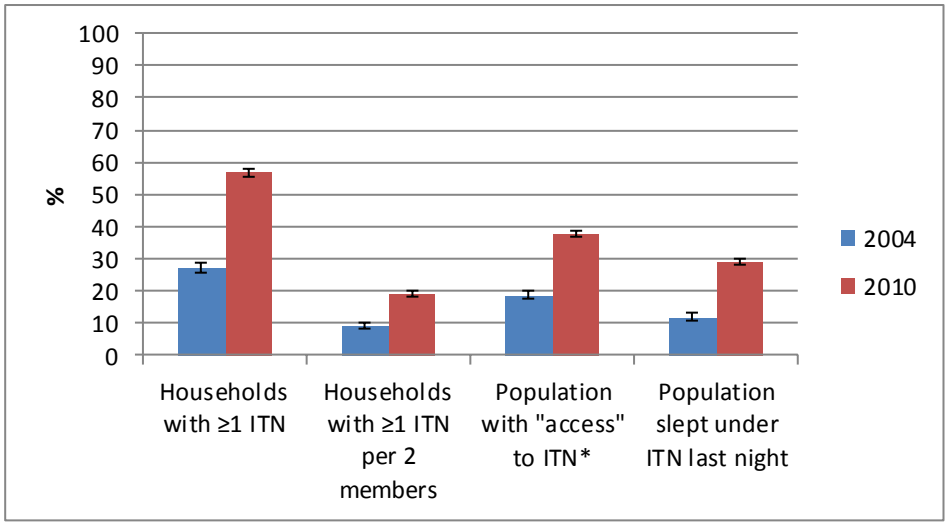
Figure 13: ITN use by children under five, by region (2004–2010)



Gaps in ITN Programs

Examining a cascade of four RBM-recommended ITN indicators helps NMCPs gain insight on potential gaps in vector control programs. One insight that can be gleaned from Figure 14 is that although close to 60% of households own at least one ITN, only about 20% own enough ITNs to cover the household population (at one ITN per two people). The percent of the population with access to ITNs was less than 40% but, closer to 30% reported using an ITN the previous night.

Figure 14: Ownership, access, and use of ITNs, (2004–2010)



*Access refers to having the option to use an ITN assuming that every ITN can be used by two people in a household.

ITN Summary

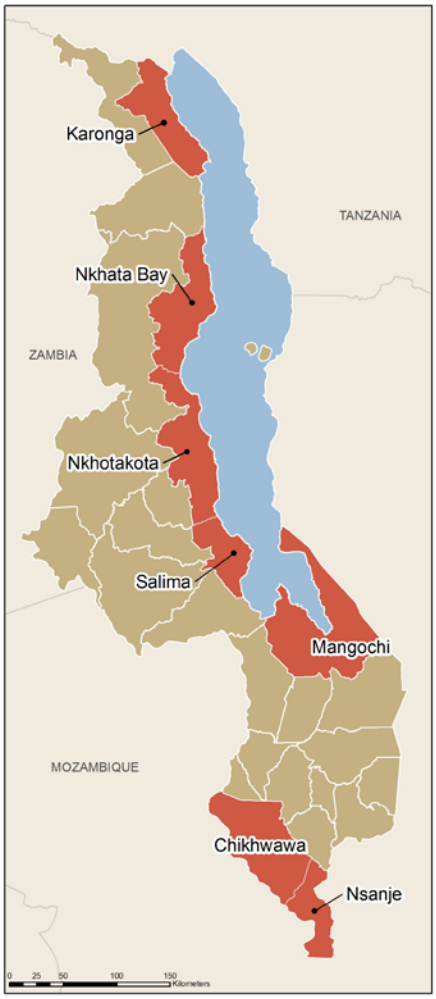
The various ITN campaigns over the past ten years have resulted in an increase in household ITN ownership from below 13% in 2000 to 27.4% in 2004 and to 56.8% in 2010. Following the 2008 campaign to distribute LLINs to pregnant women and children under five years of age, ITN ownership in households with children under five years increased to 65.3%. This was accompanied by an increase in ITN use by children under five years of age from 2.8% in 2000 to 39.4% in 2010, and ITN use by pregnant women reached 35.2%, in 2010. ITN use increased based on wealth quintile and other background characteristics; however, the unequal distribution of ITN use by children under five years of age and pregnant women that were present in 2000, persisted in 2010. Similarly, the difference between ITN ownership in urban and in rural households evident in 2000 became less pronounced by 2010. Given the large increase in ITN ownership since 2004, and use since 2000, and the documented protective effects of ITNs on child mortality [39, 42, 50-52] it is plausible to expect an associated reduction in malaria-related morbidity and ACCM among children under five years of age over this period.

Indoor Residual Spraying

In 2006, WHO reaffirmed their recommendation for indoor residual spraying with insecticides for malaria control in sub-Saharan Africa. A total of four insecticide classes are currently available for IRS [53]. A recent meta-analysis of IRS studies suggests that use of IRS reduces the prevalence of malaria parasitemia by 62% [54]. Despite its apparent effectiveness, no countries in sub-Saharan Africa use IRS at a national scale, as costs are often an impediment [55]; nonetheless, in 2009, IRS conferred vector control protection to 10% of the population of Africa [56].

The Ministry of Health (MoH) launched a pilot IRS program in Nkhotakota District, a lakeshore district with intense transmission, in 2007. Lessons learned from this pilot were used to scale-up IRS interventions to a total of seven high malaria prevalence districts along the lakeshore and in the Shire Valley, covering a population of 2.7 million people as of December 2010 Figure 15.

Figure 15: Districts with IRS programs as of December 2010, Malawi



The DHS survey results from 2010 found that 2.2% of households in Malawi had been sprayed in the past 12 months by the government or a private company (Table 9) thereby conferring protection to 2.4% of the population. It is important to note that at the time of fieldwork for the 2010 DHS, IRS activities had been limited to Nkhotakota

District and limited private spraying in Blantyre City and Sugar Estates in Nkhotakota and Chikwawa Districts. As IRS is a local strategy typically reserved for high prevalence regions, measuring coverage at a national level is not very informative. According to the 2010 DHS, IRS coverage in Nkhotakota District, in the Central Region, was much higher than the national average, with 59% of surveyed households reporting IRS within the past 12 months protecting 61% of the district's population (Table 9).

In a national-level impact analysis, IRS is unlikely to play a significant role at this level of coverage (2% nationally). IRS could have important sub-national effects, however, due to the high coverage in targeted districts.

Table 9: Percent of households with indoor residual spraying (IRS) and percent of population covered by IRS, 2010 DHS

	Percent of households with IRS in past 12 months (95% CI)	Percent of households with ≥ 1 ITN or IRS in past 12 months (95% CI)	Weighted sample size	Percent of population protected by IRS in past 12 months
National	2.2 (1.8 – 2.7)	57.5 (56.2-58.7)	24,825	2.4
Nkhotakota District	59.4 (53.1 – 65.5)	82.8 (78.3-86.5)	588	60.9

Intermittent Preventive Treatment in Pregnancy

Background

Malaria prevention and control during pregnancy has a three-pronged approach, including IPTp, ITN use, and diagnosis and treatment of clinical illness. ITN use by pregnant women was previously discussed (ITN section). Data on case management of clinical illness in pregnant women are not collected in national household-based surveys and therefore are not included in this evaluation.

Malaria in pregnancy significantly raises the risk of severe anemia, miscarriage, intra-uterine growth retardation, pre-term birth and low birth weight [57, 58]. In high transmission settings, malaria is expected to be a significant indirect contributor to maternal death [59]. Malaria in pregnancy is thought to affect neonatal mortality risk via low birth weight and anemia in the newborn [60]. Use of ITNs and IPTp during pregnancy has been found to be protective against neonatal mortality and low birth weight [61]. In Malawi, use of ITNs and IPTp has been shown to protect against parasitemia and low birth weight babies [48, 62].

IPTp Implementation

Although the first WHO IPTp recommendations were released in 2002, Malawi has recommended using SP for chemoprophylaxis during pregnancy since 1993 [63, 64]. The original WHO IPTp guidelines recommended that all pregnant women living in countries with endemic malaria take at least two treatment doses of sulfadoxine-pyrimethamine (SP) (three tablets each containing 500mg of sulfadoxine and 25mg of pyrimethamine) during routine antenatal care visits from the second trimester onwards, at least four weeks apart.[4] In Malawi, utilization of antenatal services is high (97.6% of pregnant women attending at least one ANC visit); however the 2010 DHS data reveal that IPTp coverage is much lower with only 55% of women receiving two or more doses. Previous formative research in Malawi found that inadequate knowledge or confusion among health staff regarding the proper timing of the second dose of SP, stock shortages of SP and apprehension among pregnant women to take SP may have played a role in discouraging women from taking the recommended doses [65, 66].

IPTp coverage

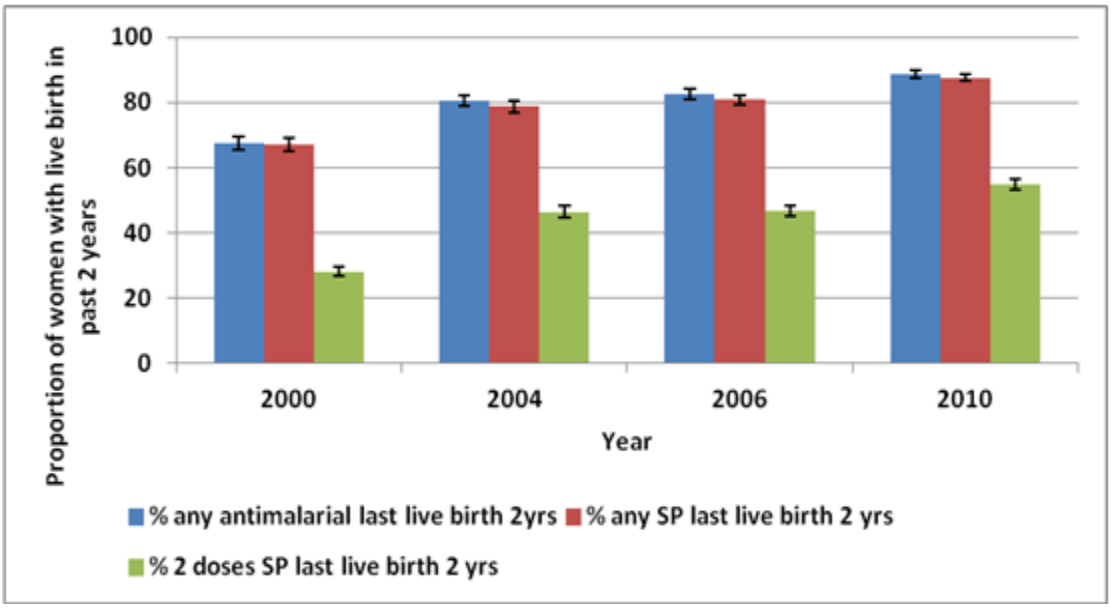
The IPTp coverage indicator refers to women who received at least two doses of SP for malaria prevention, of which at least one dose was received at an antenatal clinic. The indicator is restricted to the most recent pregnancy that resulted in a live birth, 0–2 years prior to the survey. Unfortunately, data on source of SP were not collected in all of the national surveys; thus, this indicator can only be calculated for 2004 and 2010

[4] A new WHO recommendation was issued in October, 2012. The recommended regimen is now to administer a dose of SP, beginning as early as possible in the 2nd trimester and at each subsequent ANC visit until delivery, with at least 1 month intervals. A schedule of four ANC visits is recommended by WHO. http://www.who.int/malaria/iptp_sp_updated_policy_recommendation_en_102012.pdf

(42.9% and 53.8%, respectively). It is possible to examine trends in use of SP regardless of its source for all of the survey years (Figure 16).

Trends over the decade in preventive use of any antimalarial, and of SP by pregnant women, regardless of the source of the medication are depicted in Figure 16. The proportion of pregnant women receiving at least two doses of SP increased from 28% to 55% from 2000 to 2010. Almost all of the antimalarials taken for prevention of malaria in pregnancy were SP. A significant gap is evident in those receiving one dose of SP and those receiving two or more.

Figure 16: Proportion of women (15–49 years) with live birth 0–2 years prior to survey receiving any antimalarial for malaria prevention, proportion receiving at least one and at least two doses of SP*, 2000–2010.



*Two doses of SP regardless of the source of medication

Equity in IPTp

Changes in the equity of IPTp coverage with respect to residence, wealth and women's education are presented in Table 10. Across all strata, use of IPTp increased between 2000 and 2010. In 2010 use of IPTp did not vary greatly by any of these background characteristics. Confidence intervals for these estimates are presented in Annex A.3.1 (Table A.3.1.6).

Table 10: Distribution of IPTp* by background characteristics, 2000–2010

	2000	2004	2006	2010	Absolute
Residence					
Urban	31.5	53.8	55.2	55.9	24.4
Rural	27.8	45.4	45.4	54.8	27.0
Household Wealth					
Lowest	25.7	42.1	42.2	52.7	27.0
Second	27.2	42.6	44.2	54.3	27.1
Middle	28.9	46.2	47.1	56.9	28.0
Fourth	29.8	47.8	48.3	56.2	26.4
Highest	29.9	57.0	54.4	55.1	25.2
Woman's Education					
None	25.9	39.7	39.7	52.5	26.6
Primary	28.3	47.1	46.7	54.7	26.4
Secondary or Higher	36.7	57.0	61.4	58.9	22.2

*Two doses of SP regardless of the source of medication

Summary IPTp

Progress has been made in IPTp coverage over the evaluation period. Improvements in IPTp coverage were seen across all wealth quintiles and other background characteristics. In 2010, 55% of women giving birth in the past two years received IPTp (at least two doses SP) during her most recent pregnancy and 86% of eligible women received at least one dose of SP at an ANC visit. This level of IPTp coverage is far above the average for African countries (23% for the 12 surveys between 2009–2011 with available data) [67] and was one of the highest in sub-Saharan Africa in 2010 [67].

Malaria Case Management

Background

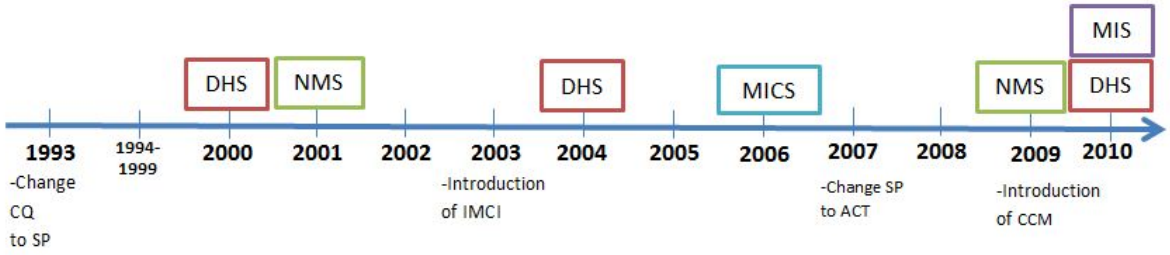
Malaria case management, including the identification, diagnosis, and rapid treatment of all malaria cases with appropriate and effective antimalarial drugs, is one of the key strategic areas for malaria control recommended by the WHO [10]. Most malarial fevers occur at home, and prompt and effective treatment is critical to prevent severe morbidity and mortality related to malaria.

Case Management Policy

Effective antimalarial drugs are one of the principal tools for combating malaria today. Over the years, the Malawi government has changed malaria treatment policies because of the emergence of resistance to recommended drugs (Figure 17). In 1993, Malawi was the first country in sub-Saharan Africa to replace chloroquine (CQ) with SP as the first-line treatment for uncomplicated malaria. In 2007, Malawi changed its first-line antimalarial in the national malaria treatment policy from SP to artemether-lumefantrine (AL) [this is referred to as lumefantrine-artemether (LA) in Malawi], an ACT, following significant scientific evidence of malaria parasite resistance to SP. With international donor funding, AL is being provided free of cost to all fever patients regardless of age presenting at health facilities across the country. The second-line treatment is artesunate-amodiaquine (ASAQ), also an ACT. Intravenous quinine was the recommended treatment for severe malaria during this evaluation period. Severe malaria treatment is mainly provided at hospitals where there are facilities for supervised treatment and other supportive care.

During the evaluation period from 2000 to 2010, Malawi relied on presumptive treatment of all suspected cases of malaria (those presenting with current or recent fever), supplemented by the limited use of microscopy in MoH facilities such as central and district hospitals, and a few peripheral facilities. Currently about 25% of health facilities have the capacity for malaria microscopy, which is provided for free by trained and qualified laboratory staff. Because of this low coverage of microscopy services, microscopy is used primarily to confirm treatment failures, in research studies, and to diagnose patients admitted to hospitals. The main constraints to expanding utilization of microscopy have been a lack of trained and qualified health workers, lack of electricity, and inadequate laboratory supplies [68].

Figure 17: Milestones in case management of malaria in Malawi



*CQ = Chloroquine; SP = Sulfadoxine-pyrimethamine; IMCI = Integrated Management of Childhood Illness; ACT = Artemisinin-based Combination Therapy; CCM = Community Case Management; DHS = Demographic and Health Survey; NMS = National Micronutrient Survey; MICS = Multiple Indicator Cluster Survey; MIS = Malaria Indicator Survey.

Although prompt administration of antimalarial treatment is a key objective in the malaria treatment policy, the scale-up of this intervention has proven difficult [69]. Prompt access to treatment in Malawi over most of the evaluation period was a challenge because of poor health system infrastructure and lack of human resources, barriers to accessing care and drug stockouts [1]. According to the SWAp Review Progress Report 2010, the ratio of doctors to the population was 1/41,045 and the nurse to population ratio 1/2,643 [70].

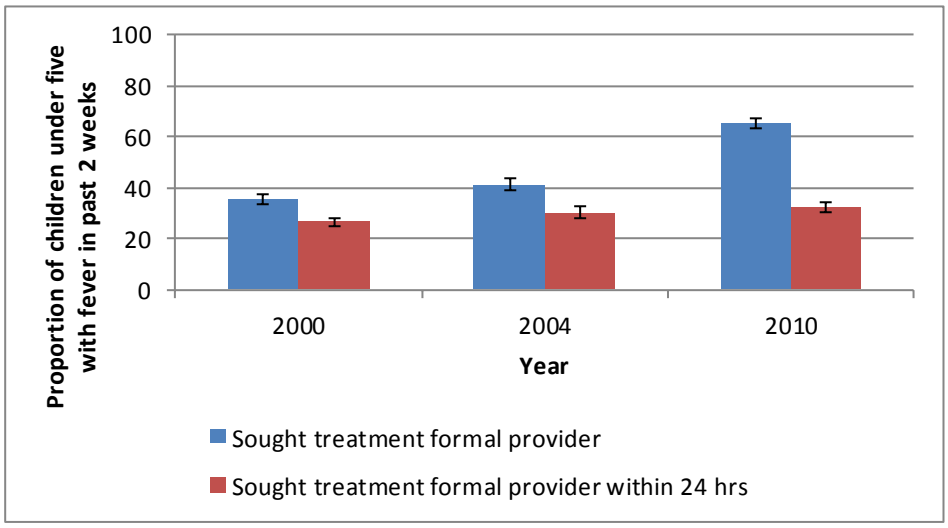
In order to address the three leading causes of child mortality: pneumonia, diarrhea and malaria, the WHO in collaboration with UNICEF developed the integrated management of childhood illness (IMCI) approach to child health. Malawi adopted IMCI in 1998 in an initial five districts. In 2003, Malawi introduced IMCI in additional districts and by 2005 the total number of districts implementing IMCI had reached 18 out of the 28 districts. National scale-up to all districts was achieved by 2008. This health care strategy was designed to reduce death and morbidity and to promote growth and development in young children. Despite the investments in IMCI, sick children in areas with few doctors or hard-to-access health facilities often were not receiving the care that they need. An extension of IMCI to the community level, known as community case management (CCM), was adopted in 2009 (with district-level pilots beforehand), to provide essential care to this population. Studies have shown that CCM reduces childhood mortality [71, 72]. The initial goal of this program was to service 4,000 hard-to-reach areas covering 10% of the national population. Availability of antimalarial treatment near the home and in the community has been proven to significantly reduce malaria morbidity and mortality in children and to increase equity in access [72-74]. The CCM service delivery package is not malaria-specific and includes treatment for other diseases such as pneumonia, diarrhea, and eye infections. CCM is being provided by HSAs in village clinics in hard to reach communities (more than 8 km from a health center). HSAs are paid government employees trained to diagnose and treat such illnesses. For cases of suspected malaria, HSAs follow child illness algorithms to diagnose sick children and dispense prepackaged antimalarial medications when necessary. Plans are in place to supply HSAs with RDTs for diagnostic purposes in the near future. International non-governmental organizations provide these services for approximately 30% of the total population with over 10,000 HSAs currently employed [28]. The 2010 estimate of HSA to population ratio is 1/1,368 [70].

Coverage Trends of Malaria Case Management in Children

Monitoring malaria case management in Malawi is challenging. Correct and timely care of children with malaria depends on many factors including access to health facilities, facility reporting of visits and diagnoses, diagnostic capacity, and availability of appropriate medicines. Measuring trends in malaria case management is further complicated by the many policy changes that have occurred in the past decade, affecting both first-line medications and diagnostic procedures. As a result, the historic RBM indicator measuring the proportion of children with recent fever who receive antimalarial treatment has been supplemented in this report with two new RBM indicators: an estimate of care-seeking for fever and an estimate of the proportion of treated children receiving recommended treatments.

The DHS surveys ask mothers to report history of fever in children under five years of age during the two weeks prior to the survey (see Annex 5 for information on fever trends). Of children who experienced fever, a series of further questions are asked about care seeking – including the source of advice and/or treatment, the timing of care seeking, treatment received, and type of antimalarial used, if any. Figure 18 presents trends over the period 2000–2010 in care-seeking from a health provider, facility or pharmacy. Although overall care-seeking has increased significantly over the decade, timely care seeking has not.

Figure 18: Percentage of children under five years of age with fever during two weeks prior to interview who ever sought care from a formal provider*, and the percentage who sought care within 24 hours of fever onset, 2000–2010.

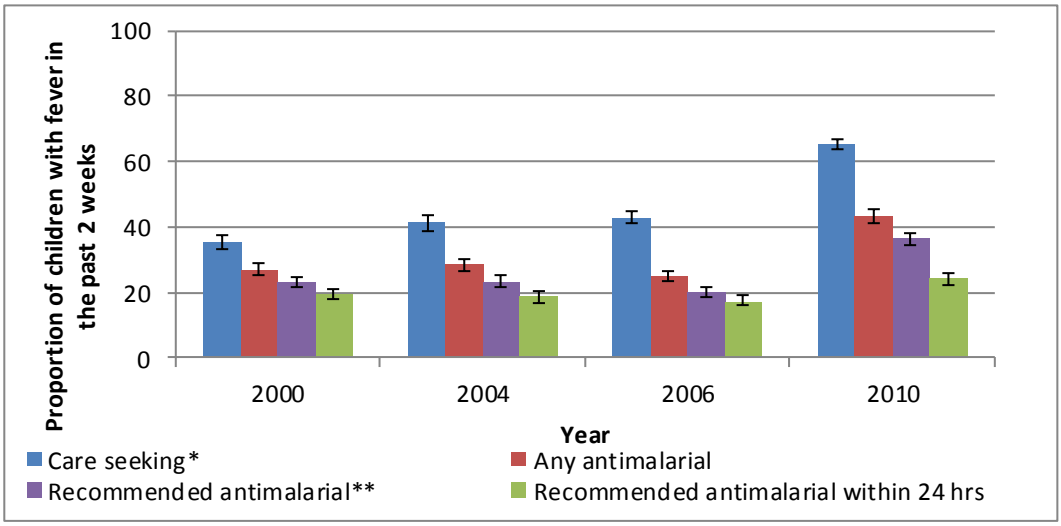


*Formal provider is defined as a health provider, facility or pharmacy. Includes HSAs, but excludes shop and traditional healer.

Of all children who experienced fever in the two weeks prior to survey, the proportion treated with a recommended (first-line) antimalarial drug the same day or the day following fever onset did not change significantly between 2000 and 2006; however, a dramatic increase occurred between 2006 and 2010 in overall antimalarial use and use of recommended antimalarials (Figure 19). These trends are challenging to interpret due to changes in recommended antimalarials, and differences in cost and availability of

the medications. As the observed trends in antimalarial use mirror those in care seeking behavior, it is possible that the increase in treatment of fevers with antimalarials is simply due to increased care seeking.

Figure 19: Percentage of children under five years with fever during two weeks prior to interview who sought care and were treated with antimalarial drugs, 2000–2010.



*Care seeking = sought advice or treatment for fever from a public or private health professional or from a pharmacy. Excludes shop and traditional healer.

**Recommended antimalarial is SP in 2000, 2004 and 2006 and ACT in 2010.

As shown in Figure 19, use of any antimalarial by children under five years of age with fever increased over the study period from 27% to 43%. A shift occurred between 2006 and 2010, corresponding to changes in recommended antimalarials, from SP to ACT use. Although the proportion of children taking SP was similar from 2000 to 2006 (approximately 20%), use of ACT in 2010 was higher (35%) (data not shown). However, when the distribution of specific antimalarials used is examined among children who took any antimalarial (Table 11) a similar proportion of children received recommended treatment across the study period (ranging from 81 to 86%).

Table 11: Among children under five with fever in two weeks prior to survey who received any antimalarial drug, proportion receiving each antimalarial, 2000–2010.

Antimalarial	2000 (n=1189)	2004 (n=1032)	2006 (n=1990)	2010 (n=2696)
ACT	n/a	n/a	0.7	83.9§
SP	86.0§	82.2§	81.1§	4.5
Quinine	10.6	16.1	15.0	11.1
Amodiaquine	0.4	0.3	1.0	0.2
Chloroquine	4.9	2.7	2.8	n/a
Other	0.5	3.1	2.5	3.0
Total Any Antimalarial	1189	1032	1990	2696

§ - first-line treatment in respective survey years

Note: Responses allowed multiple treatments to be selected so totals may exceed 100%.

Equity and Factors Associated with Treatment Access

Table 12 provides a summary of the use of first-line antimalarials in children under five years of age with recent fever who received antimalarials stratified by sex, residence, wealth and mother's education. No obvious trends in this indicator are apparent when stratified by background characteristics. Interestingly, for all survey years, there is a small difference in this indicator by wealth which favors those in the lowest wealth quintile. 95% confidence intervals for stratified estimates are available in Annex A.3.1 (Table A.3.1.8).

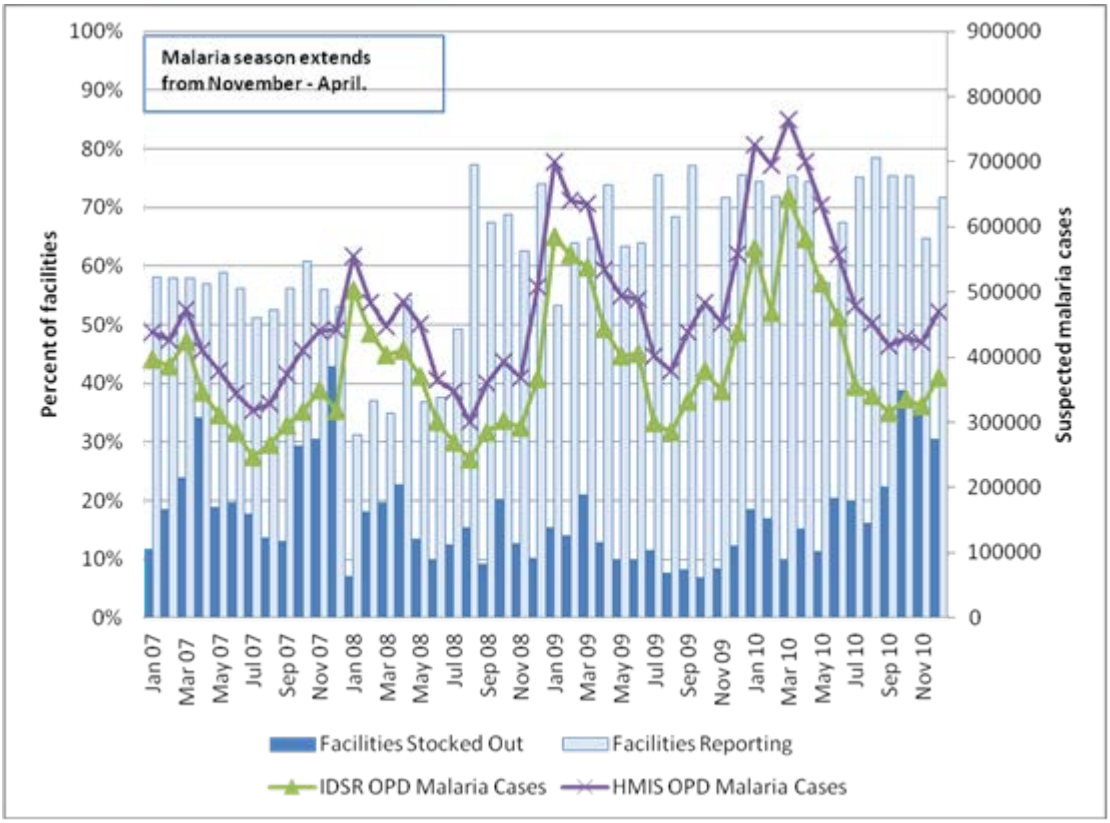
Table 12: Use of first-line antimalarial drugs by children under five years of age with fever in the two weeks prior to interview who took antimalarial drugs, by background characteristics, 2000–2010

	2000	2004	2006	2010	Absolute Change
Sex					
Male	84.6	83.7	79.0	81.8	-2.8
Female	87.4	80.7	83.3	86.0	-1.4
Residence					
Urban	81.8	81.7	78.9	80.8	-1.0
Rural	86.6	82.3	81.5	84.3	-2.3
Wealth					
Lowest	88.8	83.6	83.2	86.0	-2.8
Second	90.4	85.0	83.1	87.7	-2.7
Middle	83.0	79.6	81.0	86.3	3.3
Fourth	91.5	83.9	79.8	80.7	-10.8
Highest	76.5	78.3	78.3	75.1	-1.4
Mother's Education					
None	88.1	82.6	82.4	84.6	-3.5
Primary	85.9	83.2	81.4	85.1	-0.8
Secondary or Higher	79.1	76.5	78.2	77.2	-1.9

Antimalarial Drug Stockouts

One important factor that affects malaria treatment indicators is adequate supply of appropriate antimalarial drugs at access points. Shortages or stockouts of recommended antimalarials can have direct effects on malaria morbidity and mortality [75]. An analysis of AL stockouts was conducted for 2007–2010 to look for trends in availability of medications that might have driven trends in malaria outcomes such as parasitemia or severe anemia prevalence. Data for this analysis come from the LMIS which tracks supplies of commodities in all MoH and CHAM facilities (609 in total)[76]. Figure 20 presents the proportion of facilities reporting stockouts of first-line antimalarials from 2007 to 2010, by month. Recommended first-line antimalarials changed from SP to AL between the beginning of this period and the end. Stock–outs of AL were defined as having no supply of all four presentations of AL medications, meaning that recommended first-line antimalarials were not available. More information on the LMIS in Malawi is included in Annex A.1.8. The trends in suspected malaria cases are described in the morbidity section to follow.

Figure 20: Outpatient suspected malaria cases and percent of facilities stocked out of first-line antimalarials, 2007–2010.*



*Data source = LMIS. Stocked out refers to having no supply of all four AL presentations.

Malaria Treatment Summary

In summary, access to first-line antimalarial treatment in children with fever has increased by 24% from 2000 to 2010. However, in 2010 only one quarter of children with fever received recommended antimalarial treatment within 24 hours of fever onset. Nonetheless, it is noteworthy that 65% of children with fever sought treatment from a health provider, facility or pharmacy in 2010, and that this proportion has increased significantly over the past decade. Similarly, over 80% of children with fever who receive antimalarial treatment were given the recommended medications in all survey years between 2000 and 2010, even as the first-line antimalarial changed.

Perhaps the most important change over this period from a public health perspective is the transition from SP for the treatment of uncomplicated malaria to drugs with lower treatment failure rates and gametocidal properties (ACTs). In 1993, Malawi became the first country to change its recommended first-line antimalarial from chloroquine to SP in response to high treatment failure rates [77]. Subsequently malaria parasites developed resistance to SP and in 2007 Malawi changed its recommended first-line treatment for uncomplicated malaria from SP to ACTs [78, 79]. It seems likely that these improvements in treatment efficacy could have resulted in higher rates of parasite clearance, fewer chronic infections and better treatment outcomes [80, 81].

MALARIA MORBIDITY

Malaria Parasitemia

Background

Reductions in malaria parasitemia prevalence should have the desired effect of reducing malaria-attributable morbidity and mortality at the population level. Few data on malaria parasitemia prevalence at the national level were collected until recently.

Measuring malaria parasitemia prevalence is a challenging task; malaria transmission dynamics are quite sensitive to climatic variability [82] and are heterogeneous over small areas [82, 83], complicating interpretation of national trends. For example, as described in the Further Analyses section (Chikwawa rolling MIS), parasitemia prevalence can fluctuate drastically between seasons within the period of one year (intra-annual variation). In addition to seasonal trends, fluctuations in climate patterns over several years may contribute to similar fluctuations in parasitemia levels (inter-annual variation) which could mask successes or lapses in malaria control efforts, as was seen recently in Zambia [84-86]. Thus, parasitemia is a challenging impact measure to interpret in many settings, although it is arguably the most direct measure of success in malaria control efforts; to make best use of parasitemia prevalence data, many data points are needed for analysis of robust trends.

Malaria Parasitemia in Malawi in 2010

The 2010 Malawi MIS tested children aged 6–59 months for the presence of *P. falciparum* antigens using SD Bioline© RDTs and for malaria parasites using microscopic examination of thick and thin blood smears. The survey was conducted during the high transmission season, in March and April of 2010. Table 13 examines variations in malaria parasitemia among children under-five, stratified by various individual and household characteristics.

For Malawi as a whole, 43.3% of children under five tested positive for malaria in 2010 measured by microscopy. Childhood malaria parasitemia increased with age. The odds of malaria parasitemia measured by microscopy increased by 13% per age category (OR=1.13; 95% CI = 1.04–1.23; p=0.003).

Table 13: Malaria parasitemia in children 6–59 months of age measured via microscopy* from national Malaria Indicator Survey, Malawi, 2010

Background characteristics	Percentage of children with malaria parasitemia	95% CI	Weighted sample size
Age (in months)			
6–11	35.6	28.3, 43.7	301
12–23	41.0	34.7, 47.7	450
24–35	43.3	36.6, 50.2	487
36–47	46.2	39.6, 52.9	426
48–59	48.5	41.4, 55.6	408
Sex			
Male	45.1	39.8, 50.4	1026
Female	41.5	36.3, 46.8	1046
Residence			
Urban	14.7	9.9, 19.6	232
Rural	46.9	41.7, 52.1	1840
Region			
Northern	22.8	9.7, 35.8	218
Central	49.7	43.5, 56.0	856
Southern	42.3	34.4, 50.1	998
Household wealth			
Lowest	51.4	44.7, 58.1	613
Second	52.4	45.0, 59.7	309
Middle	46.8	38.9, 54.7	491
Fourth	34.5	26.5, 42.5	353
Highest	22.5	16.6, 28.3	306
ITN use			
No	45.2	39.4, 50.9	1175
Yes	41.9	36.6, 47.2	897
Severe anemia (Hb<8g/dL)			
No	38.7	34.5, 43.2	1826
Yes	77.1	68.1, 84.1	246
Altitude			
<1000m	46.2	36.9, 55.8	711
1000m+	41.8	36.8, 46.9	1362
Total	**43.3**	**38.7, 48.1**	**2072**

*Refers to positive thick smears

The proportion of children under five testing positive for malaria parasitemia was much higher in rural areas (47%) compared to urban areas (15%). Malaria parasitemia prevalence was higher in children from the Central (50%) and Southern Regions (42%) of the country compared to the Northern Region (23%). Children from poorer households were much more likely to test positive for malaria than children from least poor households (51% and 23%, respectively), a finding that might be partially due to collinearity between rural residence and wealth (r = -0.5386). No significant differences were observed in parasitemia prevalence in children using ITNs the night before the

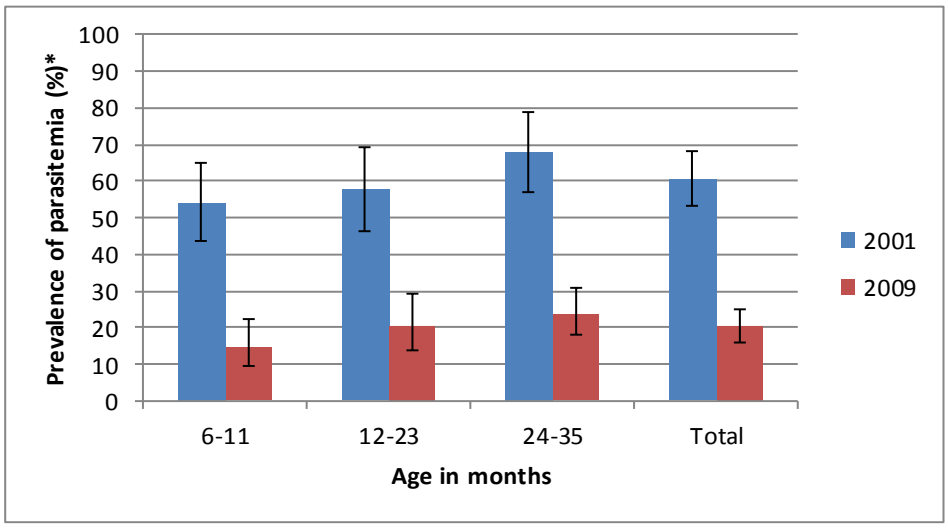
survey and those not using ITNs. Even when adjusting for urban/rural residence, odds of malaria parasitemia are not significantly lower in children who used ITNs (OR = 0.83, 95% CI = 0.65–1.06). Although counterintuitive, this is not unexpected, as national-level associations often mask dynamics at smaller spatial scales. In addition, the reported association is not adjusted for other potential confounding factors. A recent, multi-country analysis found a lack of association between ITN use and prevalence of parasitemia in three of seven nationally-representative surveys, even after controlling for potential confounders [52]. An analysis of the association of malaria parasitemia in children 6–59 months of age residing in houses with and without a net is included in the Further Analyses section below. As expected, children with severe anemia (hemoglobin <8g/dL) were much more likely to test positive for malaria parasitemia than were those without severe anemia (77% vs. 39%).

Parasitemia Trend – National Micronutrient Surveys, 2001, 2009

In addition to the 2010 MIS, two other nationally representative cross-sectional household surveys collected data on parasitemia in children using microscopy for diagnosis. The 2001 data were collected in September and October of 2001 whereas the 2009 data were collected in July and August of 2009. The typical rainy season in Malawi runs from November to April, thus both surveys were conducted in the dry season; however, variation in malaria transmission exists within the dry season as well, with lowest transmission occurring during the months of July and August when temperatures are low. The 2001 data were collected for children 6–35 months of age and the 2009 data were collected for children 6–59 months of age. The 2009 data were reanalyzed for children 6–35 months of age for comparison purposes with the 2001 survey.

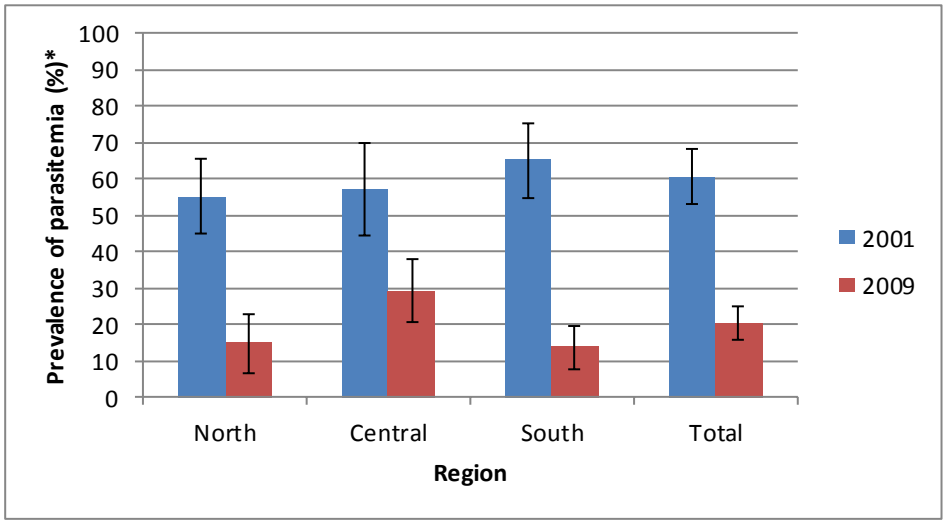
Figure 21 and Figure 22 show trends in parasitemia prevalence in children 6–35 months of age over the two survey years (2001, 2009), stratified by age and by region, respectively. Parasitemia prevalence decreased dramatically between 2001 and 2009 (61% to 20%). This trend was consistent with large declines across age categories and across regions, with the largest declines in the Northern and Southern Regions.

Figure 21: Parasitemia prevalence in children 6–35 months by age, Malawi, 2001, 2009, NMS†



†2001 survey conducted September-October; 2009 survey conducted July-August
*Measured via microscopy

Figure 22: Parasitemia prevalence in children 6–35 months by region, Malawi, 2001, 2009, NMS†



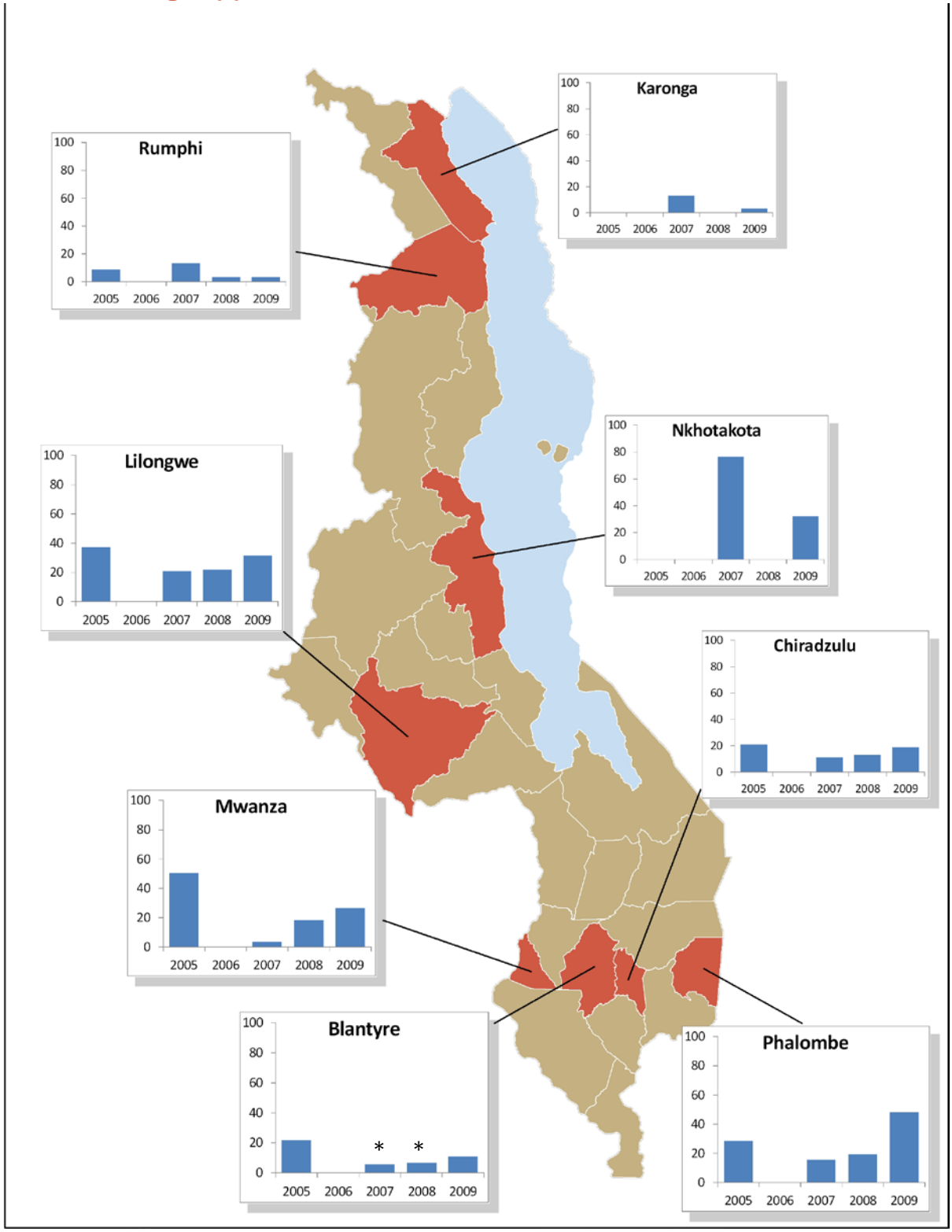
†2001 survey conducted September-October; 2009 survey conducted July-August
* Measured via microscopy

Parasitemia Trend – Sub-national Anemia and Parasitemia Surveys, 2005–2009 [87]

Cross-sectional surveys were conducted to measure malaria parasitemia and anemia in children 6–30 months old in six districts in 2005 and 2006 and in eight districts in 2007, 2008, and 2009. These surveys were conducted in April of each year, which represents the latter portion of the high transmission season. As a result, these surveys likely capture some of the highest parasite prevalence estimates within each year. The six districts surveyed in 2005 and 2006 included four from Southern Region (Chiradzulu, Mwanza, Phalombe, and Blantyre), and one each from Central Region (Lilongwe) and Northern Region (Rumphi). In 2007, 2008, and 2009, an additional district was sampled

in both Central Region (Nkhotakota) and Northern Region (Karonga). A map of surveyed districts and trends in parasitemia over time in these districts is shown in Figure 23. Parasitemia was measured by microscopy.

Figure 23: Districts surveyed and trends in malaria parasitemia prevalence in children 6–30 months of age, by year, 2005–2009, A&P†



*p<.05 (reference category is 2007 for Karonga and Nkhotakota and 2005 for all other districts)
† No data were collected in 2006. Data were not collected in 2008 in Nkhotakota or Karonga.

Trends in parasitemia prevalence were not regionally-specific over the time period. The map shown in Figure 23 contains parasitemia prevalence estimates by district and by year. In the Northern Region, parasite prevalence estimates decreased in Karonga District from 13% in 2007 to 4% in 2009. Parasite prevalence increased in Rumphi District from 2005 to 2007, but declined significantly from 13% in 2007 to 3% in 2009. In the Central Region, parasite prevalence in Lilongwe District decreased from 37% in 2005 to 21% in 2007, but increased to 31% in 2009. The change from 2005 to 2007 and 2008 was statistically significant. Parasite prevalence decreased significantly from 2007 to 2009 in Nkhotakota District. In the Southern Region, parasite prevalence decreased significantly from 2005 to 2007 in three of the four surveyed districts. Parasite prevalence declined from 22% to 6% in Blantyre, from 50% to 3% in Mwanza, and from 28% to 16% in Phalombe. However, parasite prevalence increased from 2007 to 2009 in all districts. Overall, parasite prevalence only decreased significantly in 2009 compared to 2005 in Mwanza and increased significantly over this time period in Phalombe. Values and associated confidence intervals for these estimates are shown in Annex 3.3.

While these data illustrate annual trends in parasitemia not available from the other national surveys, they were only collected in eight districts and are not representative of patterns for the whole country. In general, comparing baseline and endline survey years, parasitemia prevalence did not change between 2005 and 2009. More data points over time are required for meaningful inference to be drawn from these trend data. More in-depth interpretation of these results and regression analyses of the data are included in the Further Analyses section (page 87) and in Annex 3.3.

Severe Anemia

Background

Severe anemia, defined as blood hemoglobin levels <8 g/dL[5], is a potential impact measure for total malaria-related disease burden as it is associated with malaria-related mortality and it is measurable at the population level with less seasonality than parasitemia [9, 11-13]. Infection with malaria parasites leads to anemia through the sequestration and lysis of red blood cells, as well as to suppressed production of new cells in the bone marrow (dyserythropoiesis) [88]. In addition to malaria parasites, iron deficiency, deficiencies in other nutrients and diseases such as soil-transmitted helminthes are all causes of anemia [88]. Declines in severe anemia have been found to be associated with malaria control interventions [89]. Severe anemia prevalence has also been collected in many more population-level surveys than parasitemia, and therefore, trends are more easily established using retrospective survey data. In sub-Saharan Africa, between 17% and 54% of malaria-attributable deaths are estimated to be due to severe anemia [89-92].

[5] A hemoglobin cutoff of <7 g/dL is used to classify severe nutritional anemia, whereas a cut off of <8g/dL is used to classify malaria-related anemia. Intervention trials have shown that malaria control interventions reduce moderate-to-severe anemia (Hb <8g/dL).

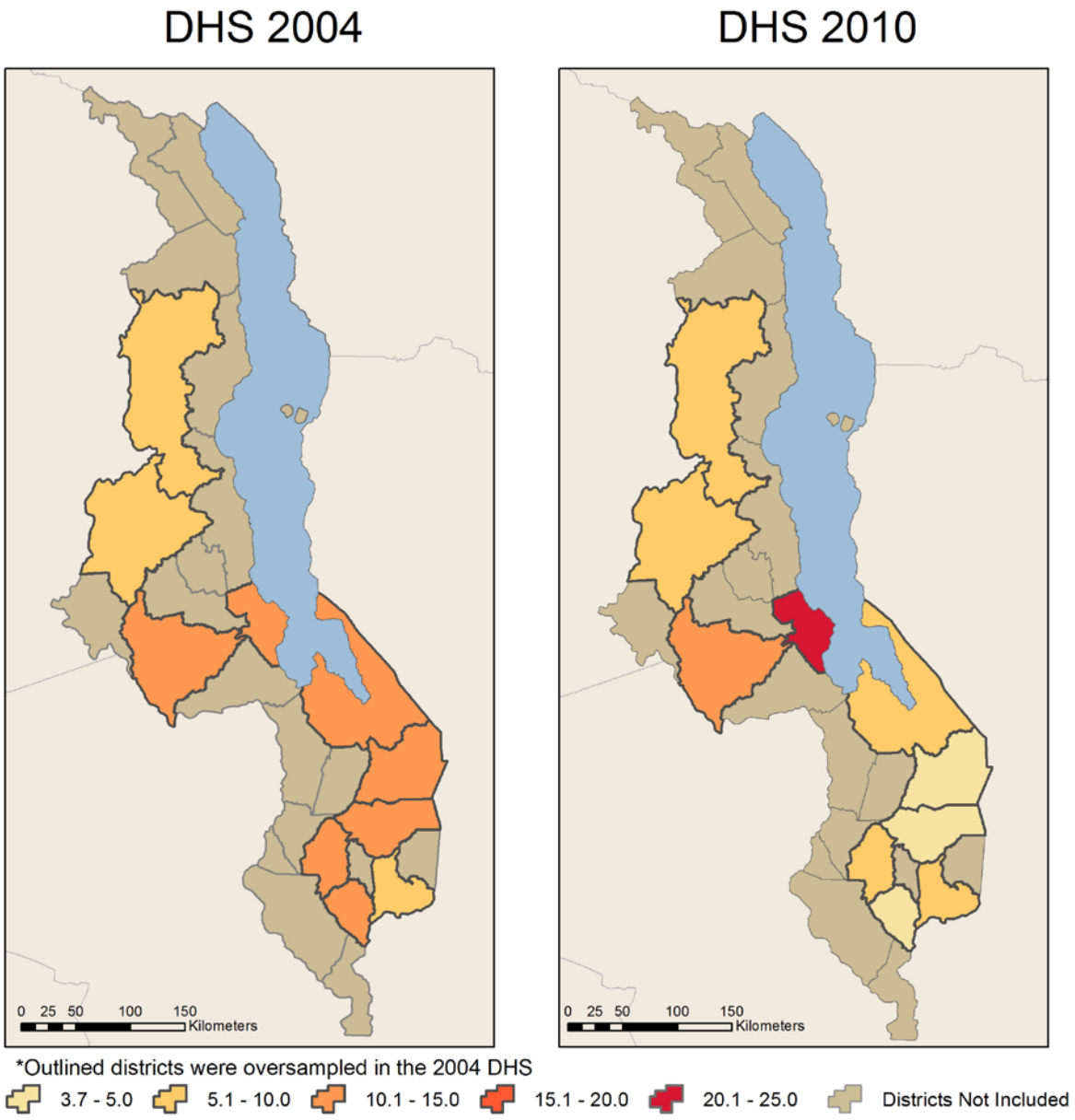
Severe Anemia in Malawi 2001–2010, Nationally-representative Survey Data

National estimates of the prevalence of severe anemia (hemoglobin <8 g/dL) in children aged 6–59 months of age are available from the two most recent DHS surveys and from the 2010 MIS. Children under six months of age are not included in the results because they have higher levels of hemoglobin at birth and just after birth. The 2010 DHS results are presented for trend analysis instead of the 2010 MIS results due to the comparability with the 2004 season in which field work was conducted. Hemoglobin values from DHS surveys were adjusted for altitude using the CDC formula[6] [93].

Geographical differences in severe anemia in children 6–59 months of age are depicted in Figure 24. Severe anemia prevalence decreased in districts in the Southern Region but increased in the Central Region between 2004 and 2010.

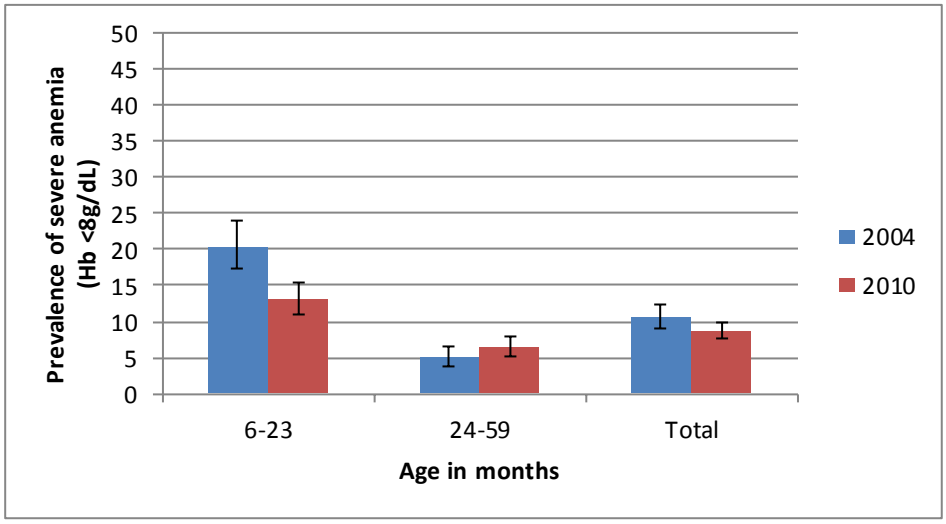
[6] Hemoglobin requirements differ substantially depending on altitude, therefore an adjustment to sea-level equivalents is made before classifying children by level of anemia.

Figure 24: Prevalence of severe anemia in children 6–59 months, by oversampled districts, Malawi, 2004 & 2010, DHS



Although the prevalence of severe anemia did not decrease significantly between 2004 and 2010 in children aged 6–59 months, significant decreases were evident in subgroups of younger children (Figure 25); 20% of children 6–23 months of age had hemoglobin levels <8g/dL in 2004 and the prevalence declined to 13% in 2010, a relative change of 36% (Figure 25). Similar declines were not seen in older children 24–59 months of age. In settings of high malaria endemicity the burden of disease and the impact of malaria control are largely concentrated in infancy and early childhood [94]. Thus, the observed trend is consistent with expected changes in anemia due to malaria control interventions, in that impact on malaria has been found to be larger in younger age groups (under two or three years of age) compared to those four or five years of age [89].

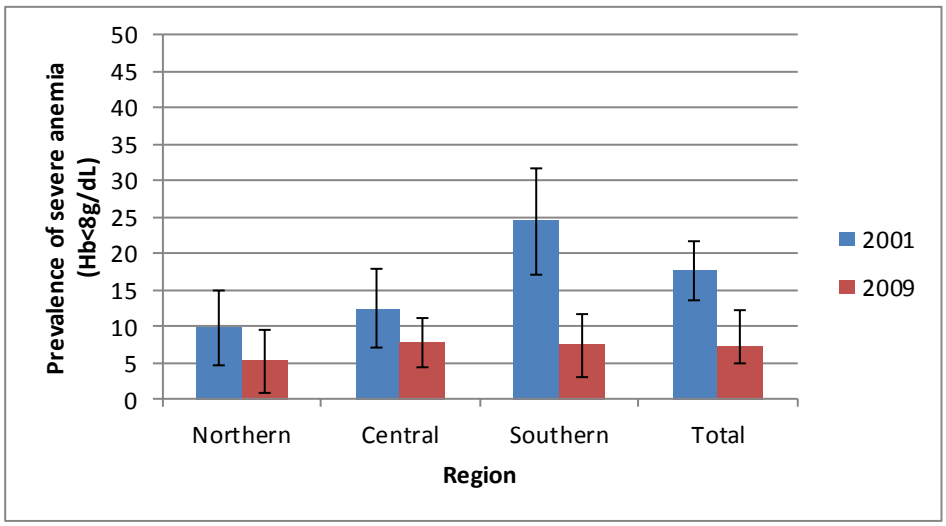
Figure 25: Trends in severe anemia (hemoglobin <8g/dL) prevalence in children 6–59 months, by age group, Malawi, 2004–2010, DHS



Nationally-representative data on severe anemia in children 6–35 months are available from the 2001 and 2009 NMS. The age range differs from that of the DHS/MIS reports (6–59 months).

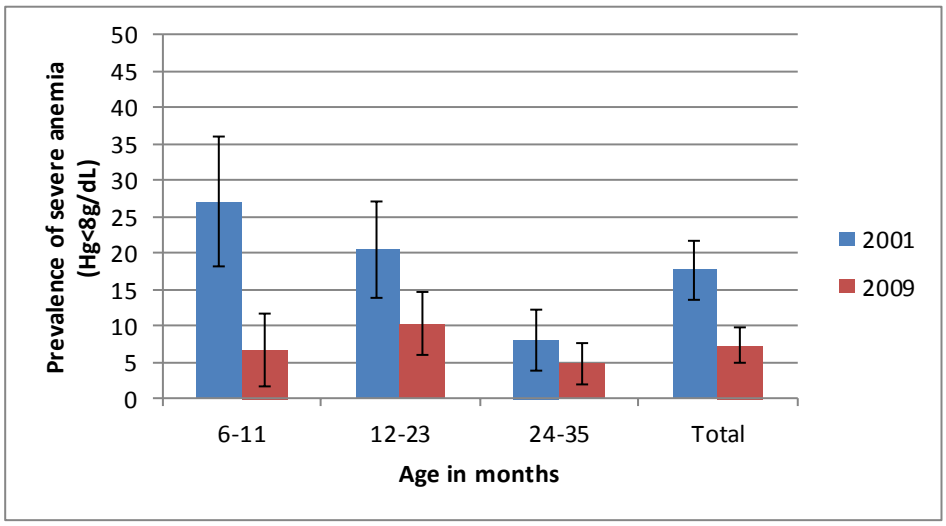
Figure 26 shows regional trends in severe anemia in children 6–35 months in 2001 and 2009. Similar to the trends observed in the DHS data, overall national decline in prevalence of severe anemia in this age group appears to be driven by a significant decrease in the Southern Region. Severe anemia prevalence did not significantly decrease in the Northern or Central Regions.

Figure 26: Anemia prevalence in children 6–35 months by region (hemoglobin <8g/dL), Malawi, 2001 & 2009, NMS



Similarly, Figure 27 shows trends in severe anemia by age category in children 6–35 months in 2001 and 2009. The most substantial decline in severe anemia occurred in the youngest children, aged 6–11 months. Declines in the other age groups were not significant.

Figure 27: Anemia prevalence in children 6–35 months by age (hemoglobin <8g/dL), Malawi, 2001 & 2009, NMS



Combining all nationally-representative survey data available on severe anemia in children, regional and age-specific trends can be examined for children 6–35 months (Figure 28 and Figure 29). Over the evaluation period, significant decreases are evident in the Southern region but not elsewhere. Although severe anemia appears to be declining over the evaluation period in the youngest children (6–11 months and 12–23 months) these differences are not significant between 2001 and 2010.

Figure 28: Anemia prevalence in children 6–35 months by region (hemoglobin <8g/dL), Malawi, 2001, 2004, 2009, 2010, NMS, DHS

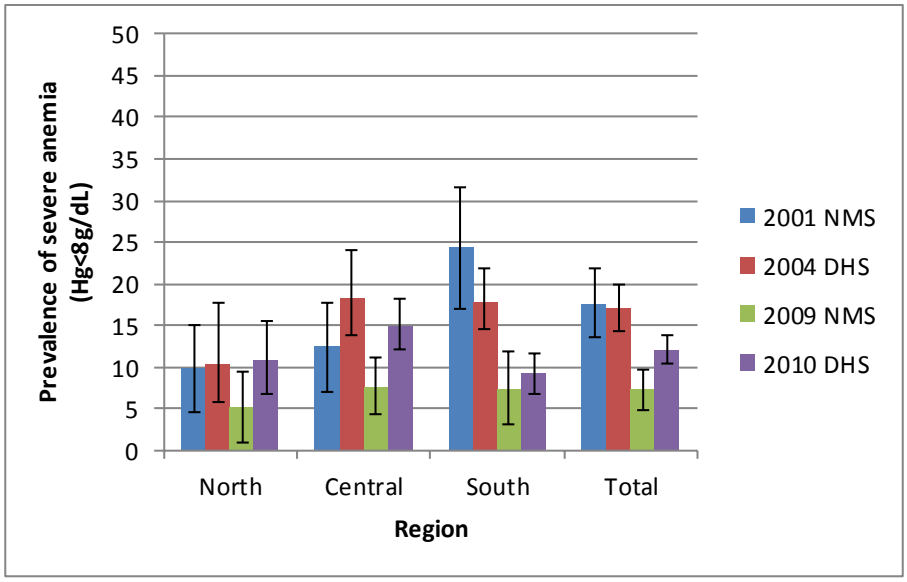
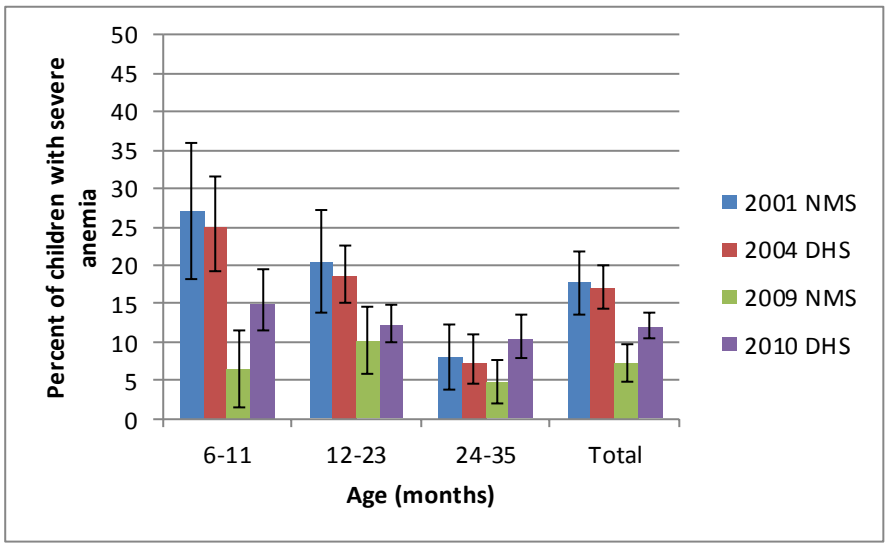


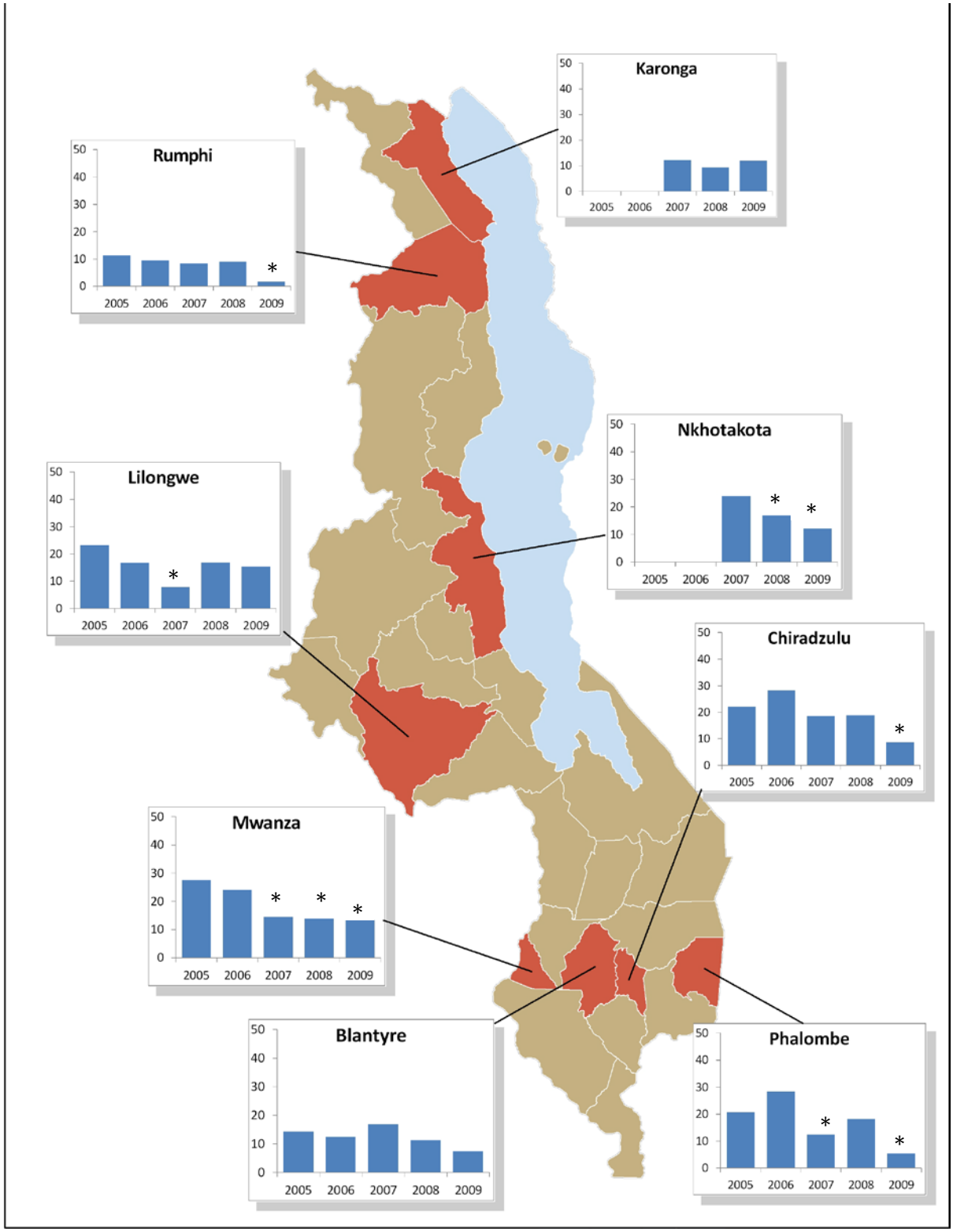
Figure 29: Anemia prevalence in children 6–35 months by age (hemoglobin <8g/dL), Malawi, 2001, 2004, 2009, 2010, NMS, DHS



Severe Anemia in Malawi 2005–2009, Sub-National Data

Anemia data were also collected in A&P surveys in eight districts between 2005 and 2009 in children 6–30 months of age. Figure 30 presents trends in severe anemia prevalence by district over this time period. Clear patterns of decreasing prevalence of severe anemia can be seen between 2005 and 2009. Further analyses of these data are included in the Further Analyses section (page 87) and tables of anemia estimates including 95% confidence intervals can be found in Annex 3.3.

Figure 30: Severe anemia prevalence in children 6–30 months by district (hemoglobin <8g/dL), Malawi, 2005–2009, A&P



*p<.05 (reference category is 2007 for Karonga and Nkhotakota and 2005 for all other districts)

Gender and Socio-economic Disparities

Estimates of severe anemia prevalence stratified by gender and socio-economic characteristics are shown in Table 14 using data from the two DHS surveys (data stratified by background characteristics were not collected or were not reported in publically available reports for the relevant age groups from the NMS). Although most of the observed changes in severe anemia prevalence between 2004 and 2010 are declines, the magnitude of change is small. In both survey years, prevalence of severe anemia is higher in children from households in the lowest wealth quintiles compared to those in the highest wealth quintile. 95% confidence intervals for these estimates are available in Annex 3.1 (Table A.3.1.12).

Table 14: Severe anemia (hemoglobin<8g/dL) prevalence in children 6–59 months of age, by background characteristics, Malawi, 2004–2010

Characteristic	2004	2010	Absolute Change
Sex			
Male	11.6	9.1	-2.5
Female	9.7	8.2	-1.5
Residence			
Urban	4.9	6.8	1.9
Rural	11.3	9.0	-2.3
Wealth			
Lowest	13.4	11.4	-2.0
Second	14.2	9.3	-4.9
Middle	9.4	9.3	-0.1
Fourth	10.0	7.9	-2.1
Highest	3.8	5.3	1.5
Mother's Education			
None	14.3	10.7	-3.6
Primary	10.2	8.9	-1.3
Secondary or Higher	10.6	6.4	-4.2
Missing	2.1	5.8	3.7
Total	10.6	8.7	-1.9

Severe Anemia Trends and Malaria Risk

Malaria transmission is not homogenous across Malawi. In order to explore the relationship between malaria endemicity and malaria-associated outcomes, risk terciles were created. The cluster locations from the 2010 DHS were overlaid on a 2007 map of parasitemia data from the Malaria Atlas Project (MAP) [95](see Annex 1.7 for detailed methods). This map contains estimated prevalence rates of *P. falciparum* infection in children 2–10 years of age (*Pf*PR_{2-10}). Terciles of *Pf*PR_{2-10} values were then created at the cluster-level. Respective malaria parasitemia prevalence for the three categories was: 0–33.7% (Lower); 33.8–45.2% (Medium); and 45.3%–100% (Higher). A map of the risk terciles is available in Annex 1.7.

If the reduction in anemia is associated with malaria decline, we would expect to see a higher baseline and greater reduction in severe anemia prevalence in areas with relatively higher risk of malaria. Trends over time for severe anemia prevalence in these three categories are shown in Figure 31.

Figure 31: Trends in severe anemia (hemoglobin <8g/dL) prevalence in children 6–23 months, by malaria risk areas, Malawi, 2004 and 2010, DHS

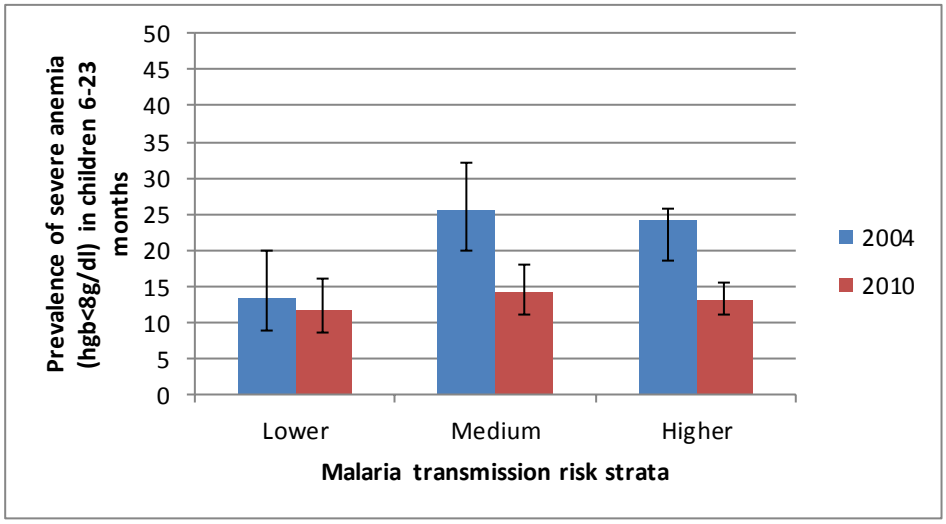


Figure 31 shows that the prevalence of severe anemia in children 6–23 months declined significantly in areas of medium and high malaria transmission but not in areas of low malaria transmission. Anemia in young children is multifactorial. The relative contribution of malaria to the overall anemia burden in young children would be expected to be greater in areas of medium-high transmission, thus control of parasite transmission would be expected to reduce anemia in these populations. In populations with low malaria transmission, successful malaria control may not lead to reductions in anemia as most cases of anemia are likely to be due to other causes.

Routinely-collected Facility-based Malaria Data

Data from the health management information system (HMIS) and from the Integrated Disease Surveillance and Response (IDSR) system were used to investigate trends in suspected malaria cases. Data from both systems are limited by incomplete reporting and by lack of diagnostic confirmation of most reported malaria cases. The percent of facilities reporting on malaria cases is presented whenever possible as an important factor that could bias trends in malaria cases. Although these reporting systems have not been formally evaluated for accuracy, they represent some of the only sources of national-level data on clinical malaria over time.

Trend in Suspected Malaria Cases, HMIS, 2005–2010

According to the HMIS, the number of reported cases of malaria in all age groups increased from 3.7 million in 2005 to about 6.7 million in 2010 (Table 15). Why this number increased during a period when antimalarial interventions were being scaled up is unclear, but likely explanations include improved reporting and increased use of

health services. Age-specific data on annual outpatient department visits are not available from HMIS records. Annual suspected malaria incidence can be roughly estimated using annual total population estimates as denominators. Similarly, incidence for children under five years of age can be estimated using the proportion of the total population that is under five years of age as the denominator. The incidence estimates reported in Table 15 do not account for variations in care-seeking between 2005 and 2009 due to the lack of age-specific outpatient department visit data which would be necessary to make the adjustment, therefore caution should be used when drawing conclusions from this data.

Table 15: Number of suspected malaria cases, with or without parasitological confirmation, in health facilities, 2005–2010

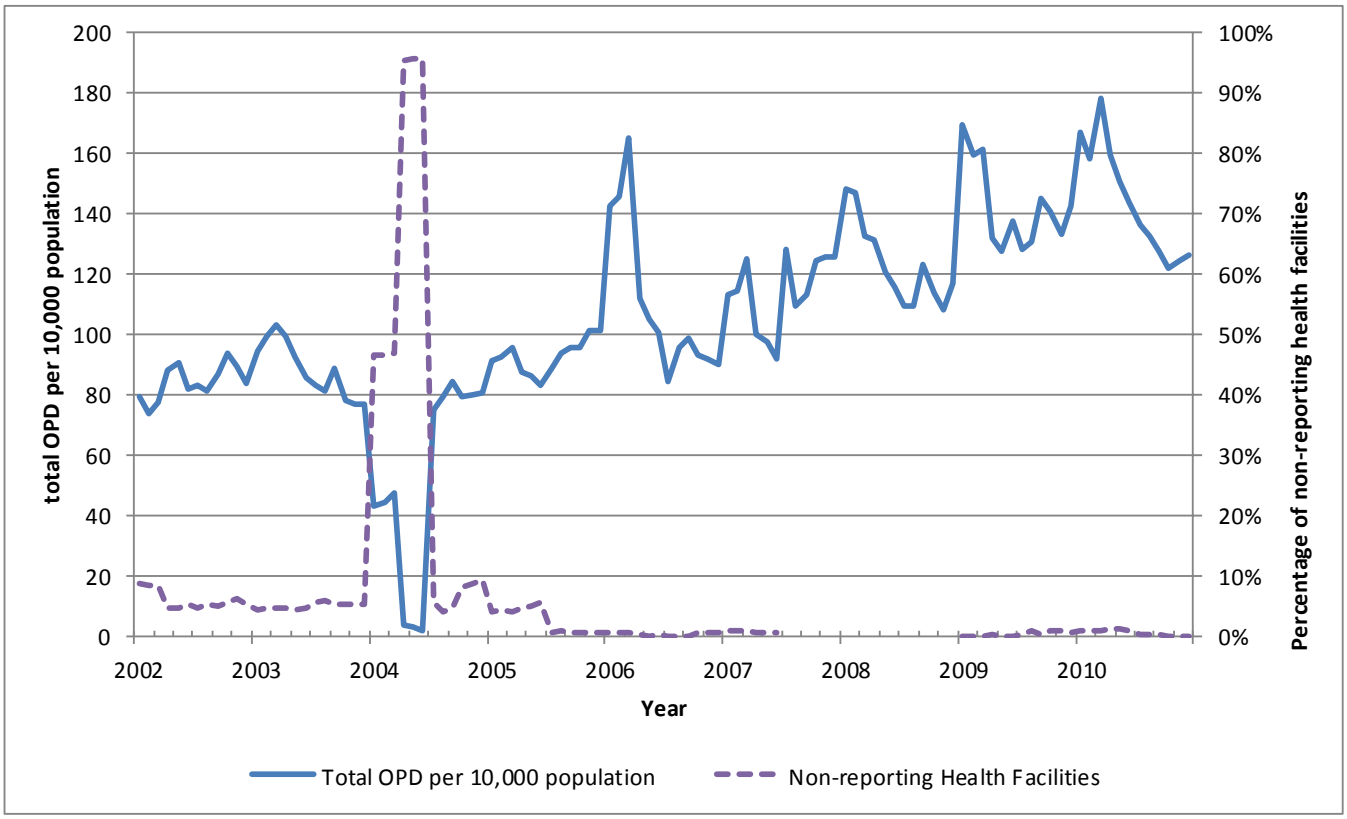
Year	Total population	Suspected malaria cases (Outpatient Department)			Suspected malaria cases per 1,000 population	Suspected malaria cases per 1,000 children <5*
		< 5 years	≥ 5 years	All ages		
2005	11,999,585	1,686,040	1,977,451	3,663,491	305	817
2006	12,345,253	2,162,316	2,339,219	4,501,535	365	1018
2007	12,700,877	2,282,360	2,505,346	4,787,706	377	1045
2008	13,066,746	2,576,931	2,608,151	5,185,082	397	1147
2009	13,432,615	3,027,629	3,133,792	6,161,421	459	1310
2010	13,808,728	3,238,259	3,510,276	6,748,535	489	1363

*Assumes children under five years of age comprise 17.2% of the total population [21]
Source: HMIS

Survey data support the hypothesis that care-seeking increased over the evaluation period. Care-seeking among children under five years of age with fever increased from 41% in 2004 to 65% in 2010, according to DHS estimates. Similarly, data from local research studies show evidence of increased care seeking for malaria. For example, research from a hospital in Blantyre, Malawi found evidence of increasing outpatient department visits in the pediatric ward from 2001 to 2010 [96]. The 2007 implementation of a policy to provide free ACTs in health facilities may have contributed to increased health care seeking thus leading to greater identification and reporting of cases. Another factor that could have contributed is an increase in the number of health facilities.

Trends in reporting and use of health services by all ages (measured by total outpatient department visits) from HMIS data are shown in Figure 32. The percent of facilities not reporting has decreased over the evaluation period and the percent of total outpatient department (ODP) visits of all ages has increased even during periods of sustained, high reporting.

Figure 32: Total outpatient department (OPD) visits and percent of facilities not reporting, Malawi, 2002–2011*



*Data on non-reporting health facilities are not available for July-December of 2007 and for all of 2008.

Trends in Suspected Malaria Cases, IDSR Health Facility-based Morbidity Data, 2005–2010

Data from the IDSR system were analyzed to look at trends in outpatient and severe inpatient suspected malaria cases as well as deaths attributed to malaria (confirmed and unconfirmed malaria deaths as reported by health facilities to IDSR). All suspected cases of malaria, diarrhea with severe dehydration, and severe pneumonia in children under five years of age were considered. Other technical and methodological details of the data and the analyses are included in Annex 1.11. Additional figures containing temporal trends in these outcomes plotted against rainfall data on a regional level are also included in Annex 4.1.

Total outpatient suspected malaria cases and outpatient malaria cases in children under five were markedly seasonal over the period of highest reporting (2006–2010). In the Northern Region, cases peaked in January to March of 2006, 2007, and 2009 (Figure 33). In the Central Region, cases peaked substantially in January to March of 2009 and 2010 (Figure 34). In the Southern Region, cases peaked in 2008 and 2009 (Figure 35). From these data it appears that cases may have increased between 2005 and 2010 in the Central Region, even after accounting for the percent of facilities reporting. No increase was evident in the Northern Region and trends are unclear in the Southern Region.

Figure 33: Total outpatient malaria diagnoses in children under five years of age per 10,000 population, Northern Region, 2005–2010, IDSR

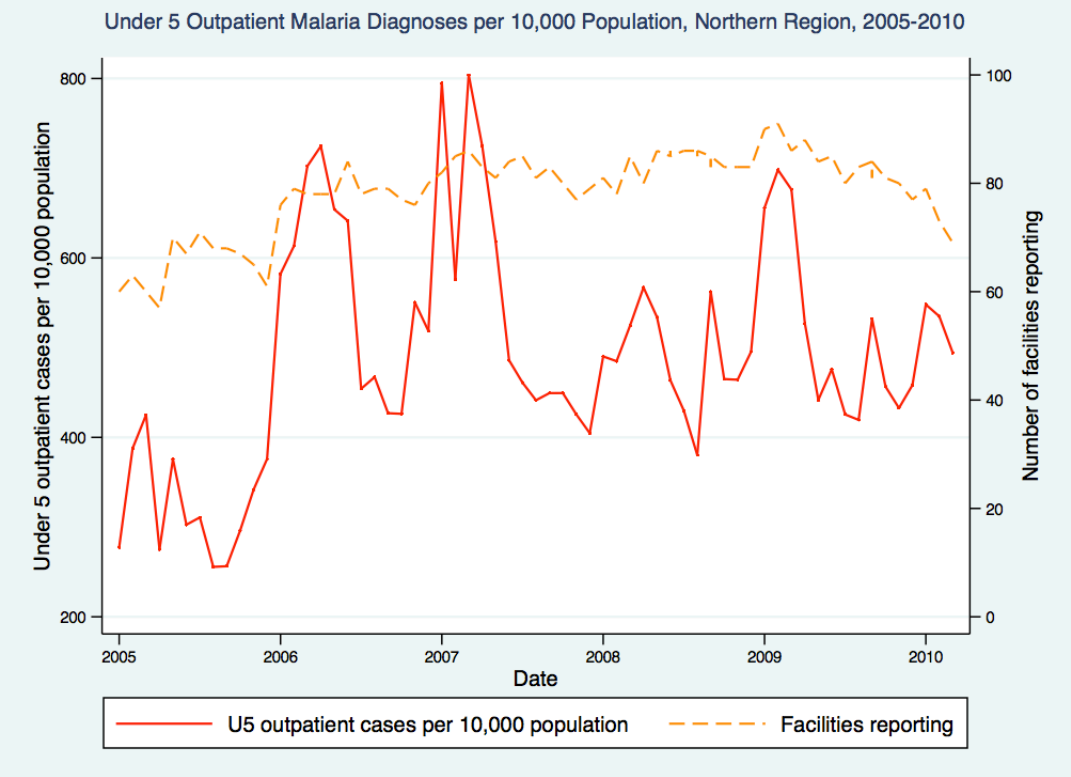


Figure 34: Total outpatient malaria diagnoses in children under five years of age per 10,000 population, Central Region, 2005–2010, IDSR

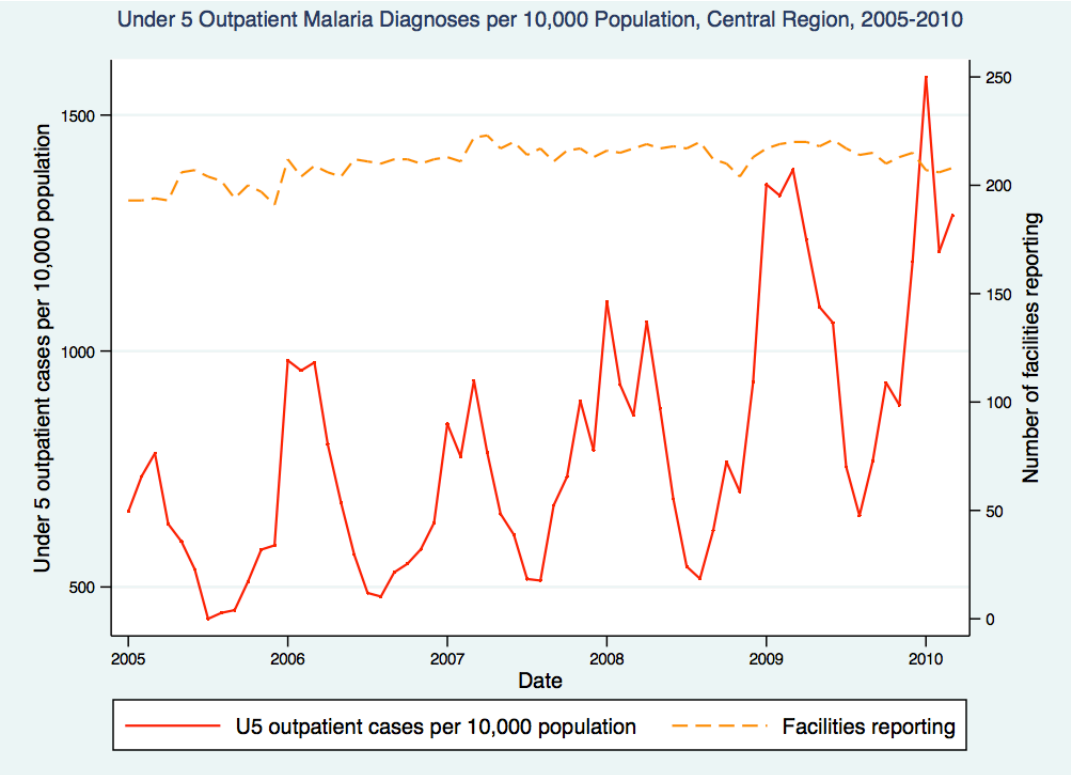
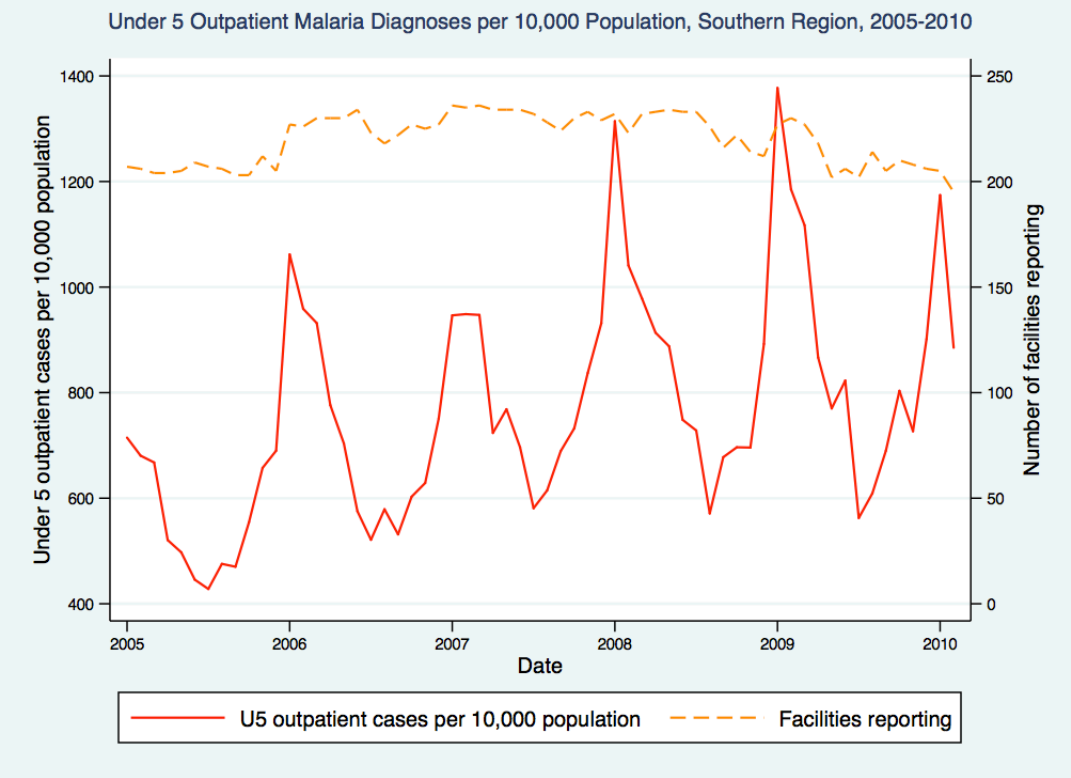
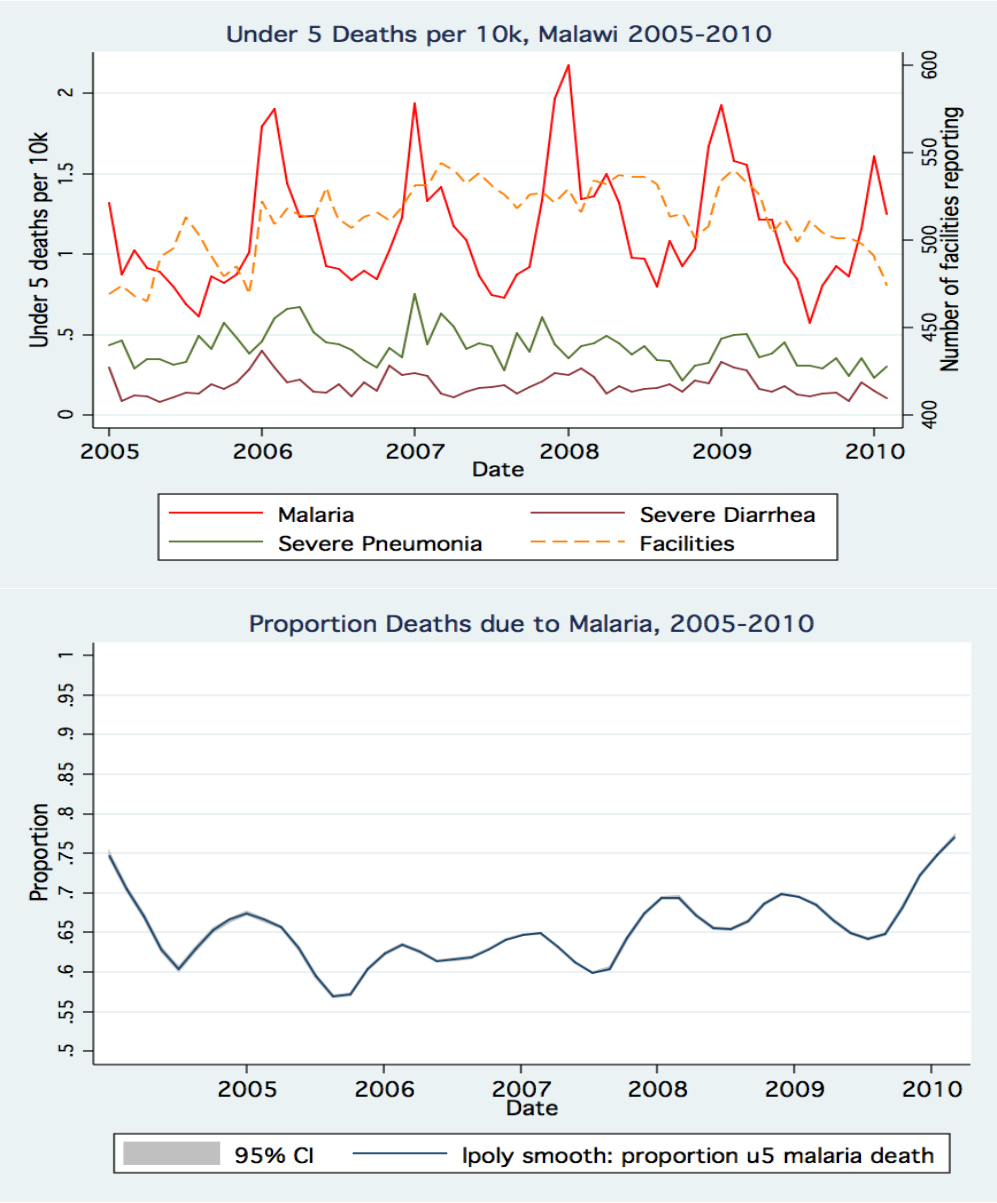


Figure 35: Total outpatient malaria diagnoses in children under five years of age per 10,000 population, Southern Region, 2005–2010, IDSR



Trends in inpatient severe malaria cases and malaria-attributable deaths in children under five were also examined. Details on trends in severe malaria cases are included in Annex 4.1. In brief, peaks of severe malaria cases and deaths were regionally specific without clear national trends. Nationally, the relative importance of malaria as a cause of deaths in children under five years of age, as compared to pneumonia and diarrhea, appears to have increased over the scale-up period (Figure 36b). This could possibly be due to contemporaneous gains in the prevention and clinical management for these other causes of under-five mortality. Supporting this hypothesis, deaths due to all three causes declined from 2005 to 2010 (Figure 36a).

Figure 36: a) Total **severe malaria**, severe pneumonia, and severe diarrhea deaths in children under five, and b) Proportion of severe malaria deaths out of all severe pneumonia, severe diarrhea, and severe malaria deaths in children under-five, Malawi, 2005–2010



These results show high seasonality but little consistent change in outpatient or severe inpatient suspected malaria cases over the scale-up period. Observed trends in severe inpatient malaria cases will be discussed in more depth in the Annex 4.1. The ratio of deaths to severe malaria inpatient cases (case-fatality rate) has declined in all regions (see Annex 4.1), indicating potential successes in case management of severe disease.

Summary of Malaria Morbidity

Although measuring trends in parasitemia prevalence can provide useful data on national successes in malaria control, the intra-annual and inter-annual variations can also complicate interpretation. Many data points are necessary to properly adjust for these variations. Unfortunately, in Malawi, national parasitemia estimates are only

available for two survey years during low transmission seasons and for one survey year during high transmission season.

Repeat cross-sectional data from NMS indicate that a significant decrease in malaria parasite prevalence occurred between 2001 and 2009 in children 6–35 months. Sub-national anemia and parasitemia surveys in eight districts did not reveal a straightforward temporal trend in parasitemia, as parasitemia prevalence decreased in some districts but not all between 2005 and 2009. A recent study, using model-based geostatistical methods to predict mean $Pf\text{Pr}_{2\text{-}10,}$ found no evidence of change in the national population-adjusted $Pf\text{PR}_{2\text{-}10}$ between 2000 and 2010 [29]. In another study also using geostatistical models, the authors reported no change nationally in the intensity of *P. falciparum* transmission between 2000 and 2010, and found only a few districts with a reduction in malaria risk over this period [97].

Available evidence suggests that the prevalence of severe anemia declined over the period of malaria control intervention scale-up in young children most at risk of malaria (6–23 months of age). The decline was significant among young children living in medium to high risk malaria transmission areas but not in those living in low risk areas. These trends are consistent with expectations in areas with multifactorial causes of childhood anemia. Southern Region has had the highest malaria burden of the three regions (although the difference is not statistically significant), therefore the differential drop in severe anemia in this region supports the notion that malaria control was a primary driver of this reduction in severe anemia.

Suspected malaria cases in children under five years of age reported by health facilities have increased between 2005 and 2010. HMIS data show a rise in the number of suspected malaria cases per 1,000 children from 817 to 1,363 over this period; however, the total number of out-patient visits and the number of health facilities reporting have also increased during this period. Similarly, IDSR data show increases in numbers of suspected malaria cases in children under five years of age from 2005 to 2010, although trends varied by season and region. As with the HMIS data, the numbers of facilities reporting to IDSR have increased throughout the period, particularly in the Northern and Central Regions. Thus, available facility-based data in Malawi suggest a trend of increasing malaria cases between 2005–2010, which may be in part due to other secular trends in care seeking for childhood illness and by trends in reporting. However, the lack of wide-spread confirmatory diagnosis means only trends in suspected and not confirmed malaria cases are available from the HMIS and IDSR. The lack of decline in confirmed malaria cases between 2001 and 2010 was noted in a study in Queen Elizabeth Central Hospital in Blantyre [96].

In conclusion, between 2001 and 2010, in national surveys conducted during similar periods in the malaria transmission cycle, parasitemia prevalence and severe anemia have decreased in young children (6–35 months), but facility-based data show increasing cases of malaria between 2005 and 2010. Declines in severe anemia prevalence have been greatest in the children most susceptible to malaria-related morbidity (6–23 months) and in those living in the highest transmission areas. Additional analyses of these trends are presented in the Further Analyses section on page 87.

MORTALITY

Mortality

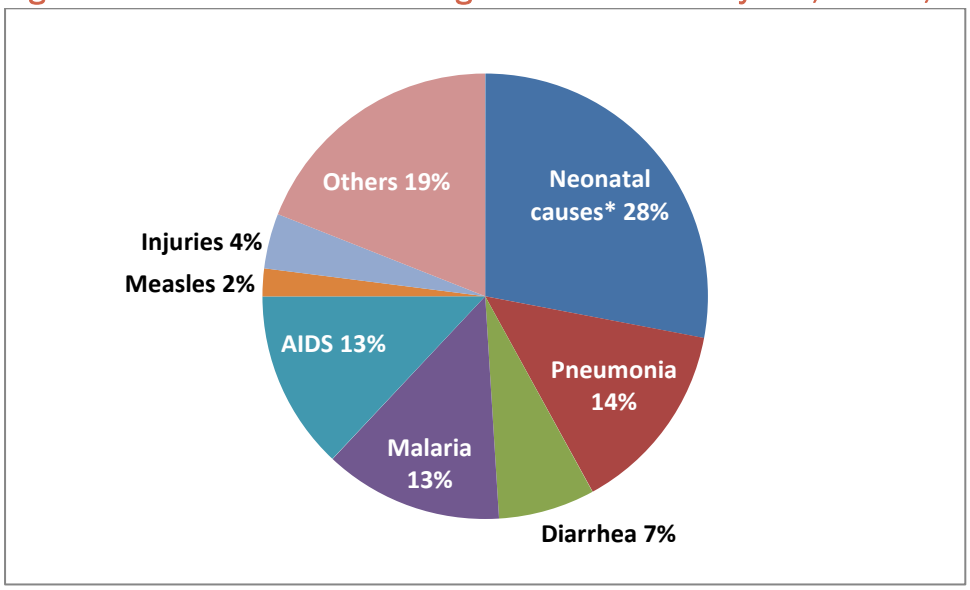
Background

This section reviews recent trends in ACCM, with a view to assessing the magnitude, timing, and age-pattern of change between the 2000 and 2010 surveys. In addition, it includes an ecological analysis that examines changes in mortality with respect to malaria risk. Mortality estimates for 1988 -1992, from the 1992 DHS, are described in order to put recent trends in a longer-term context. All mortality figures represent direct estimates, and unless otherwise stated, represent the period 0–4 years before each survey. ACCM trends from the United Nations Inter-Agency Group for Mortality Estimation (IGME) are included in figures where relevant for comparative purposes.

Mortality estimates presented in this evaluation are derived from multiple Demographic and Health Survey (DHS) datasets and a Multiple Indicator Cluster Survey (MICS) rather than mortality estimates available from the Inter-Agency Group for Mortality Estimation (IGME). The level and detail of stratification needed to inform the plausibility design of this evaluation was not possible using IGME estimates. IGME and other mortality estimates are presented and discussed when applicable.

Malawi ranks 31st out of 195 countries in the world for ACCM according to a recent UNICEF Progress Report which relies on IGME data [98]. In Malawi, in 2010, malaria was estimated to account for 13% of deaths in children under five years of age (Figure 37).

Figure 37: Causes of death among children under five years, Malawi, 2010



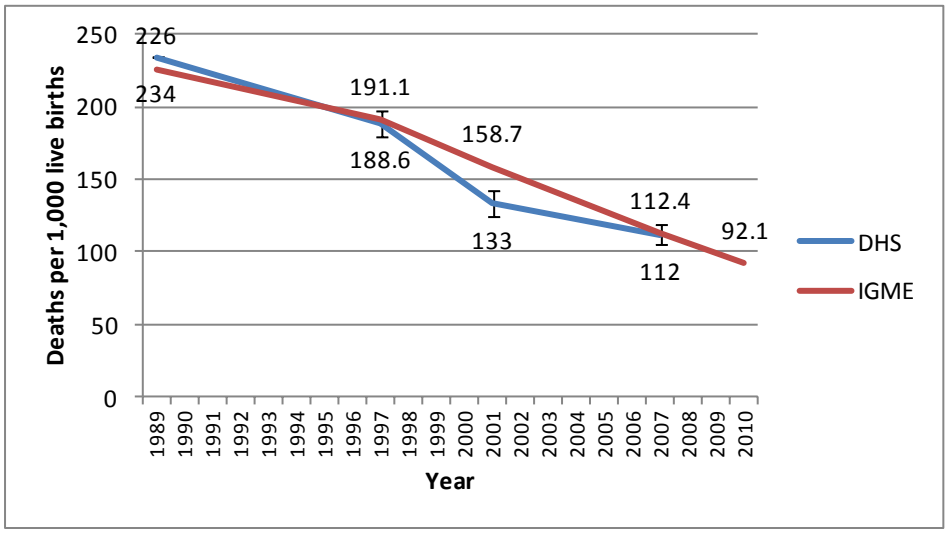
*Includes all neonatal causes except neonatal pneumonia and diarrhea.

Source: UNICEF Progress Report 2012. Committing to Child Survival: A Promise Renewed. [98]

Trends in All-cause Under-five Mortality

Estimates of ACCM from successive DHSs conducted between 1992 and 2010 are presented in Figure 38 along with the corresponding ACCM estimates from IGME. Estimates prior to 2000 are included to examine the secular trend.

Figure 38: All-cause under-five mortality (ACCM) rates from DHS data, Malawi, 1988–1992, 1996–2000, 2000–2004, 2006–2010*, and IGME trend

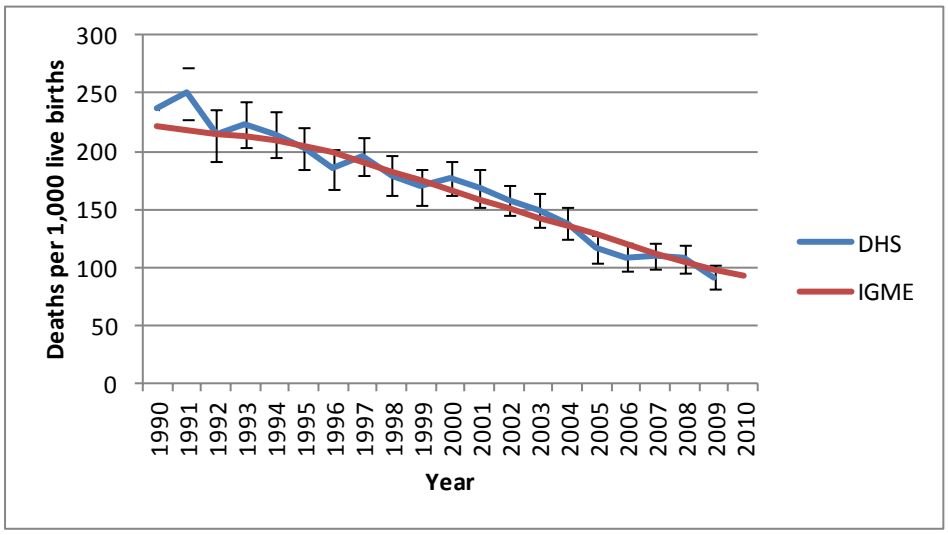


*DHS estimates are for the five years preceding the survey. Data points have been put at the mid-point of the five year range to accurately represent the timing of the estimate.

According to the DHS mortality estimates, significant reductions in ACCM are evident between all five-year periods with the most drastic decline (29%) occurring between 1996–2000 and 2000–2004.

Although DHS reports typically present five-year estimates of mortality it is possible to generate annual mortality estimates using DHS data. These estimates typically have greater levels of uncertainty due to smaller samples sizes, but allow examination of more fine-scale trends. Annual DHS estimates show very close correlation with the IGME estimates. As was seen in the five-year estimates, ACCM has been declining dramatically since 1990 and most of this decline occurred over the past 15 years (Figure 39).

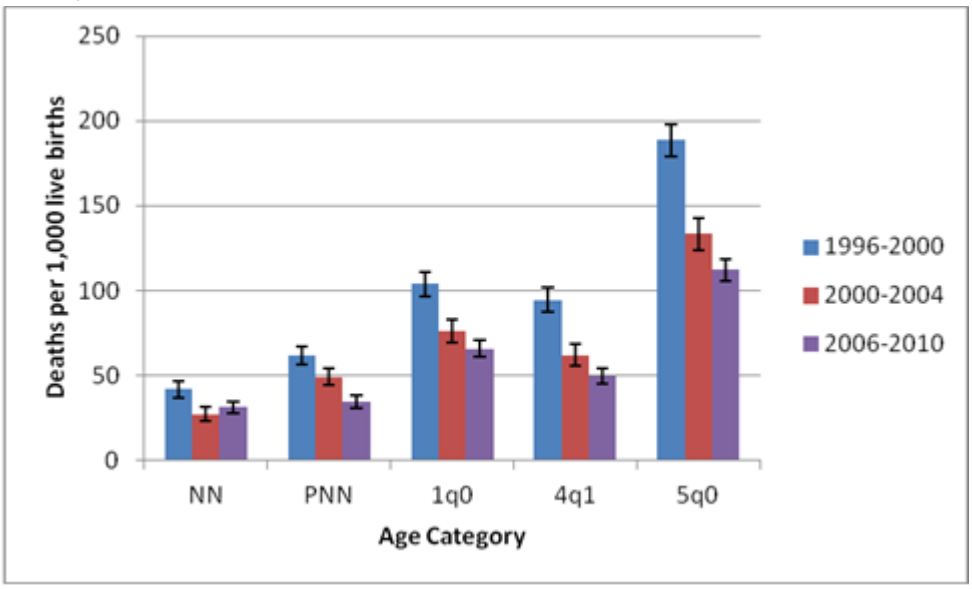
Figure 39: DHS and IGME estimates of annual all-cause under-five mortality (1990–2010)



Age-specific Childhood Mortality

Trends in age-specific childhood mortality across the last three DHS surveys are presented in Figure 40. Childhood mortality has been steadily decreasing over the past decade with the exception of neonatal mortality.

Figure 40: Trends in age-specific childhood mortality, Malawi, 1996–2000 to 2006–2010, DHS



Key: NN = neonatal mortality (first month), per 1,000 live births; PNN = post-neonatal mortality (age 1–11 months), per 1,000 live births; ${}_1q_0$ = infant mortality (first year), per 1,000 live births; ${}_4q_1$ = child mortality between exact age 1 and exact age 5, per 1,000 children surviving to 12 months of age; ${}_5q_0$ = under-five mortality, per 1,000 live births. Error bars represent upper and lower 95% confidence limits for the estimates.

The mortality estimates and relative change in these estimates by age categories are shown in Table 16 and Figure 41. Five additional age categories are included: 6–23 months (where malaria-related mortality would be expected to be concentrated) and 1–5 months, 24–59 months, 1–59 months and 6–59 months (for comparison).

A more drastic decline is evident between 1996–2000 and 2000–2004 than between 2000–2004 and 2006–2010 for infant (1q0) (27% vs. 14%) and child mortality (4q1) (35% vs. 20%). The decline was similar between these time periods for post-neonatal mortality (21% vs. 29%). Although neonatal mortality declined between 1996–2000 and 2000–2004, no decrease was evident between those time periods and 2006–2010.

Table 16: Age-specific mortality (deaths per 1,000 live births) and relative change in age-specific mortality, 0–4 years prior to the survey by period of estimation

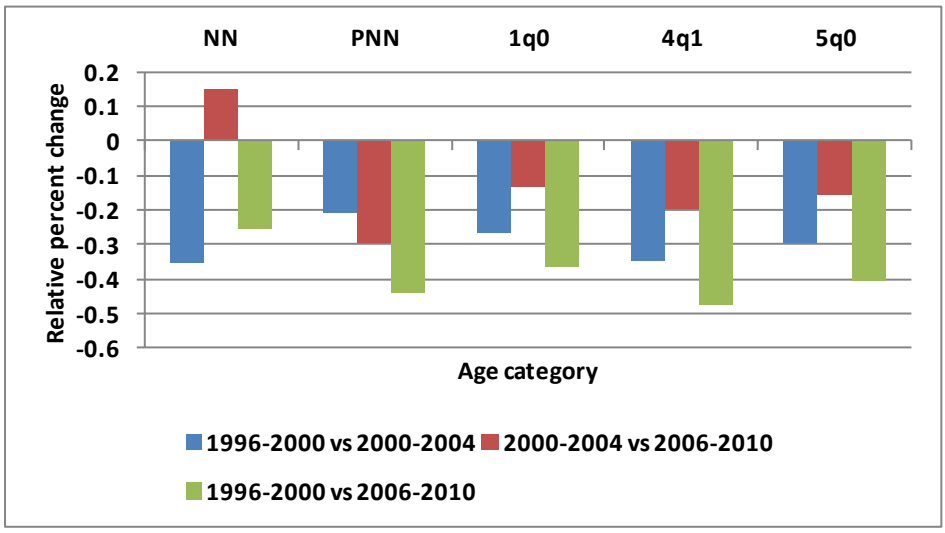
Age Category	Mortality (0–4 years prior to the survey)			Relative change	Relative change	Relative change
	A 1996–2000	B 2000–2004	C 2006–2010	A–B	B–C	A–C
Neonatal (NN)	41.8	27.1	31.2	-35.1%	+14.9%	-25.5%
Post-neonatal (PNN)	61.9	49.0	34.7	-20.8%	-29.3%	-44.0%
Infant ($_1q_0$)	103.7	76.1	65.8	-26.6%	-13.5%	-36.5%
Child ($_4q_1$) [a]	94.6	61.8	49.6	-34.7%	-19.8%	-47.6%
Under-five ($_5q_0$)	188.6	133.2	112.1	-29.4%	-15.8%	-40.5%
1–59 months [b]	152.9	109.0	83.5	-28.7%	-23.4%	-45.4%
6–59 months [c]	125.2	86.5	68.9	-31.0%	-20.3%	-44.9%
1–5 months [b]	31.6	24.6	15.6	-22.2%	-36.6%	-50.6%
6–23 months [c]	74.7	51.4	40.3	-31.2%	-21.6%	-46.1%
24–59 months [d]	54.8	37.1	30.0	-32.3%	-19.1%	-45.3%

[a]Child mortality ($_4q_1$) is per 1,000 live-born children surviving to 12 months of age
[b]1–59 month mortality and 1–5 month mortality is per 1,000 live-born children surviving to 1 month of age
[c]6–59 month mortality and 6–23 month mortality is per 1,000 live-born children surviving to 6 months of age
[d]24–59 month mortality is per 1,000 live-born children surviving to 24 months of age

The relative decline between the 1996–2000 and 2006–2010 mortality estimates was comparable for children aged 6–23 months (46%) and children 24–59 months (45%).

Relative change in mortality decreased over time for most age categories; the relative decline in mortality between 1996–2000 and 2000–2004 was greater than that for the second half of the decade, 2000–2004 to 2006–2010 (blue bars vs. red bars in Figure 41).

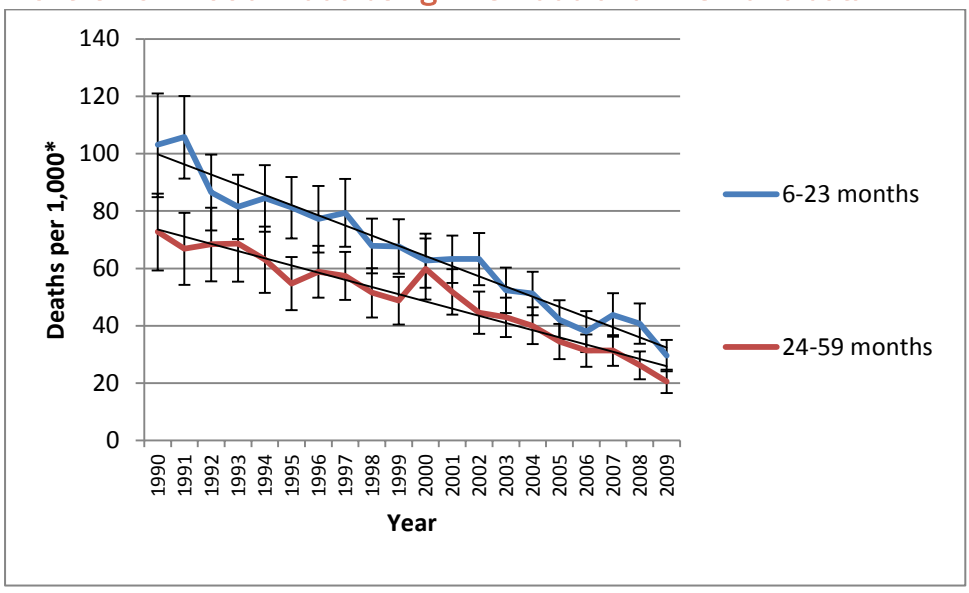
Figure 41: Relative percent change in age-specific childhood mortality in children in Malawi; a comparison of five-year estimates from the 2000, 2004 and 2010 DHS



Key: NN = neonatal mortality (first month), per 1,000 live births; PNN = post-neonatal mortality (age 1-11 months), per 1,000 live births; ${}_1q_0$ = infant mortality (first year), per 1,000 live births; ${}_4q_1$ = child mortality between exact age 1 and exact age 5, per 1,000 children surviving to 12 months of age; ${}_5q_0$ = under-five mortality, per 1,000 live births.

If a major proportion of ACCM was due to malaria, declines in malaria deaths over the period of scale-up in malaria control interventions should be greatest in the children most susceptible to severe malaria outcomes. Figure 42 shows the annual estimates of mortality in 6–23 month old children compared to those of 24–59 month old children. Both age groups experienced similar decreases in mortality over the two decades, although the mortality rates are greater in the younger age group.

Figure 42: Annual estimates of all-cause mortality in children 6–23 months and 24–59 months from 1990–2009 using DHS 2000 and DHS 2010 data**

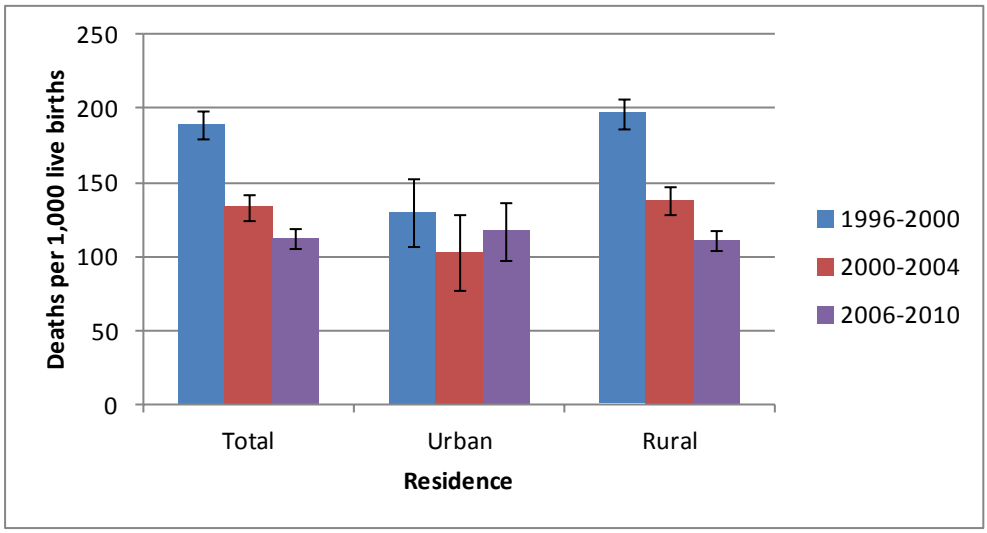


*6–23 month mortality is measuring annual deaths per 1,000 children surviving to 6 months; 24–59 month mortality is measuring annual deaths per 1,000 children surviving to 24 months.
**Estimates from 1990–1999 are derived from DHS 2000 data and estimates from 2000–2009 are derived from DHS 2010 data.

Mortality Change by Residence

Figure 43 shows mortality rates from 1996–2000, 2000–2004 and 2006–2010 stratified by rural and urban residence. ACCM in rural areas declined from 197 deaths per 1,000 live births in 1996–2000 to 111 deaths per 1,000 live births in 2006–2010; representing an absolute decline of 86 deaths per 1,000 live births and a relative decline of 44%. In urban areas, the absolute and relative difference in mortality decline (13 deaths and 10%, respectively) was much smaller (130 deaths per 1,000 live births in 1996–2000 to 117 in 2006–2010) and was not statistically significant.

Figure 43: All-cause childhood mortality in children under five years of age by residence, Malawi, five-year estimates from the 2000, 2004 and 2010 DHS.



Mortality Change by Malaria Risk

If a major part of the decline in ACCM was malaria-related, we would expect to see a greater decline in mortality, from a higher baseline, among children living in areas of greater malaria risk – as compared to areas of lower malaria risk [99, 100].

To test this hypothesis, we looked at trends in childhood mortality rates stratified by malaria risk zones as defined previously (Morbidity section, page 52; Annex 1.7). For infants between birth and one year of age, the mortality rates from 1996–2000 were 104, 108, and 97 per 1,000 live births in the higher, medium and lower risk categories, respectively (Figure 44). By the 2006–2010 estimation period, the mortality rates had dropped to 57, 61 and 81 per 1,000 live births respectively in the higher, medium and lower risk categories. These changes are statistically significant in the medium and higher malaria risk tercile but not in the lower risk tercile. For children under five years of age, mortality rates in the three risk categories in the 1996–2000 time period were 191, 201 and 165, respectively (Figure 45). These had changed to 113, 112 and 111 by 2006–2010, statistically significant changes from baseline in all three malaria risk terciles, although the decline was larger in the medium and higher risk terciles. Taken together, these results are consistent with the hypothesis that malaria control interventions have contributed to declines in ACCM.

Figure 44: Trends in infant mortality in higher, medium and lower malaria risk areas, Malawi 1996–2000, 2000–2004 and 2006–2010

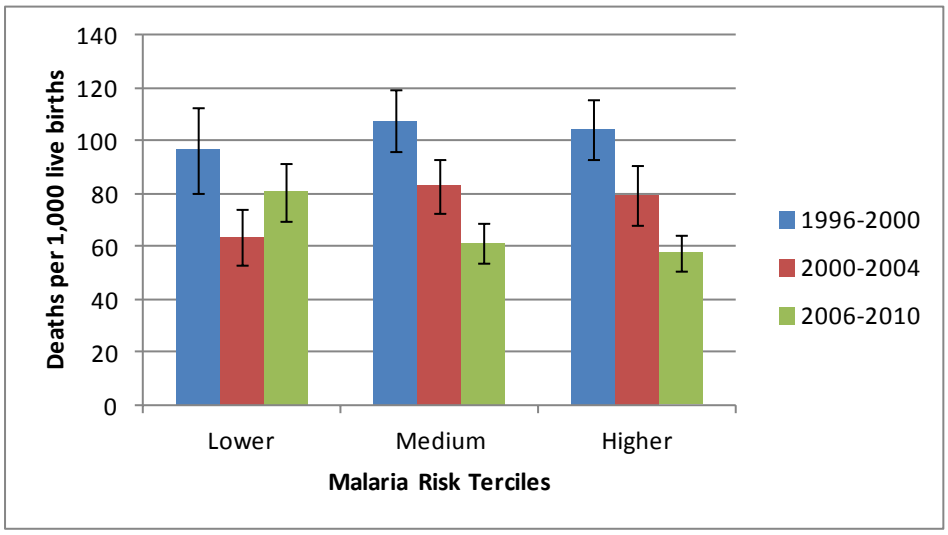
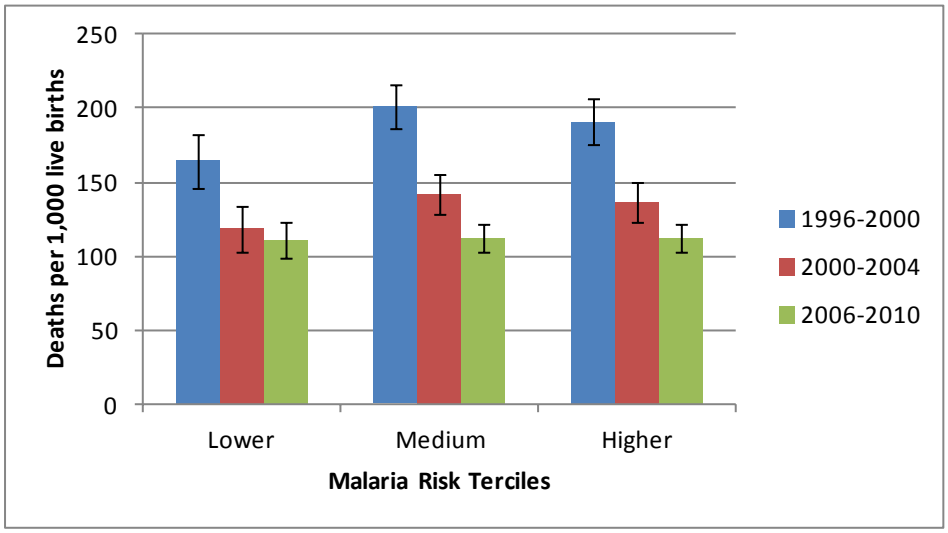


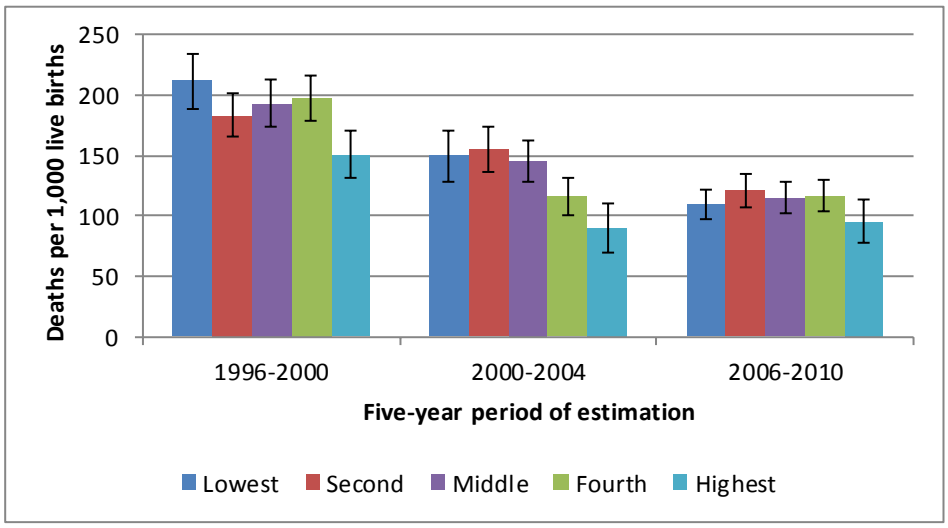
Figure 45: Trends in ACCM in higher, medium and lower malaria risk areas, Malawi 1996–2000, 2000-2004 and 2006–2010



Equity

It is conceivable that mortality changes described in this section could have occurred through disproportionately large gains in higher socio-economic groups. If this were the case, the differential in mortality by wealth quintile would have widened over time. Figure 46 presents trends in ACCM by wealth quintile. These data are for the five-year periods preceding the 2000, 2004 and 2010 DHSs. Whereas significant differences in ACCM are evident between children in the highest and lowest wealth quintiles in the 1996–2000 time period and in the 2000–2004 time periods, this difference is not evident in the most recent time period, from 2006–2010. Estimates and 95% confidence intervals are available in Table A.3.1.17 in Annex A.3.1.

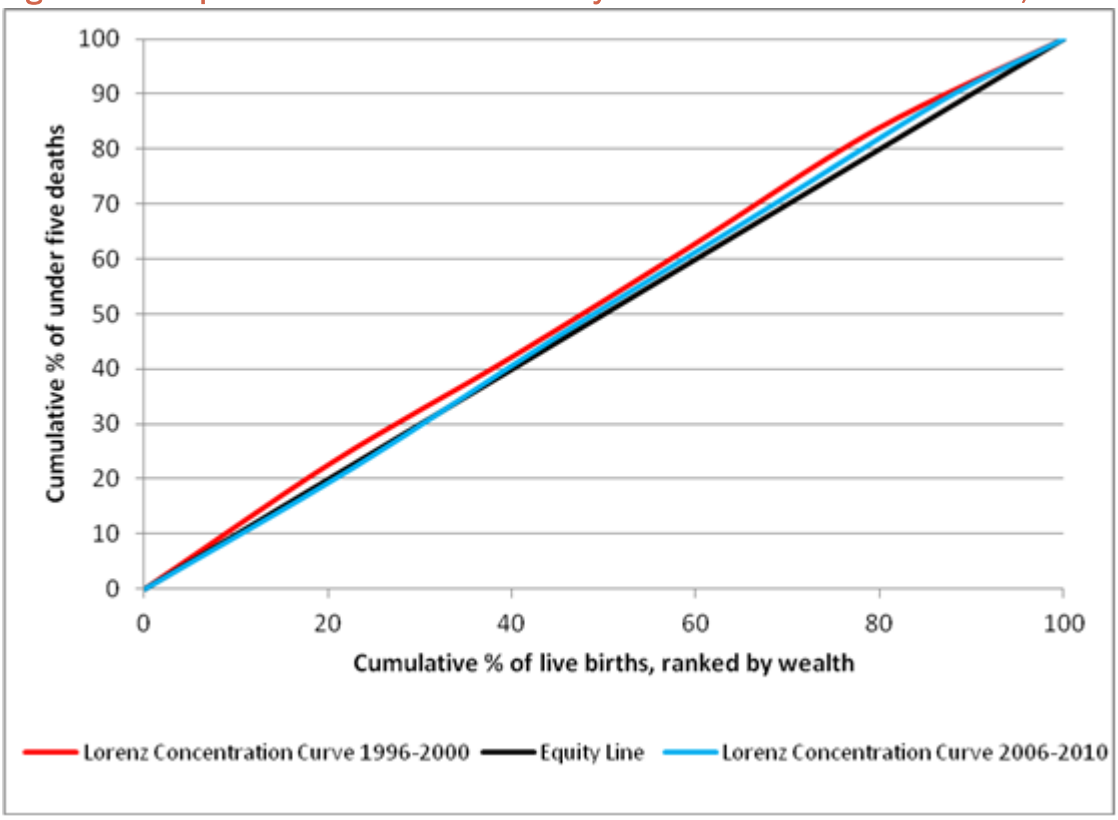
Figure 46: All-cause childhood mortality by wealth quintile, Malawi, 1996–2000, 2000–2004 and 2006–2010



Another way to view these data is to look at inequalities in mortality by wealth quintile using concentration curves – where the straight line represents perfect equity (with a concentration index of zero), and "upward" departure from the diagonal indicates excessive mortality in poorer population quintiles (with a negative sign on the concentration index).

Figure 47 shows the results of this analysis for ACCM estimates during the time periods 1996–2000 and 2006–2010, derived from the 2000 and 2010 DHS. The concentration index in 2006–2010 (-0.0145) was closer to "equality" than in that from 1996–2000 (-0.0468), indicating that equity of child survival between households of different wealth quintiles improved between these two survey periods.

Figure 47: Inequalities in under-five mortality 1996–2000 and 2006–2010, DHS



Concentration Index
1996–2000: -0.0468 (95% CI: -0.1023, 0.0087)
2006–2010: -0.0145 (95% CI: -0.0623, 0.0333)

Summary of All-cause Childhood Mortality

In summary, the data show that a significant decline in ACCM has occurred in Malawi between 2000 and 2010, a period of intense investment in malaria control interventions. This decline did not begin suddenly; data show a steady decline from 1990 through the end of the evaluation period in 2010. Within the evaluation period from 2000–2010, significant declines in ACCM occurred in the early part of the decade (2000–2004), at a time when malaria control interventions were not yet fully scaled-up (e.g. ITN use among children under the age of five was only 15% in 2004). Therefore, during this period, other child health interventions certainly played a role in the sharp decline in mortality. The effect of other interventions, referred to in this report as contextual factors, on mortality trends is addressed in the next section. From 2004–2010, when malaria control was intensified, mortality continued to decline at a significant rate.

The mortality decline over the last decade was greatest in children 1–5 years of age and in children living in rural areas. In rural areas, the reduction in mortality in this age group was significant, whereas this was not the case in urban areas. Stratification of child mortality by malaria risk showed the greatest reduction in ACCM in children living in higher and medium malaria risk areas. Infant mortality also decreased significantly in

the highest and medium malaria risk areas over the time period but no change was evident in the lowest malaria risk area.

Many aspects of mortality analysis presented in this section (timing, residence differentials, and relationship to malaria risk) are consistent with the results that would be expected if improvements in malaria control were a major factor underlying the mortality change in Malawi. It is also clear that other factors must have contributed to the observed decline in ACCM before the major investments in malaria control efforts began. These factors could have continued to contribute to the observed decline in ACCM post-malaria control interventions. The Further Analysis section of this report presents results of analyses in which associations between malaria control interventions and mortality are assessed with adjustment for other variables known to affect child mortality.

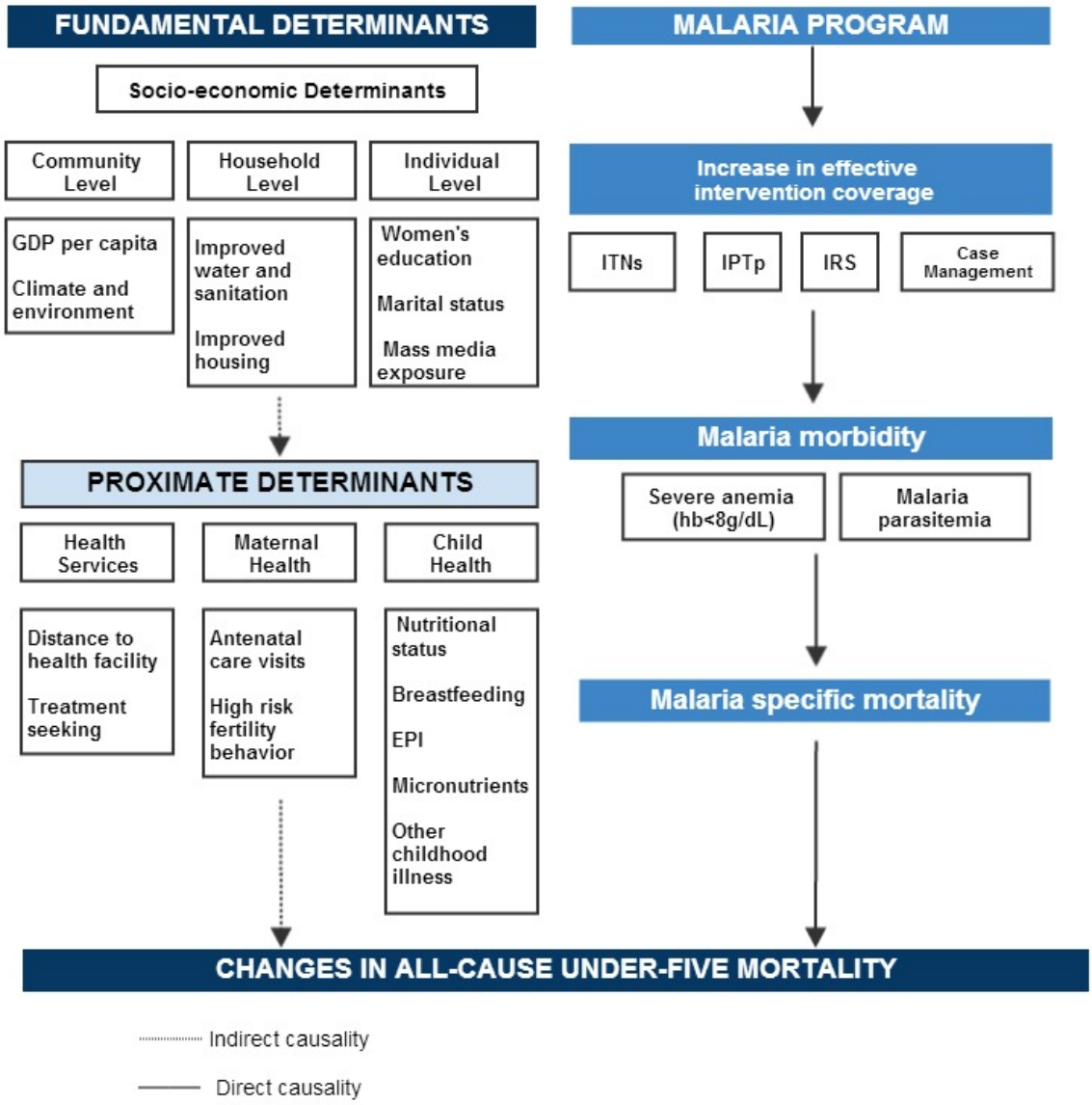
CONTEXTUAL FACTORS

Accounting for Contextual Factors

Appropriate considerations of contextual factors are essential for ensuring the internal and external validity of evaluations of large-scale health programs [101], particularly for evaluations that are conducted when rapid changes are under way in many other aspects of health services [102].

Contextual factors associated with childhood mortality and illness, including malaria, can be broadly categorized into the fundamental and proximate determinants of disease [103-110]. Fundamental determinants are the social and economic conditions under which people live, while proximate determinants are biological risks. The conceptual framework [6, 102, 111, 112] for the evaluation design in Malawi, Figure 48, incorporates numerous contextual factors within various subcategories of the fundamental and proximate determinants of disease. In the following sections, relevant information and levels and trends of various contextual determinants – fundamental and proximate – of childhood mortality and illness are reviewed. Data on contextual factors were obtained from large population-based household surveys (e.g., DHS, MIS, MICS), as well as other sources such as WHO/UNICEF, World Bank and UNAIDS.

Figure 48: Conceptual framework for the evaluation of the malaria control program, Malawi, 2000–2010



Fundamental Determinants

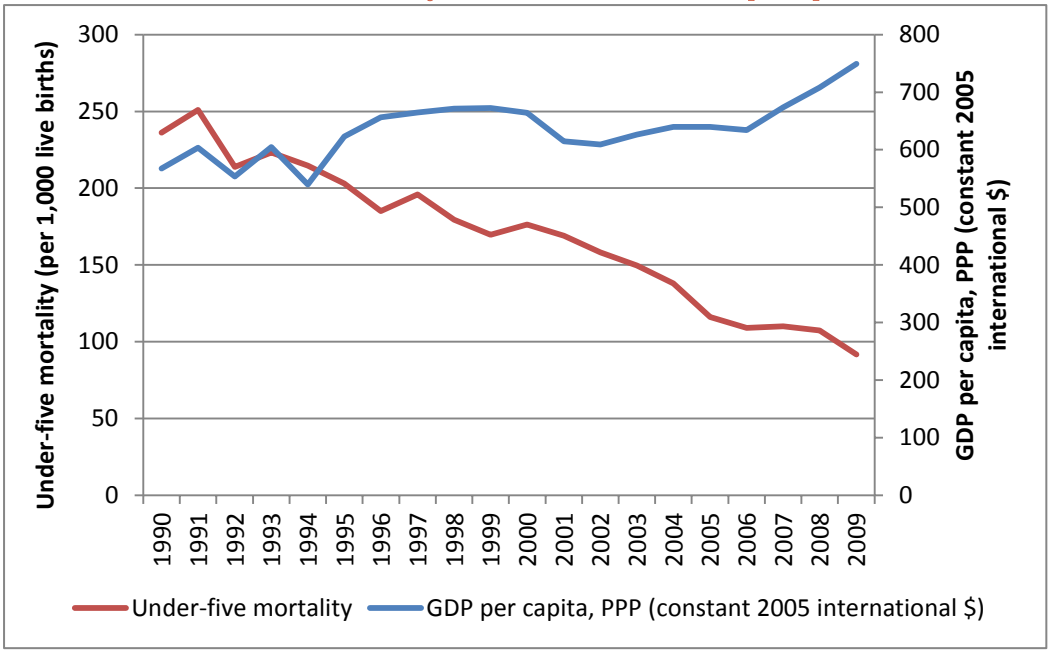
Socioeconomic Factors

A range of socioeconomic determinants at the community, household, and individual level are associated with child survival [106, 113, 114], as shown in the conceptual framework in Figure 48.

Economic poverty, either at the country or individual level, strongly correlates with poorer health outcomes [115]. GDP per capita income, a measure of population wealth in a country, is considered to be a typical macroeconomic determinant of health [114]. Relationship between GDP per capita and under-five mortality indicate that a 1% annual increase in GDP per capita is associated with a 0.4–0.6% reduction in under-five

mortality [116]. Trends in GDP per capita, purchasing power parity and ACCM in Malawi are shown in Figure 49. GDP per capita, PPP fluctuated over the period 1990–2009, remaining between 609 and 664 from 2000 to 2006, and then rising from 634 in 2006 to 749 in 2009.

Figure 49: Trends in Gross Domestic Product (GDP) per capita, PPP and annual estimates of under-five mortality, Malawi, 1990–2010 [117]



Source: GDP: World Bank. http://data.worldbank.org/country/malawi. Under-five mortality: Annual estimates derived from DHS 2000 and 2010.

Household and microeconomic factors are important determinants of child health and malaria risk [113, 118]. Socio-economic differentials at the household level are associated with access to malaria interventions [119-121], thereby increasing the vulnerability of the poorest to malaria [122]. Levels and trends in household attributes and other proxies of socio-economic status are summarized in Table 17.

Safe water and sanitary facilities contribute to improved child health and survival [119]. In 2010, 80% of households surveyed reported an improved water source (i.e., protected, borehole, piped), as compared to 65% in 2000. The proportion of households with a water source within 15 minutes of the household did not change significantly over the decade. During 2000–2010, access to improved water and sanitation generally improved although the changes were not as dramatic as those seen with malaria control interventions.

Housing construction, such as flooring and roofing material, has been used to assess household socioeconomic status, but house construction also can directly affect malaria risk [120, 121]. From 2000 to 2010, households with an improved roof (i.e., not thatch, grass, or mud) increased from 26% to 35%, while the proportion with modern floor materials (i.e., not earth, sand, or dung) was 19% in 2000 and 23% in 2010. No data are available on the proportion of houses that have sealed or screened eaves or ceiling boards – two important factors associated with malaria risk [123-126]. The proportion

of households with a telephone increased seven fold rising from 5.1% in 2000 to 39.3% in 2010.

Table 17: Household attributes and asset ownership, Malawi, 2000–2010

Survey year	2000			2010				
	%	95% CI	n	%	95% CI	n	% change	Sig.
Improved water source (protected, borehole, piped), (% households)	**65.2**	62.1-68.2	14,213	**79.7**	77.7-81.5	24,825	**22.2%**	S
Time to water source <15 min, (% households)	**33.4**	31.2-35.7	14,213	**34.7**	32.9-36.6	24,825	**3.9%**	NS
Improved roof (not thatch/grass/mud), (% households)†	**25.8**	24.5-27.3	30,553	**35.0**	32.9-37	24,825	**35.7%**	S
Modern floor material (not earth/sand/dung), (% households)	**18.8**	16.5-21.4	14,213	**23.3**	21.3-25.3	24,825	**23.9%**	NS
Electricity, (% households)	**4.8**	3.6-6.4	14,213	**8.7**	7.6-9.9	24,825	**81.3%**	S
Telephone (landline or mobile), (% households) ‡	**5.1**	3.8-6.9	13,664	**39.3**	37.6-41.1	24,825	**670.6%**	S

† signifies 2006 MICS source; ‡ signifies 2004 DHS source for the baseline estimate

Sig.= Statistical significance. Statistics with non-overlapping 95% confidence intervals are considered significantly different. NS denotes not statistically significant; S denotes statistically significant.

Climate Variability

Malaria transmission in Malawi, as in much of sub-Saharan Africa, is characterized by distinct seasonal trends, dependent on patterns of rainfall and temperature. In Malawi, the rainy season typically begins in November and continues through April. May through August is typically drier and cooler, when nighttime temperatures can fall to 10–14°C (Figure 50), whereas September through mid-November is typically hot and dry, with temperatures reaching 40–42°C in some areas (Figure 51).

Mean minimum temperatures are particularly important for malaria transmission. Within the transmission season, one of the primary limitations on transmission is low evening temperatures that slow parasite development within the vector. Higher minimum temperatures allow for greater degree-day time temperatures and more rapid parasite development within the vector. Maximum temperatures late in the dry season can in some areas reach levels where increased adult mosquito mortality occurs. In addition to annual seasonal fluctuations, inter-annual climatic drivers such as the *El Niño* Southern Oscillation can affect rainfall and temperature patterns in the region

[127] within a given year, and longer-term patterns of climate change may influence rainfall and temperature patterns over many years or decades. The mean minimum temperatures were the lowest in 2008, which corresponded to a *La Niña* year (Annex 1.16), and were the highest in 2010. It is important to consider and, where sufficient data exist, control for any inter-annual or longer term climate trends when evaluating trends in malaria morbidity and mortality.

In Malawi, average annual rainfall was slightly higher from 2006–2010 (895 mm/year) compared to 2000–2005 (888 mm/year), with the lowest annual totals occurring in 2002 (769 mm) and 2008 (784 mm) and the highest total occurring in 2004 (1067 mm) (Figure 52). Large monthly spikes occurred at the beginning of the 2005 and 2007 transmission seasons.

Figure 50: Monthly Mean Minimum Temperature, Malawi 2005–2010

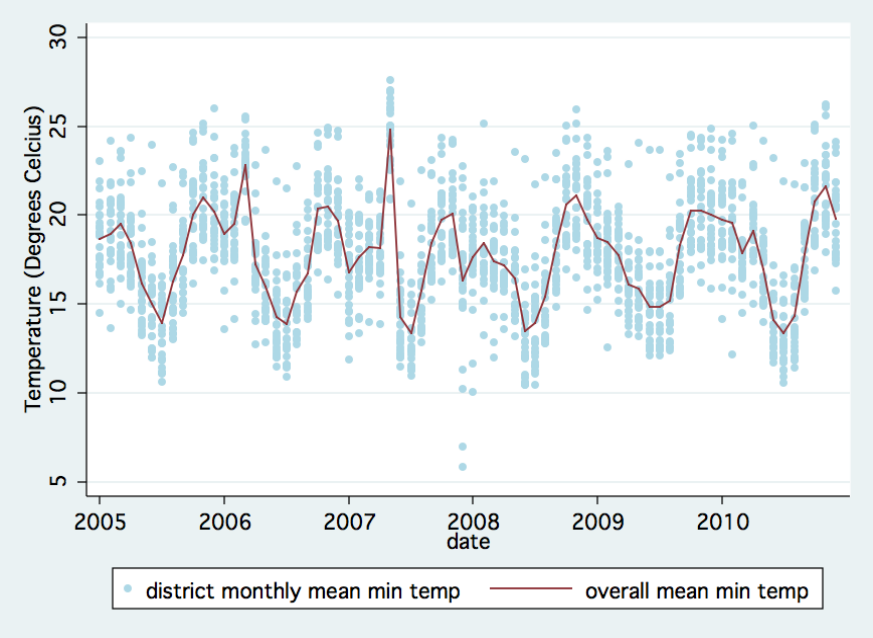


Figure 51: Monthly Mean Maximum Temperature, Malawi, 2005–2010

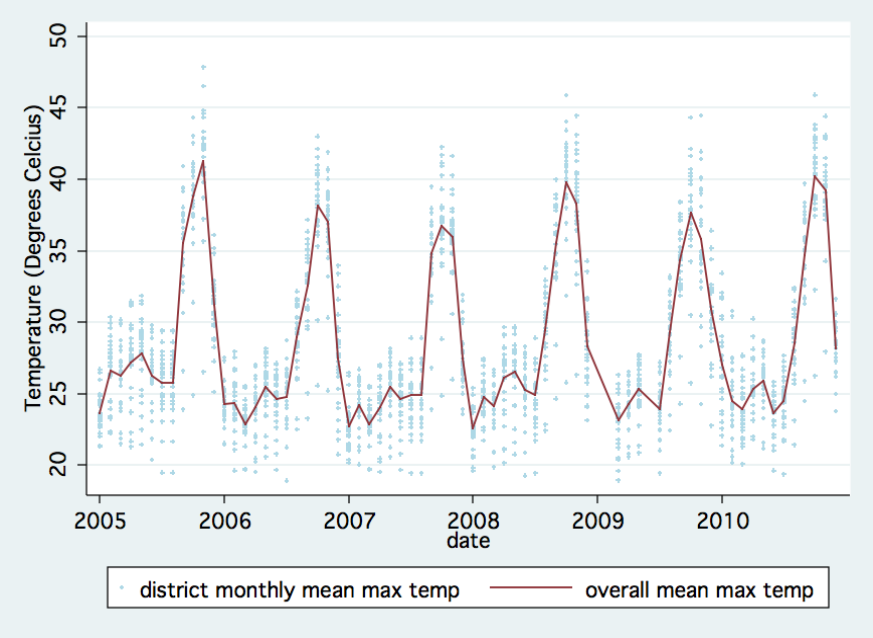
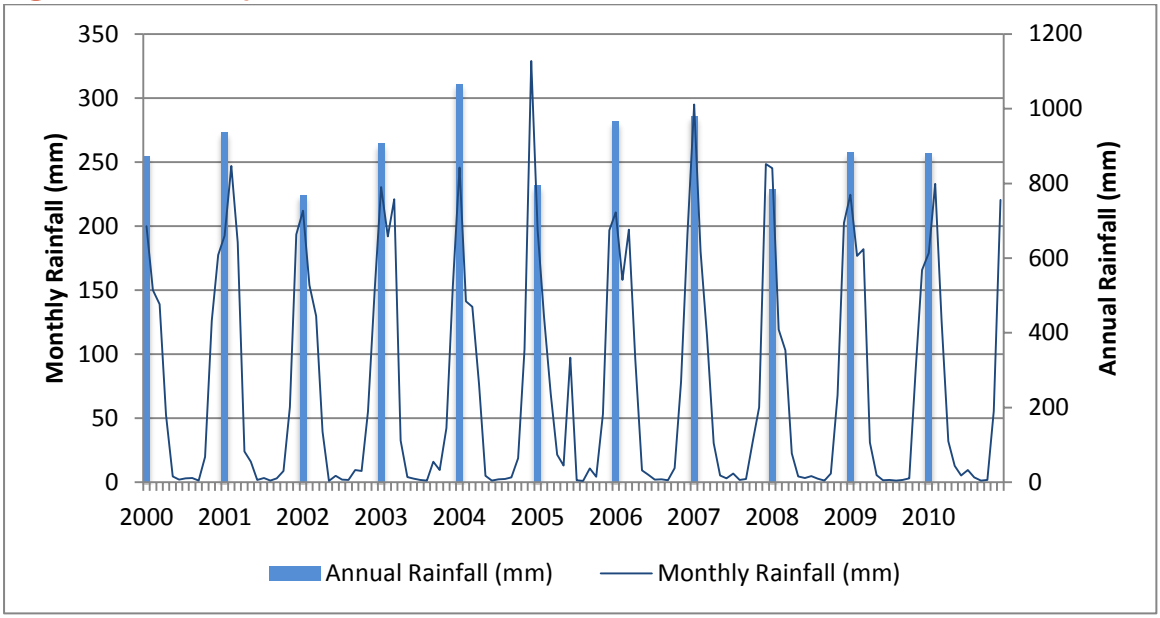


Figure 52: Monthly and annual rainfall, Malawi 2000-2010



These patterns do not suggest that any long-term climate differences existed over the period of malaria control scale-up that would have independently led to substantially different patterns of malaria morbidity and mortality at the end of the decade versus the start. Rather, inter-annual climate variability, specifically the *El Niño* Southern Oscillation, may have influenced malaria transmission within specific years. For further information on climate variability refer to Annex 1.16. In addition, these inter-annual climate factors are accounted for, wherever possible, in analyses; section Further Analyses on page 87 contains several examples.

Mother's Education and Marital Status

At an individual level, maternal education is an important determinant of maternal and child health [114, 128-133]. In Malawi, 19% of women aged 15–49 had completed primary education in 2000, as compared to 29% in 2010, and women's literacy increased from 57% in 2000 to 68% in 2010 (Table 18).

Survivorship and health outcomes of children under five years of age are better among married women [134-136]. In 2000, 72% of women were married or living with a partner, as compared to 67% in 2010.

Table 18: Women's* education, and marital status in Malawi, 2000–2010

Indicator	2000			2010				
	%	95% CI	n	%	95% CI	n	% change	Sig.
Mean years of education	**4.0**	3.8-4.2	13220	**5.4**	5.2- 5.5	23020	**34.1%**	S
Completed primary education (%)	**19.1**	17.1-21.2	13220	**29.3**	27.8-30.8	23020	**53.4%**	S
Literacy (%)	**56.5**	54.5-58.4	13220	**67.6**	66.3-69.0	23020	**19.7%**	S
Married (%)	**71.5**	70.2-72.8	13220	**67.5**	66.4-68.5	23020	**-5.7%**	S
*Women aged 15–49 years Sig.= Statistical significance. Statistics with non-overlapping 95% confidence intervals are considered significantly different. NS denotes not statistically significant and S denotes statistically significant								

Proximate Determinants

Maternal Health

Antenatal care visits are considered a key entry point for a continuum of care during and after pregnancy that offer timely opportunities for receiving health promotions, as well as preventive and therapeutic interventions aimed at improving maternal, fetal, and newborn survival and wellbeing [137]. Through antenatal visits, women benefit from various interventions, including counseling about healthy lifestyles, the provision of iron/folic acid supplements, and tetanus toxoid vaccinations to protect newborns against neonatal death in addition to malaria prevention interventions such as IPTp and distribution of ITNs. In Malawi, 52% of women attended four or more antenatal care visits (ANC4+) as recommended by WHO in 2000, compared to 43% in 2010, a decrease over the decade (Table 19).

Neonatal tetanus is often the result of infection from unhygienic cutting/cleaning of the umbilical cord at the time of delivery. To help prevent infection it is recommended for women who have never received the tetanus toxoid vaccine to receive a total of five doses: two doses given one month apart in the first pregnancy, then one dose in each subsequent pregnancy (or intervals of at least one year), to a total of five doses [138, 139]. Maternal vaccination against tetanus creates antibodies that are passed to the child *in utero* thus providing protection in the first weeks of life [140]. A conclusive reduction in neonatal tetanus mortality has been demonstrated through the scale-up in

tetanus vaccination of women of childbearing age [141]. In Malawi, the proportion of women whose most recent births (within the last two years) were protected against neonatal tetanus (two or more doses of tetanus toxoid vaccine) increased from 79% in 2000 to 87% in 2010 (Table 19).

Child birth at health facilities, usually by skilled attendants, can reduce the chances of maternal and newborn complications. In 2000, 55% of live births occurred in health facilities, compared with 73% in 2010. Births in women with high-risk fertility behavior[7] can increase the risk of early childhood mortality. From 2000 to 2010, births in any high-risk fertility category did not change (57% in both years) whereas birth in women with unavoidable fertility risk[8] declined over the decade (17% in 2000 vs. 14% in 2010).

Table 19: Maternal health in Malawi, 2000–2010

Indicators	2000			2010				
	%	95% CI	N	%	95% CI	N	% change	Sig
ANC visits 4+ (% women, most recent live birth, 0–2yrs)	**56.0**	54.0-57.8	8,057	**45.5**	44.2-46.7	13,664	**-18.8%**	S
Tetanus toxoid 2+ (% women, most recent live births, 0–2yrs)	**61.0**	59.6-62.5	8,057	**68.9**	67.8-70.0	13.664	**13.0%**	S
Delivery at a health facility (% women, live births 0–4yrs)	**55.3**	52.7-57.9	12,201	**73.2**	71.3-74.9	19,697	**32.4%**	S
Births in any high-risk fertility category (%)*	**57.3**	56.2-58.5	12,201	**56.6**	55.4-57.7	19,697	**-1.2%**	NS
Births with unavoidable fertility risk (%)**	**16.5**	15.7-17.3	12,201	**14.4**	13.7-15.1	19,697	**-12.7%**	S

Sig.= Statistical significance. Statistics with non-overlapping 95% confidence intervals are considered significantly different change. NS denotes no statistically significant change and S denotes statistically significant change
***** Births to women <18 and >34 and births <2 years apart
** First order births to women between the ages of 18 and 34

Child Health

The WHO Expanded Program on Immunization (EPI) offers vaccinations against common childhood communicable diseases and is one of the most cost-effective child survival interventions [142, 143]. Effective coverage of these vaccinations contributes substantially to reductions in ACCM. Malawi's recommended EPI schedule for children

[7] Births, in women who are less than 18 years of age or greater than 34 years of age, births less than 24 months apart, and parity greater than 3.
[8] First order births to women between the ages of 18 and 34.

includes immunizations to protect against tuberculosis (BCG), polio, diphtheria, pertussis, and tetanus (DPT), hepatitis B (HepBV), *Haemophilus influenzae (b)* (Hib) and measles. The immunization schedule calls for BCG and the first dose of polio within 14 days after birth, DPT-HepBV-Hib and polio at 6, 10 and 14 weeks after birth, and measles at or soon after 9 months of age [144]. The HepBV and Hib antigens were added to the DPT vaccine in 2002. Recommendations call for complete immunizations before one year of age and specify that they should be recorded on an immunization card. Coverage of each of these childhood vaccinations during 2000–2010, according to vaccination cards or mother's report during household surveys, is shown in Table 20. In 2000, 70% of children aged 12–23 months received all of the vaccinations recommended in the EPI schedule, as compared to 81% in 2010.

Measles vaccination, in children aged 12–23 months, was 83% in 2000 and 93% in 2010. This increase is due in part to the response to a severe measles outbreak that occurred in mid-June 2010 across Malawi and parts of Southern Africa. The outbreak led to over 100,000 reported cases of measles in 2010 as compared to 21 cases in 2009 [145, 146] and enhanced vaccination response to prevent further cases. BCG coverage in the same age group increased from 92% to 97% over the decade, coverage with three doses of DPT increased from 84% to 93% and coverage with three doses of polio from 80% to 86%, all significant increases. Although there were significant increases in immunization coverage over the decade, the baseline coverage levels in 2000 were relatively high indicating that the observed increases may not have had a very large effect on the declines in ACCM since 2000. The 2010 measles outbreak occurred too close to the endline of the evaluation period to have observable effects on mortality.

Acute respiratory infections (ARI) and diarrheal diseases, caused by a variety of viral and bacterial pathogens, are among the leading causes of illness and death in children under five years of age, both globally and in Malawi. Interventions to control these two diseases mainly include immunizations against specific pathogens, early diagnosis and treatment, improvements in nutrition and feeding practices, and safer environments, including safe drinking water. Data on the prevalence and treatment seeking practices of these two conditions were collected during household surveys in Malawi by asking mothers whether their children under five years of age had been ill with a cough accompanied by short, rapid breathing and whether they suffered from diarrhea in the two weeks preceding the survey (Table 20). In the two weeks before the surveys in 2000, 27% of children under-five were ill with symptoms of ARI (cough, and rapid breathing) as compared to 15% in 2010. Sixty-two percent of children under five years of age with symptoms of ARI sought treatment at a health facility in 2000, as compared to 76% in 2010. During the two weeks preceding the survey, 42% of children under-five had diarrhea in 2000, as compared to 35% in 2010. Sixty-two percent of children with diarrhea were taken to a health provider in 2000, as compared to 74% in 2010.

Table 20: Child health in Malawi, 2000–2010

Indicators	2000			2010				
	%	95% CI	N	%	95% CI	N	% change	Sig
BCG	**92.4**	90.7-93.8	2,238	**97.2**	96.4-97.8	3,774	**5.2%**	S
DPT3 / DPT3-HBV-Hib	**84.2**	81.8-86.4	2,236	**93.0**	91.7-94.2	3,774	**10.5%**	S
Polio3	**79.8**	77.2-82.2	2,238	**85.6**	83.9-87.2	3,774	**7.3%**	S
Measles	**83.2**	80.9-85.3	2,238	**93.0**	91.8-94.0	3,774	**11.8%**	S
All (BCG, measles, DPT3, polio3)	**70.1**	67.2-72.8	2,238	**80.9**	78.9-82.8	3,774	**15.4%**	S
Children 0–4yrs had ARI symptoms in previous 2 weeks*	**26.7**	25.3-28.1	10,559	**15.4**	14.5-16.3	18,013	**-42.3%**	S
Children 0–4yrs with ARI sought treatment	**26.7**	24.4-29.1	2,816	**65.4**	62.9-67.9	2,774	**144.9%**	S
Children 0–4yrs with diarrhea in previous 2 weeks	**17.6**	16.7-18.6	10,559	**17.5**	16.8-18.3	18,013	**-0.6%**	NS
Children 0–4yrs with diarrhea sought treatment	**28.3**	25.7-31.2	1,859	**62.4**	60.0-64.7	3,158	**120.5%**	S
Children 0–4yrs with diarrhea used ORS	**47.9**	45.0-50.7	1,859	**69.0**	66.7-71.2	3,158	**44.1%**	S

Sig.= Statistical significance. Statistics with non-overlapping 95% confidence intervals are considered significantly different. NS denotes not statistically significant and S denotes statistically significant

*Definition of ARI is based on data available in the 2000 survey: child had illness with cough in past two weeks and he/she breathed faster than usual with short, fast breaths.

Breastfeeding Practices and Undernutrition in Children and Women

In addition to serving as a source of nutrition, breastfeeding during infancy provides protection against infectious diseases, including diarrhea and ARI, the leading causes of under-five mortality [110, 147]. Early and exclusive breastfeeding is an important child survival intervention which reduces neonatal, infant, and child mortality [148]. Currently the WHO recommends early and exclusive breastfeeding for the first six months following birth [149]. In Malawi, 44% of children less than six months of age were exclusively breastfed in 2000, as compared to 71% in 2010, a significant increase (Table 21). In contrast, the proportion of children born in the five years prior to interview who initiated breastfeeding early (within one hour of birth) declined significantly, from 72% in 2000 to 67% in 2010.

Undernutrition due to chronic dietary deficiency of protein, energy, essential vitamins, and minerals (collectively referred to as micronutrients) is an important determinant of maternal and child health [150]. The continuum of maternal, fetal, and child undernutrition results in 3.5 million preventable child and maternal deaths globally, per

year [151]. There is a synergistic effect between malnutrition and infectious diseases. Pelletier *et al.* estimated that "42–57% of all child deaths (6–59 mo) are due to malnutrition's potentiating effects on infectious disease" [152].

In children under five years of age, the standardized anthropometric measures of undernutrition [153] are a) low birthweight resulting due to intrauterine growth restriction (IUGR); b) underweight, a reflection of low weight-for-age; c) stunting, a chronic restriction of growth in height indicated by a low height-for-age; and d) wasting, an acute weight loss indicated by a low weight-for-height. Undernutrition prevalence in children under five years of age was determined during a series of household surveys conducted during 2000–2010 (Table 21). In Malawi, the proportion of babies born small or very small in size (by mother's report) did not change significantly over the study period (17% in 2000 and 16% in 2010) (Table 21). In addition to mother's report of her child's size at birth, DHS collects information on children's birthweight as recorded in health cards and by mother's recall. In the 2000 survey, 11% of children born in the past five years were reported to be born with a low birthweight (<2500g) as measured by health card or by mother's recall, as compared to 12% in the 2010 survey. Underweight, stunting, and wasting prevalence in children under five, was 21%, 54%, and 6%, respectively in 2000, as compared to 13%, 47% and 4%, respectively, in 2010, all significant reductions.

Malawi experienced food shortages in 2001–2 and 2005 [154], which would be expected to have led to higher estimates of undernutrition indices and to an increase in ACCM. The food crisis in 2005 was due in part to drought conditions. A random-sampled nutrition survey conducted by the MoH, UNICEF and NGOs in December 2005 found that acute malnutrition varied by district, with four districts being categorized as precarious [154].

Vitamin A deficiency has been implicated in increased morbidity and mortality from infectious diseases such as, measles, diarrhea, and acute respiratory infections, and results in up to 600,000 under-five deaths annually world-wide [151]. Depletion of stored vitamin A occurs over a period of four to six months, when diet contains too little replacement. Periodic vitamin A supplementation (i.e., every six months) in areas with prevalent pre-existing vitamin A deficiency has been shown to replenish vitamin A stores needed for essential physiological functions and to decrease ACCM by up to 23% [155, 156]. In Malawi, vitamin A supplementation campaigns began in 2003 with biannual child health days, to complement routine supplementation after birth at health care facilities. Progress on reducing vitamin A deficiency is measured using coverage of micronutrient supplementation campaigns. In Malawi, 71% of children age 6–59 months received a vitamin A supplement in the six months prior to the survey in 2000 as compared to 87% in 2010 (Table 21).

Table 21: Breastfeeding and undernutrition in children and women in Malawi, 2000–2010

Indicator	2000			2010				
	%	95% CI	n	%	95% CI	n	% change	Sig.
Early initiation of breastfeeding	**72.1**	70.7-73.5	11,991	**67.0**	66.3-67.7	19,271	**-7.1%**	S
Exclusive breastfeeding in children <6 months of age (%)	**44.2**	40.7-47.7	1,260	**71.4**	68.0-74.6	1,656	**61.5%**	S
Small/very small size at birth (mother's estimate) (%)	**16.6**	15.7-17.6	12,201	**15.5**	14.8-16.3	19,697	**-6.6%**	NS
Low birth weight <2500g (%)	**4.9**	4.4-5.5	12,201	**12.3**	11.5-13.1	13,107	**151.0 %**	S
Under-fives stunted (%) *	**54.3**	52.6-55.9	9,343	**47.1**	45.2-49.0	4,849	**-13.3%**	S
Under-fives underweight (%) *	**20.5**	19.2-21.7	9,343	**12.8**	11.6-14.2	4,849	**-37.6%**	S
Under-fives wasted (%)*	**6.3**	5.7-7.0	9,975	**4.0**	3.3-4.8	4,849	**-36.5%**	S
Vitamin A supplementation within past 6 months (% children 6–59 months)	**70.6**	69.0-72.1	9,285	**85.5**	84.6-86.4	16,315	**21.1%**	S

* Definitions and methods per WHO reference population.
Sig.= Statistical significance. Statistics with non-overlapping 95% confidence intervals are considered significantly different change. NS denotes no statistically significant change and S denotes statistically significant change

HIV/AIDS among Children and Women

The advent of the HIV/AIDS epidemic in the 1980s, threatened child survival gains made globally since the 1960s [157]. Child survival stagnated and even reversed in many countries in sub-Saharan Africa [158] and HIV/AIDS was found to be an increasingly important cause of under-five mortality in sub-Saharan Africa. [159]

In Malawi, the first cases of HIV infection were reported in 1985 and the epidemic rapidly spread. Population trends in prevalence of HIV infection in Malawi were monitored through the 2004 and 2010 DHS. Among women aged 15–49 years HIV prevalence did not change between 2004 and 2010 with an estimated 13% infected.

Data from the Ministry of Health HIV and syphilis sero-survey and national HIV prevalence and AIDS estimates report for 2007 show large regional disparities in HIV

prevalence with 20.5% of men and women age 15–49 years in the Southern Region infected compared to 10.2% in the Northern Region and 10.7% in the Central Region [160]. Despite these regional disparities in prevalence, no differential change in HIV prevalence by region over time was observed. In addition, regional ACCM patterns did not correlate with regional HIV prevalence patterns. This suggests that HIV prevalence over the study period is unlikely to have affected trends in ACCM.

Population-based estimates of HIV infection in children under five are not available; however, analyses based on national models of HIV and AIDS show that the HIV-attributable under-five mortality per 1,000 live births (corrected for other competing causes of mortality) was around 16% in 2000 as compared to 13% in 2010 [98, 161]. Data from the UNAIDS Malawi Country Fact Sheet show the number of HIV infected pregnant women receiving anti-retrovirals (ARVs). The first year for which these data are available is 2004 and coverage was very low. A rapid increase in HIV positive pregnant women receiving ARVs occurred, from 2,179 to 33,200 between 2004 and 2009 [162]. According to UNAIDS 2012, coverage of most effective ARVs for PMTCT during pregnancy and delivery was 24% in 2009 and 53% in 2011 [98]. Data are also reported on new infections in children. New child infections rose from approximately 9,000 cases in 1990 to approximately 21,000 cases in 1999 and then subsequently declined from 20,000 cases in 2000 to 19,000 cases in 2010 [162]. It follows that PMTCT is unlikely to be responsible for the decline in ACCM from 2000 to 2004, although it could have contributed to subsequent declines between 2004 and 2010.

Summary of Contextual Factors

Malawi has experienced many positive developments during the evaluation period, many of which would be expected to lead to improved child survival. A summary of these changes and the expected relationship with under-five mortality in Malawi is presented in Table 22.

Table 22: Summary of evidence of changes in factors that could be associated with under-five mortality in Malawi, 2000–2010

	Evidence supporting lower mortality	No evidence suggesting change in mortality	Evidence supporting higher mortality
Malaria control interventions	• Household ownership of ITNs • ITN use by children under-five • ITN use by pregnant women • IRS (in selected areas) • IPTp • Care seeking for fever	• Proportion of children with fever who receive recommended treatment (of those receiving any treatment) • Use of ACTs	

Other contextual determinants	Fundamental determinants • GDP per capita growth • Maternal education • Housing conditions Proximate determinants • Nutritional status • Exclusive breastfeeding • Vitamin A supplementation • Hib vaccination • HepB vaccination • BCG, Polio, DPT, measles vaccinations • ARI prevalence • PMTCT, ART • Birth at health facility • Neonates protected from Tetanus • Diarrhea treatment (oral rehydration solution/extra fluids) • ARI care seeking	Fundamental determinants • Rainfall Proximate determinants • Diarrhea prevalence • HIV prevalence (female15-49 years) • Proportion of births that are high risk	Fundamental determinants • Women married • Food shortages in 2001 and 2005 Proximate determinants • Antenatal Care attendances 4+ • Early initiation of breastfeeding • Low birth weight

In addition to the rapid improvements in malaria control that are hypothesized to reduce child mortality, other favorable changes have occurred in fundamental and proximal determinants. GDP has increased and stunting, wasting and underweight prevalence have declined over the evaluation period. Care seeking for childhood illness increased dramatically over the time period as did treatment of diarrhea with ORS and exclusive breastfeeding of children less than six months of age. Although immunization coverage increased, fairly high coverage of most immunizations already existed at baseline. Over the evaluation period, maternal health indicators such as tetanus immunizations, facility births and PMTCT improved as well. All of these improvements are likely to positively influence child survival, although the relative importance of each factor is difficult to determine. Several contextual factors changed in a direction that would be expected to favor higher mortality, or congruously, favor slower declines in mortality. These include fewer mothers attending at least four ANC visits during her last pregnancy, decreasing proportions of married women and several significant food shortages due to unfavorable crop and/or market conditions. Overall, Malawi saw modest improvements in the coverage of many health interventions as well as socio-economic improvements between 2000 and 2010. Thus, improved malaria control was operating in this general improving environment. The next section attempts to estimate the effect of malaria control interventions on child survival while accounting for these important contextual factors.

FURTHER ANALYSES

Multivariable Analyses & Lives Saved Tool

National and sub-national datasets show significant scaling up of malaria control interventions, clear declines in malaria-related morbidity and a reduction in all-cause under-five mortality over the study period. However, factors other than malaria control are likely to have contributed to changes in these outcomes. The purpose of this section is to present results of analyses that explore the relationship between malaria control interventions and mortality and/or malaria morbidity while adjusting for other factors that could potentially confound the association. Data availability for the respective analyses is summarized in Table 23. Further detail on the datasets referred to here can be found in Annexes 1 and 4.

To address the question of whether or not increases in malaria control interventions have affected severe anemia in Malawi controlling for household, child and climate variables, sub-national anemia and parasitemia survey datasets were used in conjunction with climate data from the United States Geological Survey (USGS) Famine Early Warning System (FEWS) and satellite data from the NASA Land Processes Distributed Active Archive Center Data Pool (LPDAAC) in multivariable logistic regression models. The association between ITN ownership and odds of severe anemia was examined, as were trends in severe anemia over time.

To address the question of whether or not increases in malaria control interventions have affected malaria infection in Malawi controlling for household, child and climate variables, the same data sources and models were used with a focus on the relationship between ITN ownership and odds of parasitemia. Trends in parasitemia over time were also examined in these multivariable models.

To assess the association between household ITN ownership and mortality in children under five years of age, a Cox proportional hazards model was developed with 2010 DHS data. Matching was used and additional covariates were included in the model, such as malaria transmission levels, rainfall and temperature.

The association between household ITN ownership and all-cause childhood mortality was additionally examined in a district-level model using 2010 DHS data on child deaths, ITN ownership, and other covariates. Models also included ITN distribution data and FEWS rainfall data. Data were aggregated by district and by year and analyzed using multivariable Poisson models.

Table 23: Multivariable analysis summary

Question 1: Has increasing ITN ownership led to reductions in severe anemia?				
Dataset	***Dates***	***Location***	***Remarks***	***Data availability***
Anemia & Parasitemia surveys	2005–2009	8 districts		Hemoglobin, severe anemia, ITN ownership
Question 2: Has increasing ITN ownership led to reductions in malaria infection and/or clinical malaria?				
Dataset	***Dates***	***Location***	***Remarks***	***Data availability***
Anemia & Parasitemia surveys	2005–2009	8 districts		Parasitemia (via microscopy), ITN ownership
Question 3: Is ITN ownership protective against mortality in children under five years of age?				
Dataset	***Dates***	***Location***	***Remarks***	***Data availability***
2010 DHS data with climate, season and malaria risk data	2008–2010	National	See annexes describing 2010 DHS	Under-five deaths, SES variables, child and maternal health variables, rainfall, malaria risk, season, ITN ownership and ITN duration of ownership
Question 4: Has increasing ITN ownership led to declines in mortality in children under five years of age?				
Dataset	***Dates***	***Location***	***Remarks***	***Data availability***
District-level analysis of 2010 DHS with climate and malaria risk data	2006–2010	National	See annexes describing 2010 DHS	Under-five deaths, SES, child and maternal health variables, rainfall, malaria risk, ITN ownership and population-adjusted ITN distribution by district and year

Q1: Has increasing ITN ownership led to decreases in severe anemia?

Data sources

- Anemia and Parasitemia Surveys, 2005–2009
- NASA Land Processes Distributed Active Archive Center Data Pool from the USGS/Earth Resources Observation and Science Center, MODIS satellite (temperature data) [163]
- USGS FEWS NET data portal (rainfall data) [164]

Methodology

Survey methodology for these studies is presented on page 44 with additional details in Annex 1.10. Basic trends in severe anemia (Hb <8g/dL) were presented in Figure 30. In

this section, results of a pooled, multivariable, random-effects logistic regression model predicting severe anemia prevalence is presented. This model included a random intercept for each enumeration area (EA). The model assessed the odds of severe anemia for each survey year after controlling for child, household, region, and climatic factors. Climatic differences preceding each survey were controlled for by including anomalies from the five-year means for February and March rainfall and minimum temperature. Districts were collapsed into regional categories (Northern, Central, and Southern). Model results are presented in Table 24.

Results

Lower household wealth status (quintile), younger age (in months), not having an ITN in the home, and region (districts in the Central and Southern Region) were all significant predictors of severe anemia (Hb <8 g/dL) (Table 24). Children in households in the highest wealth quintile had 51% lower odds of severe anemia than those in the lowest wealth quintile. The odds of severe anemia are highest in the youngest children, as each month of age, up to 30 months, was associated with a 3% reduction in odds of severe anemia. In this model, high mean minimum February/March temperature anomalies were predictive of severe anemia. After controlling for these variables, the odds of severe anemia were significantly lower in 2006 compared to 2005 (Odds Ratio= 0.46, 95% CI =0.26–0.84) and marginally lower in 2009 compared to 2005 (Odds Ratio= 0.65, 95% CI =0.41–1.04). Odds of severe anemia were higher in children from the Central and Southern regions as compared to those from the Northern region. After adjusting for wealth, age, rainfall, temperature, region and year, having at least one ITN in the household reduced the odds of severe anemia by 23%.

Table 24: Multivariable random-effects logistic regression model of determinants of severe anemia (Hb<8g/dL) in children 6–30 months of age, Malawi, 2005–2009

Parameter	Odds Ratio	95% CI
Wealth		
Lowest (ref)	1	
Second	0.88	0.76-1.01
Middle	0.81*	0.70-0.93
Fourth	0.78*	0.67-0.92
Highest	0.49*	0.40-0.59
Age (months)	0.97*	0.97-0.98
Any HH ITN	0.77*	0.70-0.86
Mean rainfall February/March anomaly	1.00	0.998-1.001
Mean minimum February/March temperature anomaly	1.50*	1.27-1.76
Year		
2005 (ref)	1	

2006	0.46*	0.26-0.84
2007	1.12	0.73-1.72
2008	1.30	0.88-1.92
2009	0.65	0.41-1.04
Region		
Northern(ref)	1	
Central	2.55*	1.96-3.32
Southern	2.40*	1.92-2.99

*Significant at p<0.05

Conclusion

In this analysis of sub-national data, household ownership of ITNs was found to be protective for severe anemia in children 6–30 months of age controlling for other factors known to affect anemia such as climate, geographic location, household wealth and child's age. Additionally, after controlling for climate and other factors, there was a significant decrease in severe anemia prevalence over the scale-up period, but after controlling for climate and other factors, the decrease between 2005 and 2009 was only marginally significant. Skarbinski *et al*. demonstrated that ITN use the previous night was protective against anemia in children under five years of age (OR = 0.79; 95% CI = 0.62–0.99), after adjusting for district, socio-economic status and IRS, by analyzing the 2009 A&P survey [165].

Q2: Has increasing ITN ownership led to reductions in malaria infection and/or clinical malaria?

Sub-national Anemia and Parasitemia Surveys Analysis

Data sources

- Anemia and Parasitemia Surveys, 2005–2009
- NASA Land Processes Distributed Active Archive Center Data Pool from the USGS/Earth Resources Observation and Science Center, MODIS satellite (temperature data)[163]
- USGS FEWS NET data portal (rainfall data)[164]

Methodology

Survey methodology for these studies is presented on page 44 with additional details in Annex 1.10. Basic trends in parasitemia were presented in Figure 23. In this section, results of a pooled, multivariable, random-effects logistic regression model predicting malaria parasitemia is presented. This model included a random intercept for each enumeration area (EA). The model assesses the odds of parasitemia for each survey year after controlling for child, household, region, and climatic factors. Climatic differences preceding each survey were controlled for by including anomalies from the five-year means for February and March rainfall and minimum temperature. Districts were collapsed into regional categories (Northern, Central, and Southern). Model results are presented in Table 25.

Results

Lower household wealth status (quintile), older age (in months), not having an ITN in the home, year of survey, region (Northern, Central, and Southern) and survey year by region interaction were all significant predictors of parasite prevalence (Table 25). Children in the households in the highest wealth quintile had 54% lower odds of infection than children from households in the lowest wealth quintile. Each additional month of age of the child from 6–30 months was associated with increased odds of parasitemia (OR=1.03; 95% CI=1.02–1.04). Mean rainfall and mean minimum temperature anomalies did not have a significant effect on the odds of parasitemia. After adjusting for household wealth quintile, month of age, rainfall, temperature, year and region, having at least one ITN in the household was associated with decreased the odds of parasitemia (OR=0.81; 95% CI = 0.72–0.92).

Table 25: Determinants of malaria parasitemia in children 6–30 months of age from sub-national A&P surveys, Malawi, 2005–2009

Parameter	**OR**	**95% CI**
Household Wealth Quintile		
Lowest (ref)	1	
Second	0.89	0.76-1.04
Middle	0.91	0.78-1.07
Fourth	0.77*	0.64-0.92
Highest	0.46*	0.37-0.58
Age (months)	1.03*	1.02-1.04
Any ITNs in household	0.81*	0.72-0.92
Mean rainfall anomaly, February/March	1.00	1.00-1.01
Mean minimum temperature anomaly, February/March	1.29	0.96-1.72
Year		
2005 (ref)	1	
2007	1.95	0.97-3.90
2008	0.68	0.26-1.80
2009	0.34*	0.12-0.96
Region		
Northern Region (ref)	1	
Central Region	11.45*	4.1-32.03
Southern Region	8.60*	2.98-24.87
Year/Region Interaction		

*2007*Central*	0.88	0.32-2.41
*2007*Southern*	0.09*	0.02-0.37
*2008*Central*	0.82	0.25-2.64
*2008*Southern*	0.55	0.16-1.92
*2009*Central*	1.77	0.56-5.56
*2009*Southern*	2.43	0.85-6.96

*Significant at $p<0.05$

Conclusion

In this analysis of sub-national data, household ownership of ITNs was found to be protective against parasitemia in children 6–30 months of age controlling for other factors known to affect parasitemia such as climate, geographic location, household wealth and child's age. Additionally, after controlling for climate and other factors, there was a significant decrease in parasite prevalence between 2005 and 2009 in the districts sampled in the Northern Region, but not in the Central and Southern Regions. Parasitemia was significantly lower in the Southern Region in 2007 as compared to 2005. Analyzing parasitemia in children under five years of age from the 2009 A&P survey, Skarbinski *et al*. demonstrated that ITN use the previous night was protective against parasitemia (OR = 0.79; 95% CI = 0.64–0.98), after adjusting for district, socio-economic status and IRS [165].

Q3: Is ITN ownership protective against mortality in children under five years of age?

Data sources

- 2010 DHS birth history data, ITN ownership and contextual factors
- District-level mean *P. falciparum* prevalence rate in children 2–10 years of age (*Pf*PR_{2-10}) from MAP 2010 [166]
- Mean annual district-level rainfall and anomaly from five-year average from USGS FEWS NET data portal [164]

Methodology

Although DHS surveys are cross-sectional, data on women's birth histories can be used to create a longitudinal record of children's lives. Most other data collected in the DHS are only relevant for the time period of data collection or for a short period before (for example, history of fever in children under five years of age for the two weeks preceding interview). Although birth and child death data are available in a longitudinal format, data such as ITN ownership and ITN use only exist in a cross-sectional format; thus, the creation of individual-level mortality models requires some assumptions and the aggregation of a subset of variables to the cluster level. In order to identify an individual child's exposure to protection with an ITN, data on the duration of ownership of ITNs and the time of retreatment of nets (if any) were used to construct a time-varying variable on ITN ownership for up to three years before the survey. Using this method to model exposure to ITNs will underestimate ITN ownership as any nets that were discarded before the time of interview would not be counted. Therefore, any protective effects of ITNs resulting from this model will likely be an underestimate of the true effects. Other variables were aggregated at the cluster-level as data were only

collected for children who were living at the time of interview and thus would be missing for all deceased children. Cluster-level variables created include prevalence of diarrhea, DPT3 coverage, *Pf*PR_{2-10} and skilled birth attendance rate. Before running models, exact matching on wealth (above/below median PCA score), urban/rural, *Pf*PR_{2-10} (≥40% vs <40% from MAP 2010), DPT3 coverage at PSU level (above/below median), distance to the nearest health facility (>5km vs ≤5km), birth order (<3 vs ≥3) and mother's education (secondary+, primary, none) was performed to reduce selection bias.

The relationship between household ITN ownership and child mortality (1–59 months) over the 36 months preceding the survey was then assessed with Cox proportional hazards models with analysis time measured in months and matched strata included as a shared frailty. Additional covariates controlled for in the Cox model included household wealth quintile, child's age category, mother's age category, parity, PSU-level diarrhea prevalence (two weeks preceding survey), DPT3 coverage at PSU level (continuous), *Pf*PR_{2-10} at PSU level (continuous), season (high transmission season), and rainfall and minimum temperature lagged two months. Household improved water source and the PSU-level skilled birth attendance rate were non-significant and removed from analyses.

Results

After controlling for confounding, household ownership of at least one ITN was associated with a 25% reduction in mortality risk (HR=0.75, 95% CI 0.62 – 0.90) (Table 26). Children from households in the highest wealth quintile were less likely to die than were those from households in the lowest wealth quintile (HR=0.67, 95% CI=0.50–0.90). Children over one year experience lower mortality risk than children 1–5 months. No other variables had a significant effect on mortality in this model.

Table 26: Results of matched multivariable Cox regression on 1-59 month mortality, Malawi, 2010 DHS

Covariate	Hazard Ratio	95% Confidence Interval	p-value
Wealth			
Lowest (ref)	1		
Fourth	1.07	(0.88 – 1.31)	0.503
Middle	1.10	(0.89 – 1.35)	0.377
Second	1.12	(0.90 – 1.39)	0.311
Highest	0.68*	(0.51 – 0.90)	0.007
Child's age			
1-5 months (ref)	1		
6-11 months	0.96	(0.79 – 1.17)	0.664
12-23 months	0.42*	(0.34 – 0.52)	<0.001
24-35 months	0.29*	(0.23 – 0.37)	<0.001
36-47 months	0.17*	(0.13 – 0.22)	<0.001
48-59 months	0.10*	(0.07 – 0.14)	<0.001
Mother's age			
15-19 years (ref)	1		
20-24 years	1.01	(0.71 – 1.44)	0.970
25-29 years	0.85	(0.58 – 1.24)	0.393
30-34 years	1.18	(0.79 – 1.78)	0.420

35-39 years	1.16	(0.73 – 1.85)	0.528
40-44 years	1.12	(0.65 – 1.95)	0.679
45-49 years	1.03	(0.52 – 2.03)	0.931
Parity	1.00	(0.95 – 1.06)	0.894
Diarrhea prevalence	1.65	(0.80 – 3.38)	0.173
DPT3 coverage (continuous)	0.58	(0.26 – 1.30)	0.184
***Pf*PR$_{2-10}$ (continuous)**	1.00	(1.00 – 1.00)	0.467
Season (Dec-May)	0.90	(0.70 – 1.15)	0.395
Rainfall (lagged 2 months)	1.00	(1.00 – 1.00)	0.663
Min. temp. (lagged two months)	0.99	(0.97 – 1.02)	0.502
HH ≥ 1 ITN	0.75*	(0.62 – 0.90)	0.002

*Significant at p<0.05

Conclusion

Children between the ages of 1 and 59 months who live in households with at least one ITN are less likely to die than are children in households without ITNs, controlling for household wealth, child's age, mother's age, parity, cluster-level prevalence of diarrhea in children under five years of age, cluster-level coverage of DPT3 immunization, cluster-level *Pf*PR$_{2-10}$ and season. Results suggest that at the individual level, for the three year period before the 2010 DHS (2007–2010) owning at least one ITN in a household reduces a child's risk of death.

Q4: Has increasing ITN ownership led to declines in mortality in children under five years of age?

Data sources

- 2010 DHS birth history data, ITN ownership and contextual factors
- 2006 MICS ITN ownership and contextual factors data
- District-level ITN distribution data from PSI
- Mid-year district-level population estimates from 1998 and 2008 census data [19]
- District-level mean *Plasmodium falciparum* prevalence rate in children 2–10 years of age (*Pf*PR$_{2-10}$) from MAP 2007 [95]
- Mean annual district-level rainfall and anomaly from five-year average from USGS FEWS NET data portal [164]

Methodology

To address the limitations of cross-sectional data previously mentioned, district-level Poisson models were employed. These models use aggregated estimates of ITN ownership and other covariates including *Pf*PR$_{2-10}$ and rainfall anomaly data at the district-year-level and look for associations with counts of child deaths per district per year. In order to construct annual estimates of variables such as ITN ownership and other covariates that were collected cross-sectionally only during survey years, data from both the 2006 MICS and the 2010 DHS were used. Weighted averages of district-

level means for these variables were constructed for interim years between surveys (see Annex 1.15 for additional details).

Aside from this constructed ITN ownership variable, a second ITN ownership variable was also examined. Data on annual district-level ITN distribution were used and a decay factor was applied as per previously published methodology [167]. This decay factor accounts for some loss of ITNs per year and includes ITNs distributed in previous years to estimate ITN ownership (Figure 53). This variable was also adjusted for mid-year district-level population available through census data. Finally the variable was categorized into four categories of ITNs distributed/mid-year population (<0.25, ≥0.25 & <0.5, ≥0.5 & <1.0, ≥1.0 & <1.5). Backward elimination was used to select final models. For additional models see Annex 1.15.

Figure 53: Three-year cumulative ITN distributions by district, with 8%–20%–50% decay factor [167], as a percent of 1:2 district population size

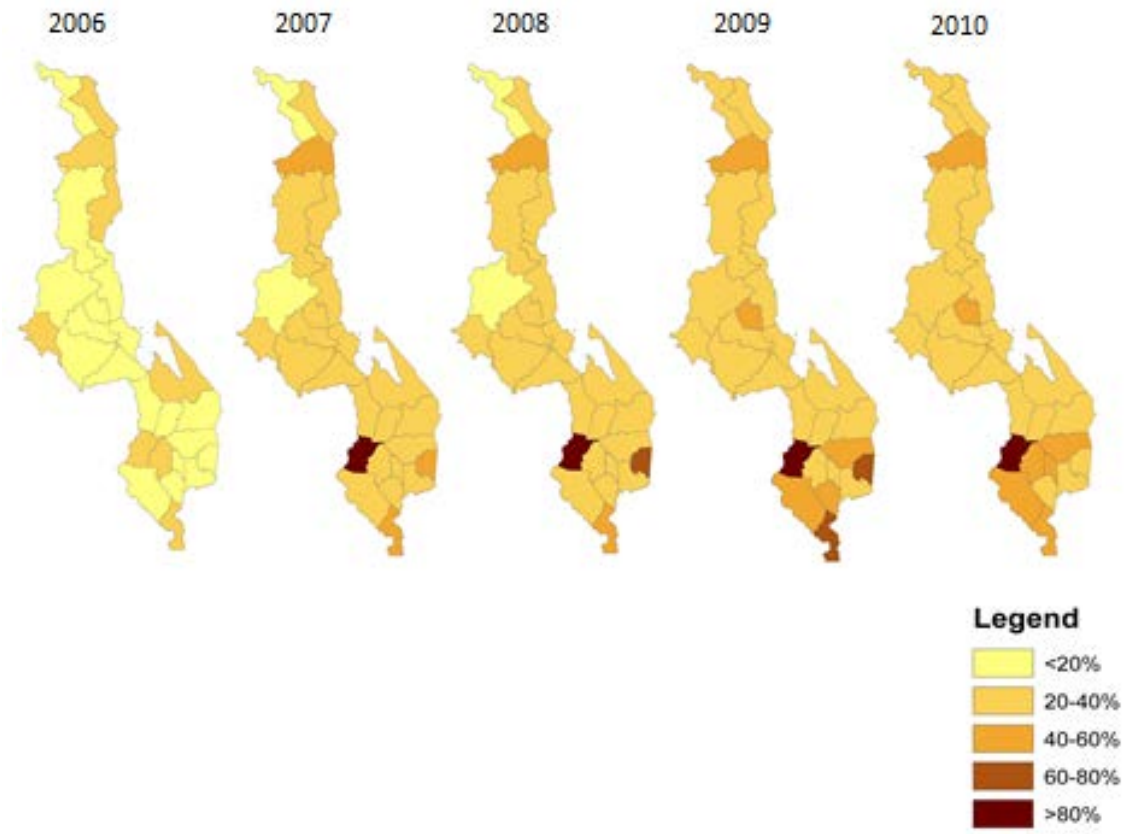


Figure 53 represents ITN distributions over the three preceding years in relation to the RBM target of one ITN to two household members. A decay factor is included, such that 92% of ITNs distributed in the previous year are presumed to be available in the year depicted, as are 80% of ITNs distributed two years prior, and 50% of ITNs distributed three years prior. In 2006, less than 20% of the population in most districts was covered at a ratio of 1 ITN per 2 persons. By 2010, all districts had at least 20–40% of the population covered with higher coverage (>40%) in many districts in the Southern Region.

Results

In multivariable models, after controlling for district, calendar year, access to improved water, mother's educational level, mother's tetanus immunization status, and prevalence of diarrhea in children, ITN ownership was significantly associated with child survival (IRR=0.55, 95%CI=0.31-0.99) (Table 27).

Table 27: IRR of under-five mortality in multivariable Poisson model using ITN ownership from DHS data*

	IRR	[95% Conf.	Interval]	P>z
ITN ownership	**0.55**	**0.31**	**0.99**	**0.048**
Year				
2004 (ref)	1			
2005	0.75	0.66	0.86	<0.0005
2006	0.80	0.71	0.91	0.001
2007	0.66	0.58	0.75	<0.0005
2008	0.60	0.49	0.73	<0.0005
2009	0.75	0.62	0.91	0.004
2010	0.54	0.37	0.79	0.001
Access to improved water	3.02	1.66	5.48	<0.0005
Mother's educational level	0.69	0.50	0.94	0.021
Mother's tetanus immunization	2.14	1.34	3.42	0.002
Diarrhea prevalence	5.89	2.14	16.17	0.001

*Model is adjusted for district and calendar year

In multivariable models controlling for district, calendar year, proportion of households with access to improved water, education of mother's, diarrhea prevalence, and vitamin A supplements, category of ITN ratio (ITNs distributed/mid-year population) was significantly associated with mortality (IRR = 0.87, 95% CI = 0.77–0.98) (Table 28). Thus, for each increase in level of ITN/population, the risk of dying decreased by 13% in children under five years of age. Risk of mortality also decreased over time (IRR=0.82, 95% CI = 0.71–0.93 for 2008 compared to 2004).

Table 28: IRR of under-five mortality in multivariable Poisson models of ITN ownership using population-adjusted ITN distribution data*

	IRR	[95% Conf.	Interval]	P>z
ITN ratio category	**0.87**	**0.77**	**0.98**	**0.018**
Year				
2004 (ref)	1			
2005	1.04	0.84	1.28	0.725
2006	1.12	0.91	1.38	0.295
2007	0.92	0.75	1.14	0.463
2008	0.82	0.71	0.93	0.003
2009†	1.00			
Access to improved water	4.13	2.05	8.30	<0.0005
Mother's educational level	0.58	0.39	0.85	0.005
Diarrhea prevalence	3.94	1.27	12.29	0.018
Vitamin A in past 6 months	0.43	0.20	0.89	0.024

*Model is adjusted for district and calendar year
†Omitted due to collinearity

Conclusion

District-year Poisson models of deaths in children under five years of age reveal significant relationships between variables measuring levels of ITN ownership and under-five mortality, controlling for other variables associated with child survival. In addition, mortality in children under five years of age decreased over time in these models. Thus, findings support the patterns of decreasing mortality trends from nationally-representative survey data discussed in the mortality section.

Other variables found to be significantly associated with under-five mortality in multivariable models included proportion of households with access to improved water sources, mother's educational level, prevalence of diarrhea, vitamin A supplementation in the past six months in children under five years of age, and proportion of women with recent births who had two tetanus immunizations. Surprisingly, several variables that would be expected to be protective against under-five mortality were found to be associated with higher mortality rates including access to improved water and mother's tetanus immunization. While significant, the confidence intervals around the estimated effect of diarrhea prevalence are very large.

In summary, ITN ownership was found to be significantly associated with decreased risk of dying in children under five years of age at the district level, adjusting for other predictors of child survival. This association was robust across several different strategies for modeling ITN ownership (see also Annex 1.15). This is strong evidence in support of the impact of malaria control intervention scale-up on reductions in ACCM in Malawi. Nonetheless, results should be interpreted with caution as the models are not

individual-level models but ecologic models which may be subject to the ecological fallacy (relationships seen at the aggregate level may not hold at the individual level).

Further Analyses Conclusion

Multivariable analyses of the effects of scale-up of malaria control interventions on parasitemia prevalence, anemia prevalence and suspected malaria cases do not yield simple results. Results of multivariable analyses support the hypothesis that increases in ITN ownership are associated with decreased risk of parasitemia and severe anemia, controlling for climate and other relevant factors. In anemia and parasitemia surveys, the odds of parasitemia were 19% lower in children living in households owning at least one ITN compared to those in households without ITNs. Similarly, ITN ownership was protective against severe anemia; the odds of severe anemia were 23% lower in children living in households owning at least one ITN compared to those in households without ITNs.

Multivariable analyses also support the hypothesis that ITN ownership is associated with decreased risk of mortality in children under five years of age, controlling for other predictors of child mortality. Cox proportional hazard models revealed that children living in households with at least one ITN had 0.75 times the risk of dying as children in households without an ITN, controlling for other variables. Similarly, the scale-up in household ITN ownership over time was shown to be associated with decreased odds of dying in children under five in multivariable Poisson models. Districts with greater proportions of children living in households owning ITNs had significantly fewer deaths among children under five years of age (IRR=0.55).

Despite clear temporal decreases in mortality evident in the multivariable analyses, temporal trends in malaria-associated morbidity and parasitemia were difficult to interpret. The anemia and parasitemia survey data show some evidence of decreasing parasitemia in 2009 compared to 2005, controlling for other potential confounders, including climate, but these trends varied by region. Temporal declines in severe anemia prevalence between 2005 and 2009 were marginally significant, although there was clear regional variation.

Lives Saved Tool

Given the evidence shown in this report of a decline in all-cause mortality in children under five years of age, a decline in anemia and some sub-national declines in parasitemia from 2000 to 2010, we estimated the potential impact malaria control interventions could have had on malaria mortality through modeling. The Lives Saved Tool (LiST) was used to estimate the deaths prevented due to the scale-up of malaria control interventions in the context of a complex set of maternal and child health interventions, but is not used as evidence for impact. For information on the LiST model, intervention coverage estimates, the cause-specific breakdown of child mortality and the protective efficacy of malaria control interventions used in this model see Annex 2. The LiST model is not used here to provide evidence of a malaria-specific

mortality decline; instead it is a modeling exercise to examine what the potential impact of malaria control intervention scale-up could look like.

One of the primary malaria prevention measures in Malawi has been ITNs. Figure 54 shows the deaths averted due to the scale-up of ITNs in Malawi from 2000–2010. The midline estimate is shown with uncertainty bounds (see Annex 2.1 for a description of uncertainty calculations). It is estimated that over the 10 years of ITN scale-up, approximately 21,400 (15,700–27,700) deaths were prevented in children 1–59 months, compared to what would have happened if no vector control scale-up had occurred since 2000 coverage levels (Table 29). The number of deaths prevented per year steadily increased throughout this period, with a slight acceleration after 2004. These estimates fall within the range of those obtained by Eisele *et al*. of 18,800 (range 11,500–29,300) child deaths prevented by vector control scale-up between 2001–2010 [7, 8].

Figure 54: Deaths prevented by ITN scale-up, children 1–59 months, 2000–2010

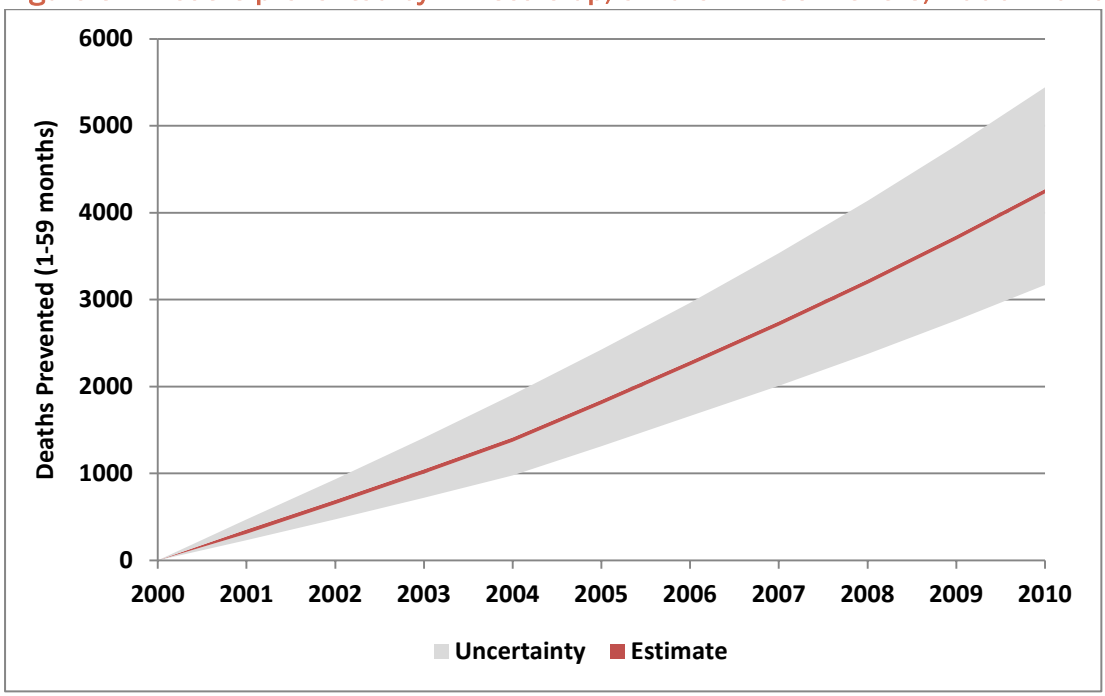


Table 29: Annual deaths prevented* by ITN scale-up, children 1–59 months, 2000–2010

	Malaria Deaths 2000	Estimated deaths prevented (1–59 months)											
		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	Total
Lower	12,764	0	232	472	720	977	1,313	1,661	2,008	2,374	2,761	3,168	15,686
Midline		0	330	671	1,023	1,389	1,821	2,268	2,724	3,205	3,713	4,247	21,391
Upper		0	446	908	1,385	1,881	2,400	2,938	3,509	4,111	4,747	5,417	27,742

*Deaths prevented are relative to 2000 coverage levels.

Under-five child mortality (specifically neonatal and post-neonatal mortality) is also affected by interventions to control malaria in pregnancy, including ITN use by pregnant women and IPTp during pregnancy. The LiST model estimated 198 (range: 111–315) deaths in children 0–59 months were averted due to the scale-up of IPTp use by pregnant women in Malawi from 2000 to 2010 (see Annex 2.4). Combined, ITN household ownership and IPTp use by pregnant women prevented 21,600 (range: 15,800–28,100) deaths in children 0–59 months in Malawi from 2000 to 2010.

The LiST analysis presented here models the potential direct effect of malaria interventions on reducing malaria-specific mortality. This estimate is likely an underestimate of the effect of malaria interventions given the conservative nature of the LiST model (see Annex 2.1 for more details). Calculations using the LiST model conservatively estimate that the scale-up of malaria control interventions during 2000–2010 prevented at least 21,600 deaths among children under five years of age in Malawi and were responsible for a 27% reduction in malaria-specific mortality in 2010 compared to what it would have been without intervention scale-up.

PLAUSIBILITY ANALYSIS AND CONCLUSION

Plausibility Argument and Conclusion

In this section, the success of malaria control intervention scale-up and changes in malaria related outcomes in Malawi are summarized, and the plausibility that the malaria intervention scale-up led to changes in malaria-related outcomes and impact during the evaluation period is assessed.

To determine if the scale-up of malaria control interventions could have contributed to the observed 41% reduction in all-cause under-five mortality and if so, to what extent, we examined the fundamental and proximate determinants of child mortality that were in the causal pathways of the impact model (Table 22, Figure 48).

Malaria control interventions have been scaled up

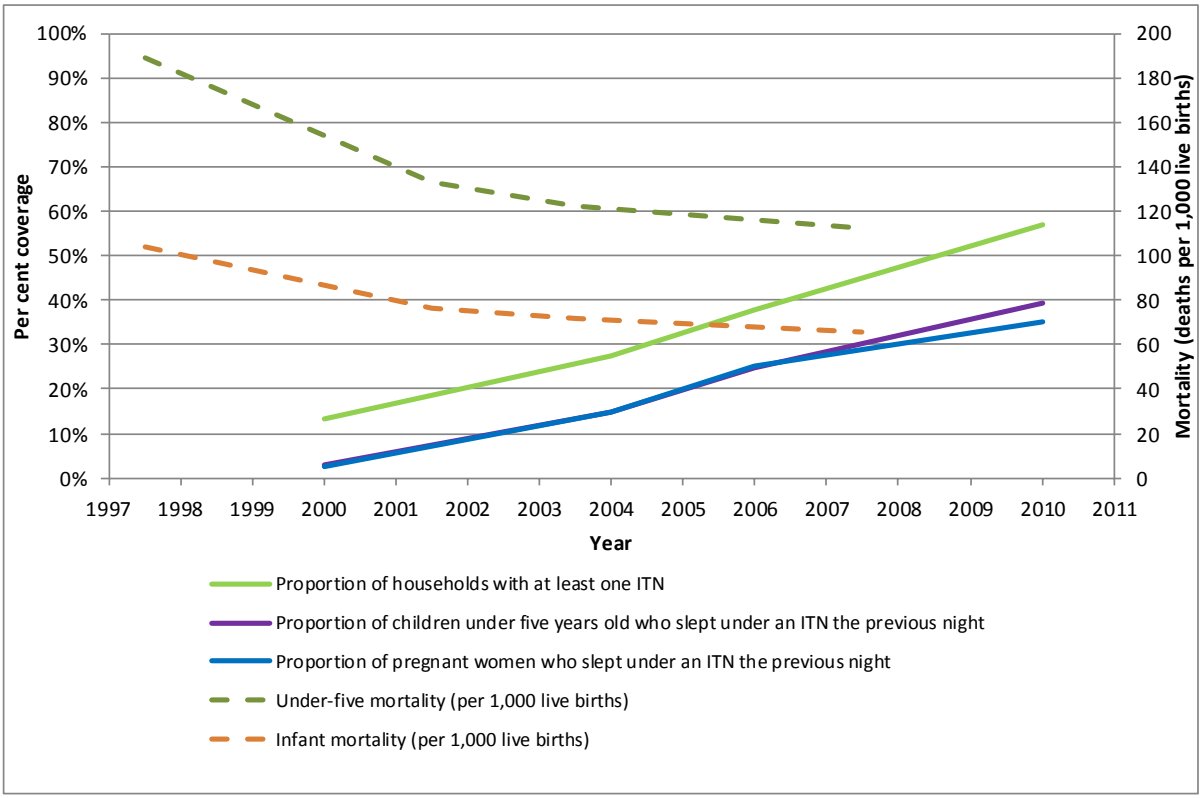
Ownership of ITNs by households increased from close to zero to approximately 57% and ITN use among children under five years of age increased from 3% to about 39% during the evaluation period (2000–2010). This coverage represents significant improvement over the evaluation period. Rowe and Steketee estimate that if malaria control interventions are scaled up from very low to reasonably high coverage levels (e.g. 70%), ACCM will decrease in high malaria transmission areas [168]. ITN coverage levels in Malawi are approaching the levels used in the Rowe and Steketee models. Despite increases in ITN ownership, socio-economic inequity in ITN ownership and use persists in Malawi despite drastic improvements between 2000 and 2010, with residents of households in the lowest wealth quintile less likely to own and to use ITNs compared to those in the highest wealth quintile.

Care-seeking for fever from formal health providers in children under five years of age rose significantly during the evaluation period from 35% in 2000 to 65% in 2010. Among children under five years of age with fever, treatment with an antimalarial increased from 27% in 2000 to 43% in 2010. ACTs replaced SP as the first-line antimalarial drug in 2007. In 2010, only 36% of children under-five received a first-line antimalarial (an ACT) on or the next day following fever onset; however, the superior therapeutic efficacy of ACTs (compared to CQ and SP) would be expected to result in higher rates of parasite clearance, fewer chronic infections, and better treatment outcomes.

Remarkably, Malawi began recommending IPTp in 1993, far before the WHO issued IPTp guidance. Despite its early inception, IPTp coverage is far from reaching the NMCP coverage target of 80%. In 2000, only 28% of women with a live birth in the previous two years had received two doses of SP during her most recent pregnancy. By 2010, this proportion had reached 55%, meaning Malawi has one of the highest IPTp coverage levels in sub-Saharan Africa [67, 169]. Thus, given the protective effect of IPTp on low birth weight [170], increasing IPTp coverage could have affected neonatal mortality and birth weight before the study period and continued to contribute to reductions in these outcomes over the evaluation period. However, given the minimal improvements in neonatal mortality and the increases observed in the proportion of babies born with low birth weight, the effect of IPTp appears to be mitigated by other confounding factors.

A summary of trends in ITN indicators and mortality are depicted in Figure 55.

Figure 55: Summary of trends in malaria control interventions and infant and under-five mortality, 2000–2010.



Malaria-related morbidity has declined

Severe anemia in children 6–59 months decreased between 2004 and 2010 but the decrease seen was not statistically significant. However, a significant decline of 36% did occur in children 6–23 months. The 6–23 month age group is relatively at a higher risk of severe malaria-related syndromes, such as anemia as well as mortality, than children 24–59 months of age [46, 47]. In addition, declines in severe anemia in this age group varied based on malaria risk zone; severe anemia in children 6–23 months declined by 46% in higher risk areas and by 44% in medium risk areas as compared to 12% in lower risk areas. Temporal trends in severe anemia in children 6–35 months from all available nationally-representative survey data show trends of decreasing prevalence between 2001 and 2010.

Trends in long-term malaria parasitemia prevalence in children 6–35 months from the NMS reveal significant declines from 60% in 2001 to 20% in 2009; however, the data from the 2010 MIS estimate a prevalence of 43% in children in this age group. The 2010 MIS estimate could reflect a marked effect of season on malaria parasitemia prevalence, as timing of survey administration varied substantially between surveys. Sub-national anemia and parasitemia surveys from eight districts show regionally variable trends in malaria parasitemia with overall trends of decreasing prevalence in the Northern Region but no significant decrease in the Central or Southern Regions. A recent study by Bennett *et al.* modeled malaria transmission intensity in Malawi in 2000, 2005 and

2010 and found no evidence of a change in mean predicted malaria parasite prevalence over this period [29].

National facility-based data on trends in suspected malaria cases reported monthly are less subject to seasonality bias compared to household survey data due to the longitudinal nature of data collection; however, they suffer from inaccurate and incomplete reporting and lack of confirmation of malaria cases. In Malawi, these data do not suggest that prevalence decreased over the evaluation period; in fact, significant increases are seen between 2005 and 2006 as are marginally significant increases between 2005 and 2009. These trends are likely to be affected by patterns of health care seeking by the population and by trends in the completeness of reporting by health facilities, and both of these factors have increased over the evaluation period. Similar findings were reported in an epidemiologic profile study of Malawi, where the authors found no change in *P. falciparum* transmission intensity between 2000 and 2010, which they said was supported by an examination of hospital admission data where they found no evidence of a sustained decline in pediatric malaria admission rates and routine HMIS data that showed if anything an increase in malaria cases (although some of this may be due to improved reporting rates) [97].

The available evidence supports a significant or marginally significant decline in malaria parasitemia prevalence and in the prevalence of severe anemia between 2000 and 2010 but a possible increase in suspected malaria cases reported by health facilities between 2005 and 2010. Inference based on these measures should be made with caution due to the previously mentioned limitations.

Mortality in children under five years of age has declined

Mortality in children under five years of age decreased by 41% percent, from 189 to 112 deaths per 1,000 live births, between 2000 and 2010. This decline may be attributable to a number of child survival interventions, including scale-up of malaria control interventions. To further examine this decline, mortality in children under-five was stratified by residence (i.e., urban or rural) and age (e.g., 6–23 months, 24–59 months). The mortality declines were larger in children residing in rural areas (43%) as compared to children living in urban areas (10%). During the same period, the relative decline in mortality in children 6–23 months (46%), who are at higher risk of severe malaria and mortality was similar to the relative decline in children 24–59 months (45%). Mortality declines from 2000 to 2010 were also larger in regions with medium- or higher-malaria risk than those with lower malaria risk. It should be noted that 73% of the decline (from 189 deaths per 1,000 live births in the 2000 DHS to 133 in the 2004 DHS) in ACCM over the period 2000–2010 occurred in the early part of the decade (2000–2004), at a time when malaria control interventions were not yet fully scaled-up (e.g. ITN use among children under the age of five was only 15% in 2004). Other child health interventions certainly played a role in this sharp decline in mortality as well. In the 2004–2010 period, when malaria control was intensified, mortality continued to decline, albeit less sharply.

Contextual factors and the plausibility argument

To examine whether the marked reduction in ACCM could be attributed to scale-up of malaria control interventions, we reviewed other determinants of child survival that could offer alternate explanations for the observed changes in mortality during 2000–2010 (summarized in Table 22).

Among the social and economic determinants of child survival, increases were seen in GDP per-capita and women's education, which could have contributed significantly to declines in ACCM between 2000 and 2010. However, the dynamics of socio-economic determinants on population health are often complex [171, 172] and these determinants, arguably [173], must operate through the proximate determinants to affect child survival [106].

Due to the high degree of temporal and spatial heterogeneity in meteorological variables, vector abundance, malaria intervention coverage, and health seeking behavior, the association between climate variability and malaria is also often complex. Multivariate analyses of severe malaria cases in children under five years of age reveal the importance of climatic variation in interpreting patterns of malarial disease. In addition to seasonal trends, *El Niño* Southern Oscillation was shown to have a significant effect on patterns of malarial disease. The observed increases in suspected malaria cases from health facility data in 2009 and 2010 specifically may in part be due to climatic factors, as is also likely to have been the case in neighboring Zambia [85]. However, potential effects of climate on all-cause mortality are difficult to quantify; however, the rainfall and temperature patterns do not suggest any long-term climate differences that would have independently led to substantially different patterns of malaria morbidity and mortality at the end of the evaluation period compared to the beginning.

During the evaluation period, several proximate determinants changed favoring lower mortality: care seeking for diarrhea and for suspected ARI, exclusive breastfeeding in children less than six months of age, use of ORS for diarrhea, improvements in nutrition and the proportion of deliveries in a health facility (Table 22; see Annex 3.1, Table A.3.1.22). Care seeking for suspected ARI and for diarrhea increased 145% and 120%, respectively over the evaluation period. While accessing formal health care is crucial, it does not guarantee effective treatment of childhood illness. Trends in treatment of diarrhea with ORS (relative 44% increase) and declining prevalence of suspected ARI (relative 42% reduction, from 27% to 15%) do suggest improvements in care and prevention of childhood illness that are likely to have contributed to reductions in ACCM.

Coverage of other child survival interventions, such as immunization services, increased less dramatically between 2000 and 2010. Sustained high coverage of BCG, measles, DPT3 and polio3 were observed during the evaluation period with coverage at levels exceeding 80% throughout. Coverage with these vaccines saved many lives over the evaluation period, but the further increases in coverage of these vaccines are unlikely to have had a great impact on the change in mortality in children under five years of age as sufficient levels for protection by herd immunity already existed in 2000. One exception may be the increase in measles immunization coverage (83% in 2000 to 93% in 2010);

measles is highly contagious, so immunization coverage levels of at least 90% need to be maintained to confer population-level protection [174]. Also, *Haemophilus influenza (b)* and Hepatitis B immunizations were added to the EPI package, as a component of the pentavalent vaccine DPT3-HBV-Hib, during the evaluation period (2002); thus coverage of these vaccinations rose from near-zero in 2000 to 93% in 2010. Although the increase in Hepatitis B vaccine coverage, as part of the DPT3-HBV-Hib vaccine, over the study period could have lowered the burden of transmission and infections, it is unlikely to have contributed substantially to reduction in ACCM as the Hepatitis B mortality burden, typically falls on the older age groups [175]. On the other hand, *Haemophilus influenza b* is a leading cause of bacterial meningitis and pneumonia in children, and thus introduction and scale-up of the Hib vaccine could have contributed to declines in ACCM during this evaluation period. While the improvements in coverage with the various vaccines may have reached statistical significance, the magnitude of changes sustained during the evaluation period was small. It is therefore possible that there was little or no relative increase in the contributions of these interventions, except possibly Hib vaccination, on the observed reductions in ACCM.

Stunting, underweight, and wasting in children under-five declined significantly relative to their 2000 baseline by 13%, 38% and 37%, respectively (Annex 3.1, Table A.3.1.22). It should be noted that nutritional improvement cannot be considered as a factor completely independent of malaria control. Recurrent illness is a major contributor to malnutrition and there is some evidence that malaria control interventions are associated with improved anthropometric indices [42]. In addition, Malawi experienced food shortages in the early part of the evaluation period (2001–2 and 2005) [154], which would be expected to have led to higher estimates of undernutrition indices and to an increase in ACCM earlier in the decade. It is therefore likely that improved nutrition between 2000 and 2010 could have contributed to lower mortality over the evaluation period.

Other changes in proximate determinants that may have favored lower ACCM include a 62% relative increase in exclusive breastfeeding of children less than six months of age (44% to 71%), improved PMTCT coverage among HIV positive pregnant women (from non-existent in 2003 to 24% in 2009), a 32% relative increase in the proportion of women giving birth in health facilities (55% to 73%), and improved coverage of tetanus immunization (61% to 69%) and postnatal vitamin A supplementation (42% to 57%) in pregnant women (comparing 2000 to 2010). Most of these improvements are likely to affect mortality in neonates or infants but less likely to have an effect on ACCM.

Several trends in proximate determinants suggest higher ACCM. A smaller proportion of women reported attending four or more ANC visits during the most recent pregnancy in 2010 compared to 2000 (56% in 2000 and 46% in 2010). The proportion of babies being born with low birth weight (<2500g) has increased over the decade from 5% in 2000 to 8% in 2010.

Overall Malawi saw improvements in the coverage of many health interventions as well as socio-economic improvements between 2000 and 2010. Thus, improved malaria control was operating in this general improving environment.

Multivariable regression analyses

Some of the multivariable analyses of sub-national data support the plausibility of the association between scale up of malaria control interventions and impact and some do not. In sub-national analyses from eight districts between 2005 and 2009, household ownership of ITNs was protective for malaria parasitemia and severe anemia in children 6–30 months of age, controlling for climate factors, geographic location, household wealth and child's age; odds of parasitemia were 19% lower in children living in households with at least one ITN and odds of anemia were 23% lower. In this study, regional differences were seen in temporal reductions in parasite prevalence, with significant declines in the Northern Region but not in the Central or Southern Regions. Total decreases in severe anemia over the study period were marginally significant. National health facility-based data do not show an association between district-level aggregated inpatient malaria cases and ITN distributions after controlling for potential confounders. No clear temporal pattern (annual) in suspected malaria cases was evident after controlling for annual numbers of ITNs distributed, climate variables and percent of facilities reporting. Cox proportional hazard models revealed that children living in households with at least one ITN had 0.75 times the risk of dying as children in households without an ITN, controlling for other variables. A nationally-representative district-level analysis showed that districts with higher levels of ITN ownership had fewer deaths in children under five, accounting for relevant district-level characteristics such as district average educational level of mothers, district average proportion of household with access to improved water, district average diarrhea prevalence in children under five and district average proportion of children with vitamin A supplementation. These results were robust to several different methods of measuring ITN coverage with incident rate ratios ranging from 0.55 to 0.87. Finally, an analysis of MIS data in Chikwawa District revealed meaningful seasonal trends in both ITN use and in malaria parasitemia prevalence, highlighting the importance of accounting for annually variable climate data in trend analyses.

Summary

There is no doubt that Malawi has made dramatic progress in scaling up malaria prevention and treatment measures: Household ownership of ITNs doubled between 2004 and 2010, reaching 57% of households; use of ITNs by children under five years of age increased 13-fold from 2000 to 2010 with 39% using ITNs in 2010; use of IPTp doubled from 28% in 2000 to 55% in 2010. Case management of malaria has also improved over this period: Care seeking for children with fever has almost doubled from 35% in 2000 to 65% in 2010 and the proportion of children receiving the recommended first-line treatment amongst those who received any antimalarial medication, remained high at over 80%. During this period of scale-up of malaria control interventions (2000–2010), ACCM has fallen by 41%. Part of this decline in all-cause mortality could be due to the improvements in the coverage of non-malaria control interventions including increased women's literacy, women giving birth in a health facility, improved water source, exclusive breast feeding, care seeking for suspected ARI and diarrhea, the introduction of the Hib vaccination and declines in malnutrition. In addition, it is likely that the decline in all-cause mortality among children under five years of age was in part due to a reduction in malaria-specific

mortality. Multivariable models support this claim; districts with more ITNs were shown to have fewer deaths in children under five years of age, controlling for other predictors of child mortality. Similarly, ITN ownership was found to be protective against severe anemia and parasitemia in children 6–30 months of age in multivariable models. Taken together this evidence suggests that malaria control interventions in Malawi contributed to reductions in ACCM between 2000 and 2010.

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