
Evaluation of the Impact of Malaria Interventions on Mortality in Children in Mainland Tanzania

Tanzania Malaria Impact Evaluation Research Group

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Paul Smithson of Ifakara Health Institute was lead author of the report. Achuyt Bhattarai (PMI-CDC) wrote the Contextual Factors and Plausibility section with inputs from Peter McElroy (PMI-CDC) and Rene Salgado (PMI-USAID). Christine Hershey (PMI-USAID) performed the LiST analysis and wrote that section. Chonge Kitojo (PMI-CDC) collected all financial data and was lead writer of the resources and inputs section. Tanya Marchant (Liverpool School of Hygiene and Tropical Medicine) and colleagues allowed their manuscript to be cited for the Mtwara-Lindi case study. Fabrizio Molteni (RTI International) contributed most of the material for the Kagera case study. Angelica Rugarabamu (Ifakara Health Institute) undertook the literature review, bibliography preparation and assembly of case study material. Special thanks are due to Lia Florey (ICF-International) who undertook most of the data analysis, with assistance from Trevor Croft (ICF-International), Honorati Masanja (Ifakara Health Institute) and Yazoume Ye (ICF-International). Special thanks are due to Rene Salgado, Lia Florey, Christine Hershey, Peter McElroy, Achuyt Bhattarai, Yazoume Ye, Fred Arnold (ICF-International) and Jessica Kafuko (PMI-USAID), all of whom were intimately involved in the planning, preparation and execution of the assignment. Administrative support was provided by Jessica Kafuko from USAID-Tanzania, and Anne Mboya and Monica Sengoda, both from Ifakara Health Institute.

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Table of Contents

Acronyms	6
Tables	8
Figures	9
Executive Summary	11
INTRODUCTION AND BACKGROUND	
Introduction	16
Purpose and Scope	16
Study Design	16
Evaluation Indicators.....	17
Data Sources	19
Report Structure	19
Country Context	20
Background.....	20
Health Services.....	21
Malaria in Mainland Tanzania	22
Malaria Strategy	24
Resources and Inputs	24
INTERVENTION SCALE UP	
Insecticide Treated Nets (ITN)	28
Background.....	28
ITN Implementation.....	28
ITN Coverage Trends	30
Equity in ITN Use.....	32
Geographic Variation in ITN Use.....	33
Other Factors Associated with ITN Use	34
ITN Summary	34
Malaria Treatment	35
Background.....	35
Drug Policy	35
Treatment Implementation	35
Coverage of Prompt and Effective Treatment	36
Equity and Factors Associated with Treatment Access.....	39
Malaria Treatment Summary.....	39
Intermittent Preventive Treatment in Pregnancy (IPTp)	40
Background.....	40
IPTp Implementation	40
IPTp Coverage.....	40
Equity in IPTp	41
IPTp Summary.....	42
Other Interventions	43
Indoor Residual Spraying (IRS)	43
Environmental Control and Larvicides	43
Intermittent Preventive Treatment in Infancy (IPTi)	44

MALARIA MORBIDITY

Morbidity Indicators and Data	46
Malaria Parasitemia	48
Malaria Parasitemia in Mainland Tanzania in 2007/8.....	48
Parasitemia Trend – NMCP Surveys 2006-2008.....	50
Parasitemia Trend, Lindi and Mtwara, 2004-2007	50
Malaria Parasitemia Trend, Ifakara Demographic Surveillance Site, 2001-2010.....	51
Severe Anemia Trends	52
Gender and Socio-Economic Disparities.....	53
Severe Anemia Trends and Malaria Risk	54
Fever Prevalence	55
Facility-Based Morbidity	58
Morbidity Summary	59

MORTALITY

Mortality	62
Background.....	62
Trend in All-Cause Under-Five Mortality	62
Age-Specific Mortality.....	63
Mortality Change by Residence	65
Under-Five Mortality Change and Malaria Risk	66
Equity.....	69
Mortality Summary	70

CASE STUDIES

Case Studies	73
Ifakara DSS Area	73
Lindi and Mtwara.....	78
IRS in Kagera Region	80

CONTEXTUAL FACTORS AND PLAUSIBILITY ANALYSIS

Accounting for Contextual Factors	84
Fundamental Determinants	85
Socioeconomic Factors	85
<i>Economic Poverty</i>	85
Proximate Determinants	89
Maternal and Child Health.....	89
HIV/AIDS among Children and Women.....	93
Plausibility Argument	94
LiST Model: Estimating Lives Saved	98

CONCLUSION

Conclusion	103
Contextual Factors and Plausibility Argument.....	104

REFERENCES	107
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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)
ACT	Artemisinin combination therapy
ALu	Artemether-lumefantrine
ANC	Antenatal care
ARV	Anti-retroviral therapy
CDC	Centers for Disease Control and Prevention
CI	Confidence interval (95%, unless otherwise stated)
CQ	Chloroquine
DDT	Dichlorodiphenyltrichloroethane
DfID	United Kingdom's Department for International Development
DHS	Demographic and Health Survey
DOTS	Directly-observed therapy (short-course)
DPT	Diphtheria, tetanus, pertussis
DSS	Demographic Surveillance System
EIR	Entomological inoculation rate
GDP	Gross domestic product
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
HB	Hepatitis B (vaccine)
Hb	Hemoglobin
Hib	<i>Haemophilus influenzae</i> type b (vaccine)
HIV	Human immunodeficiency virus
IGME	Inter agency group for mortality estimation
IPTi	Intermittent preventive treatment in infants
IPTp	Intermittent preventive treatment in pregnancy
IRS	Indoor residual spraying
ITN	Insecticide-treated net
IUGR	Intrauterine growth retardation
JICA	Japan International Cooperation Agency
KINET	Kilombero ITN project
LiST	Lives Saved Tool
LLIN	Long-lasting insecticide-treated net
M&E	Monitoring and evaluation
MERG	Monitoring and evaluation reference group
MOHSW	Ministry of Health and Social Welfare
NMCP	National Malaria Control Program
NN	Neonatal (mortality)
OPV	Oral polio vaccine
PMI	President's Malaria Initiative
PMTCT	Prevention of mother-to-child (HIV) transmission
PNN	Postneonatal (mortality)
RBM	Roll Back Malaria
RDT	Rapid diagnostic test
SMITN	Social marketing of ITN project
SP	Sulphadoxine-pyrimethamine
TDHS	Tanzania Demographic and Health Survey

THMIS	Tanzania HIV and Malaria Indicator Survey
TNVS	Tanzania National Voucher Scheme
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
WHO	World Health Organization

Tables

Table 1: Roll Back Malaria core population-based indicators used in this report.....	18
Table 2: Definition of zones in DHS Surveys from 2004/5.....	21
Table 3: Health facilities by type and ownership, Mainland Tanzania, 2010.....	21
Table 4: Equity of ITN use by under-fives and pregnant women.....	33
Table 5: Percentage of children under five with fever in two weeks prior to survey, by type of anti-malarial used for treatment	38
Table 6: Equity of IPTp 2004/5-2010.....	41
Table 7: Malaria parasitemia in children 6-59 months, by age, Mainland Tanzania, 2007/8.....	48
Table 8: Malaria parasitemia in children 6-59 months, by background characteristics, Mainland Tanzania, 2007/8.....	49
Table 9: Malaria parasitemia in children under-five years of age, Mainland Tanzania, 2006-2008.....	50
Table 10: Relative reduction in severe anemia, 2004-2010 by age group (months).....	53
Table 11: Severe Anemia (Hb<8g/dL) prevalence in children 6-59 months of age, by background characteristics, Mainland Tanzania, 2004/5-2010	54
Table 12: Age-specific mortality (deaths per 1000 live births) ^a and relative change in age-specific mortality, 0-4 years prior to the survey	64
Table 13: Case study summary.....	73
Table 14: Household attributes and asset ownership, Mainland Tanzania, 1999-2010	887
Table 15: Women's* education and marital status in Mainland Tanzania, 1999-2010	89
Table 16: Maternal and child health in Mainland Tanzania, 1999-2010	91
Table 17: Breastfeeding and undernutrition in children and women in Mainland Tanzania, 1999-2010.....	93
Table 18: Summary of evidence of changes in under-five mortality in Mainland Tanzania, 1999-2010.....	95

Figures

Figure 1: Administrative map of Mainland Tanzania showing regions.....	20
Figure 2: Distribution of malaria endemicity, Tanzania 2007	23
Figure 3: Milestones in Malaria Strategy in Mainland Tanzania	24
Figure 4: Trend in funding source for malaria control, Mainland Tanzania, 2000-2010	25
Figure 5: Malaria budget 2000-2010 by intervention.....	26
Figure 6: Evolution of ITN implementation in Mainland Tanzania.....	30
Figure 7: Household ownership of any nets and ITNs, 1999-2010.....	30
Figure 8: ITN ownership in households with/without under-fives.....	31
Figure 9: ITN use among children under-five years, pregnant women and the general population, 1999-2010.....	32
Figure 10: ITN use by children under five, by zone (2004/5-2010)	34
Figure 11: % of children 0-59 months with fever during two weeks prior to survey who were treated with recommended antimalarial same or next day after fever onset.	37
Figure 12: Treatment seeking, promptness and choice of treatment in under-fives	38
Figure 13: Intermittent preventive treatment for malaria prevention, with at least two therapeutic doses of sulfadoxine-pyrimethamine in women (15-49 years) with live birth 0-2 years prior to survey, 2004-10	41
Figure 14: Malaria morbidity (parasitemia, severe anemia and fever), Mainland Tanzania, 2007/8.....	47
Figure 15: Malaria parasitemia, in Lindi and Mtwara, Southern Tanzania, 2004-2007	51
Figure 16: Malaria Parasitemia (All Age) in Ifakara Demographic Surveillance Site, 2001-2010	52
Figure 17: Trends in severe anemia (Hb< 8g/dL) prevalence in children 6-59 months of age, by residence and age, Mainland Tanzania, 2004/5-2010	53
Figure 18: Trends in severe anemia (Hb <8g/dL) prevalence in children 6-23 months of age, by malaria risk areas, Mainland Tanzania, 2004/05, 2007/08 and 2010	55
Figure 19: Proportion of all children and those with fever in the two weeks prior to the survey who tested RDT-positive on the day of survey, by age group, 2007/8	56
Figure 20: Fever during the two weeks prior to survey, children under-five years of age, 1999-2010	57
Figure 21: Age-specific fever prevalence by age group, 1999 - 2010	57
Figure 22: Malaria admissions and blood slide-positivity, in children under-five years of age, Ifakara District Designated Hospital, 1999-2010	58
Figure 23: Malaria admissions and blood slide positivity among children under-five years of age, Bagamoyo District Hospital, 2006-2010.....	59
Figure 24: Trend in all-cause under-five mortality (5q0), Mainland Tanzania, 1992-2010	63
Figure 25: Trends in age-specific childhood mortality, Mainland Tanzania, 1999, 2004/5, 2010.....	64
Figure 26: Age-specific mortality, rural areas of Mainland Tanzania, 1999 and 2010	65

Figure 27: Age-specific mortality, urban areas of Mainland Tanzania, 1999 and 2010	66
Figure 28: Trends in infant mortality in higher, medium and lower malaria risk areas, Mainland Tanzania 1999 and 2010	67
Figure 29: Trends in under-five mortality in higher, medium and lower malaria risk areas, Mainland Tanzania 1999 and 2010	67
Figure 30: Trends in mortality in 6-23 month olds in higher, medium and lower malaria risk areas, Mainland Tanzania 1999 and 2010.....	68
Figure 31: Trends in mortality in 24-59 month olds in higher, medium and lower malaria risk areas, Mainland Tanzania 1999 and 2010.....	68
Figure 32: Inequalities in under-five mortality 2004/5 - 2010.....	70
Figure 33: ITN and any net use (all ages).....	74
Figure 34: Malaria parasitemia (all ages).....	75
Figure 35: Slide positivity, under five patients	75
Figure 36: Infant and under-five mortality rates	76
Figure 37: Entomological inoculation rate.....	77
Figure 38: Rainfall trends	77
Figure 39: Household net ownership and infant (2-11 months) net/ITN use trends, Lindi and Mtwara, 2004 - 2007.....	78
Figure 40: Malaria parasitemia, Lindi and Mtwara, 2004 - 2007.....	79
Figure 41: Map of Kagera Region showing districts with number of IRS rounds since inception	80
Figure 42: Number and % blood smears positive for malaria, Nyakahanga District Hospital, Karagwe District (2003-2010)	81
Figure 43: Malaria positivity, Chato District Hospital, Chato District	81
Figure 44: Malaria positivity, Rubya District Hospital, Muleba District.....	81
Figure 45: Impact model for the evaluation of the malaria control program, Mainland Tanzania, 1999 to 2010.....	85
Figure 46: Trends in gross domestic product (GDP) per capita and under-five mortality, Tanzania, 1990 - 2009	86
Figure 47: The 12-month Weighted Anomaly Standardized Precipitation (WASP) index, Mainland Tanzania,.....	88
Figure 48: Lives saved by ITN scale-up, children 1-59 months, 1999-2010	99
Figure 49: Lives saved in children aged 0-59 months by scale up of malaria in pregnancy interventions (ITN use by pregnant women), 1999-2010	100

Executive Summary

This report was commissioned by the Roll Back Malaria (RBM) Partnership and supported by the US President's Malaria Initiative (PMI) on behalf of the Ministry of Health and Social Welfare of Mainland Tanzania. The evaluation is limited to Mainland Tanzania and focuses on the 1999 to 2010 period, during which malaria control interventions were rapidly scaled up. The interventions were mainly: insecticide treated nets (ITN), prompt and effective malaria case-management with artemisinin combination therapies (ACTs), intermittent preventive treatment in pregnancy (IPTp) and, in selected areas, indoor residual spraying (IRS).

The evaluation is based on a "before-and-after assessment", which uses a plausibility evaluation design that measures changes in malaria intervention coverage, malaria-related morbidity and all-cause mortality and accounts for other contextual determinants of child survival. All-cause mortality in children under-five years of age (under-fives) is used as a measure of mortality, as malaria-specific mortality cannot be reliably measured in most parts of sub-Saharan Africa.

The evaluation indicators are primarily the population-based indicators recommended by RBM, which include the following three primary impact measures: (1) all-cause mortality in children under five years of age, (2) malaria parasitemia and (3) severe anemia (Hb <8g/dL) prevalence in children 6 – 59 months.

Data cited in the report stems mainly from four large population-based household surveys, representative of Mainland Tanzania, conducted by the Tanzania National Bureau of Statistics and ICF International (MEASURE DHS), during 1999, 2004/5, 2007/8 and 2010. These data are supplemented, where relevant, by programmatic data, small-area studies and other survey data. Data sources are clearly cited throughout the report.

During the evaluation period, Mainland Tanzania witnessed dramatic changes in the coverage of malaria control interventions, including: the adoption of new first-line treatments, increased access to ITNs, and introduction of IPTp. Additional interventions were undertaken at a sub-national level.

Household ITN ownership increased from about zero to 63% during the evaluation period. ITN use by under-fives and pregnant women reached 64% and 56%, respectively, in 2010. Although malaria treatment seeking showed little change from 1999 levels, Mainland Tanzania did change from a failing drug (chloroquine) to much more effective therapies (sulfadoxine-pyrimethamine in 2001 and ACTs in 2006). In 2010, 27% of children under-five years of age with a fever were treated with an artemisinin-based combination therapy (ACT) the same day, or the day following, fever onset. Since its introduction in 2001, coverage with two doses of IPTp changed very little from 20% in 2004 to 25% in 2010. The impact of IRS was more limited, as spraying focused on only two

districts in the highly endemic Lake Zone; however, IRS reached over 90% of targeted households in those two districts.

Parasitemia prevalence is a useful malaria morbidity indicator, as it is malaria-specific and can provide a rough measure of transmission. No nationally representative trend data are available for malaria parasitemia in under-fives because this was measured only once (2007/8) during the evaluation period. However, sentinel surveys by the National Malaria Control Program (NMCP) found that malaria parasitemia in children under-five declined slightly from 19% in 2006 to 16% in 2008. In addition, in the six districts of Lindi and Mtwara Regions, all-age malaria parasite prevalence halved (from 50% to 26%) and prevalence in infants aged 2-11 months fell by two-thirds (from 57% to 19%) between 2004 and 2007. Repeated cross-sectional random surveys in the well-documented Ifakara Demographic Surveillance System (DSS) area also showed a decline in (all-age) malaria parasitemia from between 18% and 25% (2001-2004) to 5% in 2009 and 4% in 2010.

Severe anemia prevalence, which is strongly associated with *Plasmodium falciparum* infection in children under five years of age, is a good measure of the health impact of malaria control interventions. Among children under-five, severe anemia declined from 11% in 2004/5 to 6% in 2010. The relative decline was greater in rural (54%) than in urban areas (24%), as would be expected if malaria was a major cause of anemia. The decline was also greatest in children 6-23 months old, the age group most vulnerable to severe malarial syndromes and mortality.

Under-five mortality (5q0) fell by 45%, from 148 deaths per 1000 live births in 1995-99, to 81 in 2006-10. This decline in mortality appears to have commenced around 1999-2000. Significant reductions in child mortality occurred in all age cohorts, but the reductions were greatest in the 1-11 month (postneonatal) age group. The relative mortality decline in children aged 6-23 months was larger (49%) than children in 24-59 months (34%). The largest mortality decline was observed in children 1-5 months (66%). Mortality declines from 1999 to 2010 were also larger in regions with medium or high malaria risk than those with low malaria risk. The timing of the change in these mortality trends broadly corresponds with the period during which malaria interventions were being scaled-up nationwide.

The evaluation used ancillary data from small studies to further verify that findings were consistent. A case study from the Ifakara DSS area adds strong evidence to the linkage between intervention scale-up, and consequent reductions in malaria morbidity and all-cause mortality. A case study from Mtwara and Lindi Regions describes a steep reduction in malaria parasitemia in children under two years of age associated with ITN scale-up. A case study from Kagera Region documents a sharp reduction in malaria cases in local hospitals following the implementation of successive rounds of IRS.

To determine whether alternate explanations for the observed changes in mortality during the evaluation period might exist, we undertook a systematic

review of contextual determinants of child survival. Among the social and economic determinants of child survival, increases were seen in per-capita gross domestic product and women's education, which could have been significant contributors to the mortality decline in children under-five from 1999 to 2010. Review of data from 23 meteorological stations suggests rainfall patterns suitable for malaria transmission persisted throughout the evaluation period, and it is unlikely that any variations in rainfall could have significantly altered malaria transmission during this period. Proximate determinants of child survival were also examined including health services, maternal health interventions and child health interventions. Two important proximate determinants of child survival notably increased during the evaluation period: *Haemophilus influenzae (b)* (Hib) vaccination and vitamin A supplementation. While both interventions have been shown to reduce child mortality and may have contributed somewhat to the declines seen in Mainland Tanzania, the introduction of Hib very late in this period (2009) and changes in coverage of vitamin A are unlikely to entirely explain the mortality declines seen between 1999 and 2010.

We also estimated the potential combined effect of changes in coverage of essential health interventions on mortality risk using the Lives Saved Tool (LiST) model. Over the period 1999 to 2010, scale-up of ITN ownership is estimated to have prevented approximately 61,300 (range: 32,100-95,100) deaths in children 1-59 months old and ITN use by pregnant women was estimated to have prevented an additional 1300 (range: 600-2100) deaths of children under-five (including neonatal deaths due to low birth weight). These deaths averted represent 15% of the overall reduction in under-five mortality that occurred between 1999 and 2010. It should be noted, however, that the model results under-estimate the impact of malaria control interventions because they omit the gains associated with improved treatment efficacy and the impact of reduced malaria burden on "indirect" malaria mortality (deaths in which malaria was a contributing cause and the death was categorized as a non-malaria death).

According to the LiST model, other (non-malaria) interventions that made a significant (>5% of all deaths averted from 1999 to 2010) contribution to mortality decline over this period include increases in breastfeeding, immunization (DPT3 and Hib), vitamin A supplementation and improved excreta disposal. Of these, only vitamin A supplementation has an impact magnitude (deaths averted) comparable to that of malaria interventions.

In summary, the 45% decline in under-five mortality and the 50% decline in severe anemia prevalence in children 6-59 months in Mainland Tanzania from 1999 to 2010 was observed following a 36-fold increase in ITN use among children under-five. Larger declines in under-five mortality and severe anemia were observed in rural areas, where the risk of malaria is higher compared to urban areas. The decline in mortality and severe anemia was also larger in children 6-23 months, who are at a greater risk of severe malaria syndromes and mortality, as compared to children 24-59 months. During the evaluation period, climatic conditions favorable for malaria transmission persisted, and no additional sustained significant increases in other child survival interventions

were observed. Based on these findings, we believe that there is strong evidence that the dramatic reductions in under-five mortality in Mainland Tanzania during the period 1999 to 2010 were at least in part due to reductions in malaria mortality that resulted from the major scale up of malaria prevention and control interventions.

INTRODUCTION AND BACKGROUND

Introduction

Purpose and Scope

This report was commissioned by the Roll Back Malaria (RBM) Partnership and supported by the U.S. President's Malaria Initiative (PMI) on behalf of the Ministry of Health and Social Welfare (MOHSW) of Mainland Tanzania and its National Malaria Control Program (NMCP).

The main objective of the evaluation is to assess the impact of malaria control interventions (regardless of the source of funding) on malaria morbidity and all-cause mortality in children under-five years of age (under-fives), between 1999 and 2010 in Mainland Tanzania.

The evaluation comes at a timely juncture. In Mainland Tanzania, malaria control intensified dramatically over the past decade, enabled by over \$450 million in malaria funding coupled with new interventions. As a result there has been 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 the burden of malaria.

The evaluation also allows Mainland Tanzania to track progress toward its national malaria targets and those agreed to in the Abuja Declaration to Roll Back Malaria, Millenium Development Goals, and other international agreements. The analysis in this report is restricted to Mainland Tanzania. A separate evaluation is required for Zanzibar owing to contrasting epidemiology, differing intervention mix and timing, and the fact that a Zanzibar-specific evaluation requires a separate process for stewardship and consultation.

The evaluation focuses on the period of 1999 to 2010 because this is the period over which most changes have taken place in malaria control interventions. Prior to 2000, intermittent preventive treatment in pregnancy (IPTp) had yet to be implemented, new drugs had not yet been introduced and the scale-up of insecticide-treated nets had not yet begun on a national scale. Data from earlier time periods are included where it helps to put recent changes into perspective.

The report does not aim to present a critique of program implementation or effectiveness. However, it does include a detailed description of intervention scale-up, sub-national variations in coverage, and factors affecting uptake. The evaluation also considers what other factors may have contributed to mortality decline over the period.

Study Design

The evaluation is based on a "before-and-after assessment", which uses a plausibility evaluation design that measures changes in malaria intervention coverage, malaria-related morbidity, and all-cause mortality and accounts for other contextual determinants of child survival. All-cause mortality in children

under-five is used as a measure of mortality as malaria-specific mortality cannot be reliably measured in most parts of sub-Saharan Africa.

The overall conceptual framework for the evaluation is a “plausibility argument.”(1) Underlying the argument is the known biological plausibility of causal association between malaria interventions, malaria-related morbidity and all-cause mortality in children under five. Therefore, the major part of the document seeks to describe in detail the changes in each of these parameters (interventions, morbidity and mortality). The plausibility of an inference of causal association is further bolstered if the magnitude of impact is consistent with intervention efficacy; if the age-pattern of change is consistent with malaria-mediated morbidity and mortality; if the timing of intervention scale-up matches the trend change in impact, and if there is an ecological association between malaria risk and the impact observed. Each of these analytical analyses is employed in the evaluation where the data set permits.

The plausibility of causal association is also examined through a number of sub-national case studies, where richer data sets permit:

- closer examination of the temporal association between relevant indicators;
- statistical tests of association between interventions, morbidity and mortality;
- description of changes in other malaria-related indices (such as malaria transmission intensity), and
- information on potential confounders that could have contributed to morbidity and mortality change.

At the national level, the report examines other factors that have the potential to mediate changes in malaria-related morbidity and/or all-cause mortality. These “potential confounders” include three broad groups of factors: contextual (rainfall, socio-economic status and fertility-related risks); other morbidities (diarrhea and acute respiratory infection) and other health interventions. The Lives Save Tool (LiST) model is then used to quantify the expected contribution of various health interventions (including, but not limited to malaria control) to changes in mortality of children under-five years of age between 1999 and 2010.

Evaluation Indicators

The selection and definition of indicators used in this study for national-level analysis was guided by the recommendations of RBM’s Monitoring & Evaluation Reference Group (MERG), see Table 1. Of the eleven recommended indicators, the “IRS + ITN indicator” (indicator 3) and “RDT indicator” (indicator 6) were omitted because implementation of rapid diagnostic tests (RDTs) in Mainland Tanzania commenced at the end of the period (2009) and neither RDTs nor indoor residual spraying (IRS) had attained national scale.

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

Indicator	Indicator Number and Description
Insecticide-treated nets (ITNs) and indoor residual spraying (IRS)	1. Proportion of households with at least one ITN.
	2. Proportion of children under 5 years old who slept under an ITN the previous night.
Prompt and effective treatment and use of diagnostics	4. Proportion of children under 5 years old with fever in last 2 weeks who received any antimalarial treatment.
	5. Proportion of children under 5 years old with fever in last 2 weeks who received antimalarial treatment according to national policy within 24 hours from onset of fever.
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 antenatal care clinics visits during their last pregnancy.
Mortality	9. All-cause under-5 mortality rate (5q0).
Morbidity	10. Parasitemia: proportion of children aged 6-59 months with a positive RDT or microscopy result.
	11. Anemia prevalence: proportion of children aged 6-59 months with a hemoglobin measurement of <8 g/dL.

Source: Guidelines for Core Population-Based Indicators Working Paper

In addition to the RBM-MERG morbidity indicators, this report includes a description of trends in fever, defined as the proportion of children under five years of age who had suffered fever within a two week period preceding the survey, as reported by their mother or caregiver. This indicator is included because an association between fever prevalence and malaria control is biologically plausible, national trend data is available, and reliable national facility-based measures of “presumed malaria” are not available in Mainland Tanzania.

In line with RBM-MERG guidance, the principal measure of impact employed in this evaluation is all-cause mortality in children under five years of age. This measure is preferable to malaria-attributable mortality for a number of reasons,

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 United Nations Inter-agency Group for Child Mortality Estimation has developed methods of HIV-adjustment of child mortality estimates and recommends this adjustment in countries where more than 5% of adult women are infected with HIV. However, other analyses of potential HIV bias by Rajaratnam and colleagues* using Demographic Health Survey data from 21 countries shows substantial variation in effect on child mortality estimates in both directions, even in countries where HIV prevalence exceeds 20%.

Available Tanzania Mainland data indicate that HIV prevalence among women attending antenatal care clinics declined by 2.6 percentage points between 2001/2 and 2007/8, so the underlying bias has changed only modestly. Finally, improvement in coverage of antiretroviral therapy (ARV) and prevention of mother to child transmission (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. In this evaluation report, the mortality estimation methods do not take into account potential selection bias arising from high HIV prevalence, which could be considered a limitation of the report.

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

including: the non-availability of national-level malaria-specific mortality; concerns about the low sensitivity and specificity of the verbal autopsy method for detecting malaria deaths;(2) and the fact that malaria is thought to make an “indirect” contribution to under-five mortality that is equivalent to 50%-100% of the mortality that can be directly attributed to malaria.(3)

The research group chose to use mortality estimates from Demographic and Health Survey (DHS) instead of estimates from the Inter-Agency Group for Mortality Estimation (IGME) because IGME estimates lag behind DHS direct estimates of mortality and do not permit stratification needed to inform the plausibility argument.

Data Sources

The data source for mortality in children under five years of age, malaria intervention coverage indicators and many contextual factors, is the series of DHS surveys conducted between 1999 and 2010. No new primary data were collected for this evaluation. Additional data sources are referred to where relevant - particularly where these shed light on variables that were not measured in the DHS surveys. Supplementary data sources include: economic reports from the Bank of Tanzania; the Tanzania [Mainland] National Household Budget Survey (2000/1 and 2007); programmatic data from project and research sites; entomological data from transmission and insecticide-resistance monitoring sites; case-study data from Bagamoyo, Ifakara, Lindi/Mtwara and Kagera, and rainfall data from the Tanzanian Meteorological Agency. Finally, the study makes reference to numerous published studies on the relationship between malaria interventions and their impact. Throughout the report, the source of data is clearly cited and caveats on data quality, comparability and assumptions are indicated. A more detailed description of the data sets, survey methods, sample sizes and other statistical parameters can be found in the annexes.

Report Structure

The main body of this report is divided into five sections. The first provides a brief description of the country context and malaria situation, including the evolution of malaria strategy and funding. The second section describes in detail the scale up of malaria interventions: ITN, treatment, IPTp, and IRS. The third section examines changes in morbidity, specifically malaria parasite prevalence, anemia and fever. Section four describes changes in mortality in children under five years of age. Section five presents the plausibility analysis, which includes evidence from case studies where additional data on the intervention-morbidity-mortality relationships are available; an assessment of “what else has changed”; and a quantitative estimate of the contribution to mortality change of malaria control and other health interventions. The report concludes with a discussion on the evidence as well as implications for the future.

Country Context

Background

Mainland Tanzania covers an area of nearly 1 million square kilometers, lying in the tropics between 1°S - 12°S and 29°E - 40°E. The population, estimated at 41.9 million in 2010, is predominantly (75%) rural. Population distribution is uneven, being most dense in the Northern Highlands, Southern Highlands, regions adjacent to Lake Victoria and Dar es Salaam. Mainland Tanzania is divided into 21 administrative regions (Figure 1) and 113 districts with 133 councils. There are approximately 10,300 villages. The definition of zones for the purpose of DHS surveys (2004/5 onwards) is shown in Table 2.

Figure 1: Administrative map of Mainland Tanzania showing regions



Table 2: Definition of zones in DHS Surveys from 2004/5

Zones	Regions
Western	Tabora, Kigoma, Shinyanga
Northern	Arusha, Manyara, Tanga, Kilimanjaro
Central	Singida, Dodoma, Morogoro
Southern Highlands	Rukwa, Mbeya, Iringa
Lake	Kagera, Mwanza, Mara,
Eastern	Tanga, Morogoro, Dar es Salaam, Coast (Pwani)
Southern	Mtwara, Lindi, Ruvuma

Source: Tanzania National Website (<http://www.tanzania.go.tz/>)

High fertility and declining mortality has resulted in population growth of over 2% per year. In spite of rapid economic growth during the last decade, gross national income per capita was \$500 in 2009, ranking Tanzania 192 out of 213 countries. The economy depends heavily on agriculture, which accounts for more than one-fourth of gross domestic product (GDP), provides 85% of exports, and employs 80% of the work force. An estimated 34% of the population lives on less than \$1 per day and 36% is living below the poverty line. Adult literacy stands at 69% (78% male, 62% female). Primary school enrollment has risen rapidly since 2000 and reached 66% of girls and 72% of boys in 2009.

Health Services

Health services in Mainland Tanzania are organized on a pyramidal structure comprising 5,400 dispensaries, 582 health centers, and 232 hospitals (including 18 regional hospitals and 8 national/referral hospitals) (see Table 3). More than two-thirds of health facilities are owned and operated by the government. In 2007, 76% of households lived within six kilometers of a dispensary or health center and 58% within 10 kilometers of a hospital.(4) Dispensaries provide basic primary health care services, but some may have an inpatient bed for deliveries. Health centers have larger in-patient capacity and may offer some specialized services. Hospitals are the third level of care and are usually located in urban centers and attend to more specialized medical needs.

Table 3: Health facilities by type and ownership, Mainland Tanzania, 2010

	Government	Parastatal	Voluntary	Private	Total
Hospitals	96	7	98	31	232
Health Centers	402	8	117	55	582
Dispensaries	3,711	166	668	855	5,400
Total	4,209	181	883	941	6,214

Source: Ministry of Health and Social Welfare, Health Statistics Abstract 2010 [draft]

After independence, many social and health indicators began a steady improvement in the late 1960s. However, by the mid-1980s such advances came to an end and from 1985 to 2000, many health indicators remained at the same level or worsened. During this period of fiscal austerity and low aid flows, growth of the health facility infrastructure was minimal and a freeze on government hiring in 1994 resulted in a net decline in the health workforce.

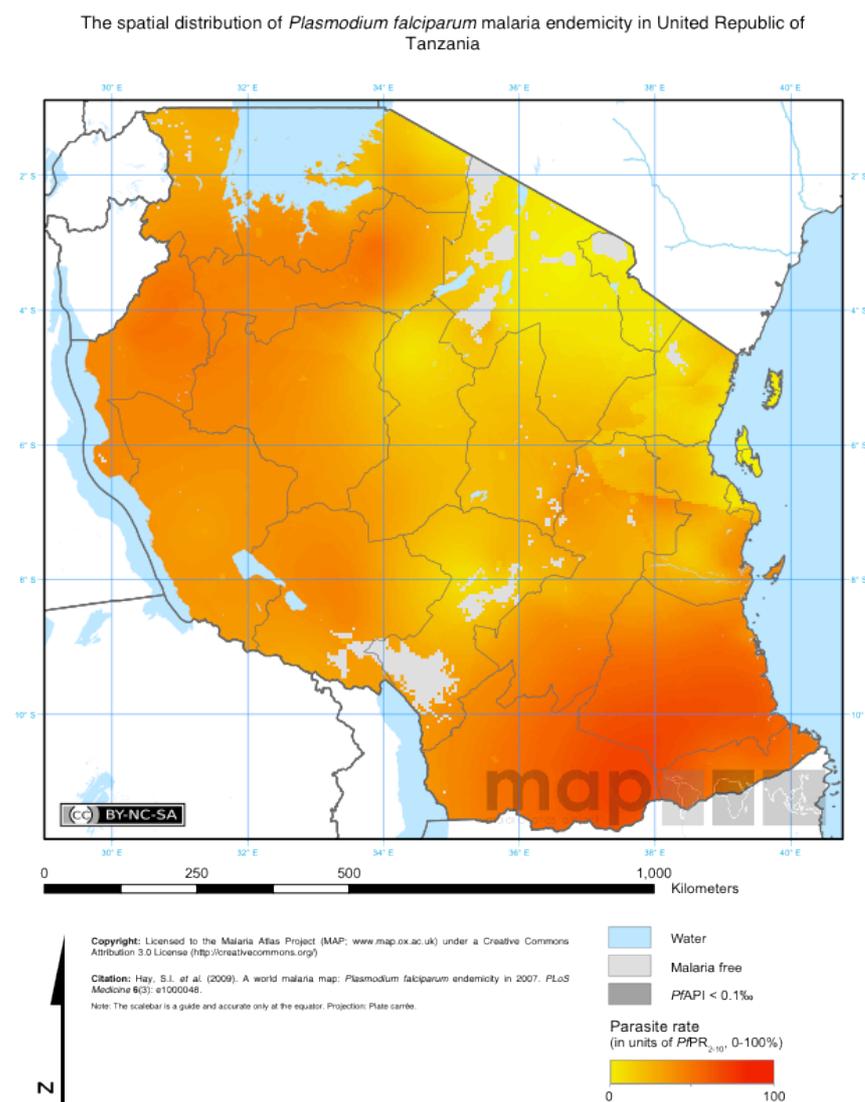
Public sector facilities continue to face a chronic shortage of personnel, with an estimated 35% of designated positions actually filled.(5) In 2002, the last year for which data are available, the physician and registered nurses per population was 0.02 and 0.37 per 1,000 respectively.(6)

Economic growth, fiscal expansion and greater aid flows have permitted some rehabilitation and expansion of the health infrastructure since 2000. Hiring of new health workers resumed in 2003, although intake of new recruits is barely sufficient to offset natural decline of the health workforce through retirement and turnover. Chronic shortage and misdistribution of health personnel, coupled with frequent interruption of drugs and medical supplies are often cited as the chief operational challenges to effective health care delivery.(7)

Malaria in Mainland Tanzania

Over 93% of the Mainland Tanzania population lives in areas where malaria is transmitted. The remaining 7% live in areas that are normally malaria-free, predominantly at altitudes above 2000 meters with mean temperatures not exceeding 20°C. Three malaria epidemiological strata exist in Mainland Tanzania: 1) Unstable seasonal malaria; 2) stable malaria with seasonal variations; and 3) perennial malaria. Unstable seasonal malaria occurs in about 20% of the country, largely in the arid central plateau. In the coastal fringe, southern lowlands and regions bordering Lake Victoria malaria transmission is stable with very high transmission intensities. Seasonal malaria peaks occur at the end of the rainy season. The southern part of the country has a single main rainy season (March-May) while northern and western Tanzania experiences bimodal rainfall (November-January and March-May). The geographic distribution of malaria endemicity, based on ecological suitability for vector propagation, is presented in Figure 2.

Figure 2: Distribution of malaria endemicity, Tanzania 2007



Source: © Malaria Atlas Project(8)

Plasmodium falciparum is the parasite responsible for 96% of malaria infections in Mainland Tanzania, the other 4% being attributable to *P. malariae*, *P. ovale* and, very rarely, *P. vivax*. Mosquitoes from the *Anopheles gambiae* complex and the *An.funestus* group are the vectors responsible for nearly all malaria transmission in Mainland Tanzania.

Malaria was the leading cause of death among children under five years of age in Tanzania, causing around 24% of under-five mortality (approximately 51,000 deaths) in 2000.(9, 10) This figure excludes “indirect malaria mortality” via chronic anemia or the exacerbation of other conditions. The magnitude of indirect malaria mortality is unknown, but it is thought to be between 50% and 100% of “direct malaria mortality”.(3) If true, this would implicate malaria in at least one-third of all deaths in children under-five years of age in Mainland Tanzania prior to the scale-up of malaria control interventions.

Around 40% of under-five outpatient consultations and inpatient admissions are diagnosed with malaria. However, the condition is over-diagnosed due to reliance on clinical assessment alone. Eleven clinical studies in Tanzania over the past thirty years found that between 4% and 81% of (all age) fever cases were malaria positive.(11) Total expenditure on malaria prevention and treatment in Tanzania was estimated in 2000 to amount to \$2.2 per capita, absorbing 39% of total health expenditure and 1.1% of GDP.(12)

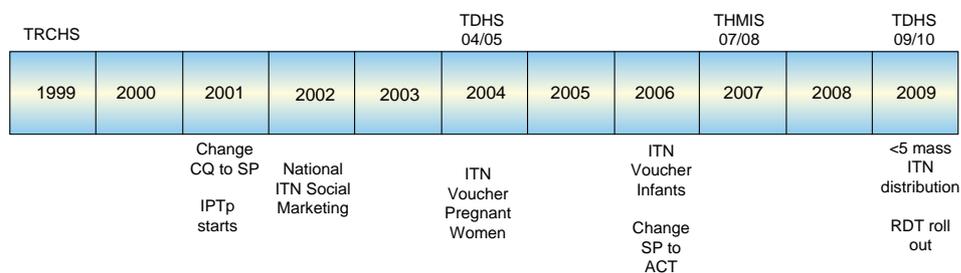
Malaria Strategy

The NMCP coordinates malaria control efforts in Mainland Tanzania. This unit, within the MOHSW's Department of Preventive Services, is responsible for designing strategies, developing guidelines, mobilizing funding, facilitating implementation and monitoring progress. Activities are coordinated under the Malaria Medium-Term Strategic Plans (2002-7; 2008-13).

Evolution of national malaria policy shows clear parallels with the global context. In the early part of the 20th century, malaria control was focused largely on protecting the colonial population and their settlements through a mixture of quinine treatment, environmental management and use of nets for personal protection. During the late 1950s, large-scale vector control using DDT was undertaken successfully in the Pare Mountains.(13) As eradication fell out of favor, Mainland Tanzania relied primarily on case-management, until the growth of chloroquine (CQ) resistance during the 1980s and 1990s worsened the malaria situation.(14, 15)

Following the formation of RBM (1998) and the Abuja Declaration (2000), a number of important developments took place in Mainland Tanzania. These include changes in first-line therapy for malaria (2001, 2006), the introduction of IPTp (2001), and a national ITN scale-up strategy (2002 onwards) using a mix of social marketing, vouchers for pregnant women (2004 onwards) and infants (2006 onwards), and free ITN distribution between 2009 - 2011. Indoor residual spraying was conducted in seven districts in Kagera Region during 2009 and 2010, see Figure 3.

Figure 3: Milestones in Malaria Strategy in Mainland Tanzania

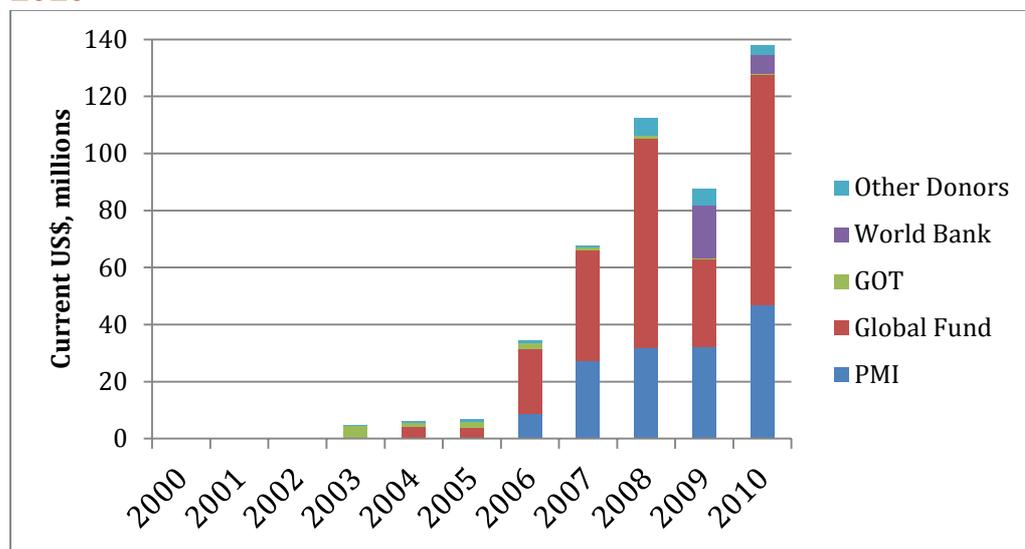


Resources and Inputs

In common with other countries in the region, a sharp rise in funding for malaria has been a driving force behind policy changes and has permitted a dramatic

scale-up of key interventions. Figure 4 summarizes over \$450 million in (budgeted) financial support for public malaria interventions from major sources, showing a 100-fold increase from 2000 to 2010. The steep increase in malaria funding commenced with receipt of the first Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) Grant in 2003. The pace of funding increased following the advent of PMI support and further Global Fund grants. Of the 2000-2010 total funding 55% came from the Global Fund, 32% from PMI, 6% from the World Bank, 4% from other donors and 3% from the Government of Tanzania. It should be noted that this estimate of Government contribution excludes large indirect expenditures on malaria, such as the substantial portion of front-line health-worker time spent on malaria-related tasks.

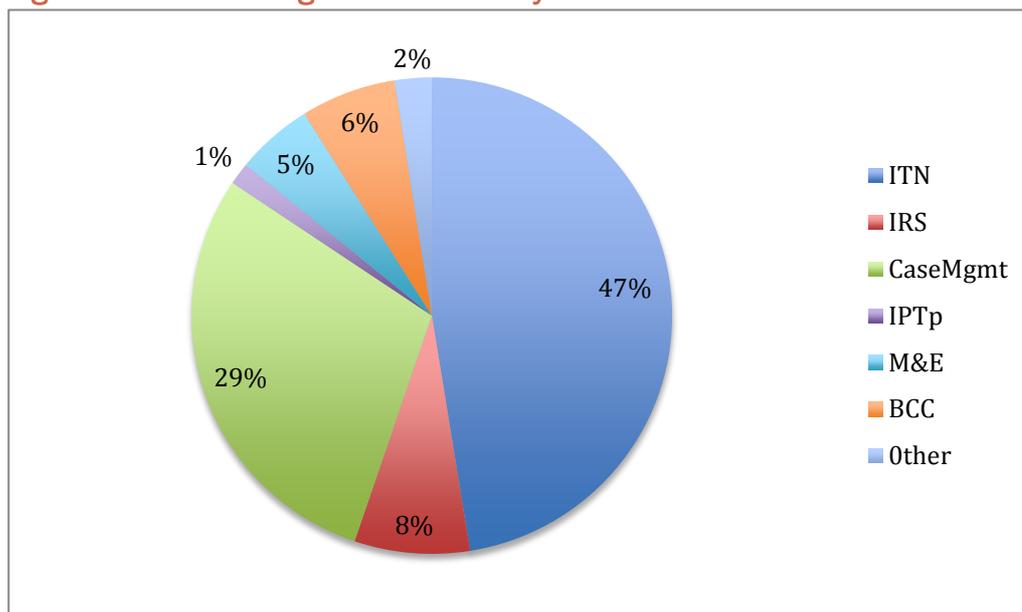
Figure 4: Trend in funding source for malaria control, Mainland Tanzania, 2000-2010



Note: Budgets as reported by the Government of Tanzania and donor agencies.

Disaggregation of total budgeted expenditures (\$450 million) over the period 2000-2010 by intervention reveals that the largest shares of funds were dedicated to ITNs and case management, which collectively absorbed two-thirds of the total resources available (Figure 5).

Figure 5: Malaria budget 2000-2010 by intervention



Note: ITN=Insecticide treated nets; IRS=Indoor residual spraying; CaseMgmt= Malaria case management; IPTp: Intermittent preventive treatment of malaria in pregnancy; M&E=Monitoring and evaluation; BCC=Behavior change communication.

Source: Budget reports 2000 – 2010.

INTERVENTION SCALE UP

Insecticide Treated Nets (ITN)

This section describes the scale-up of ITNs since the 1990s, assesses trends in ownership and use, describes equity of ITN use and analyses factors affecting ITN use. Unless otherwise stated, all data cited comes from the series of DHS surveys conducted in 1999, 2004/5, 2007/8 and 2010.

Background

Although nets have been used to protect individuals from mosquito nuisance for many decades, treatment of nets with synthetic insecticides only began in the 1970s. Dramatic results from the Gambia found that “sleeping under impregnated nets was associated with an overall reduction in mortality of about 60% in children aged 1-4 years”,(16) highlighting the potential of ITNs as a major tool for malaria control. Subsequent trials of ITNs in diverse transmission settings have demonstrated that ITNs can reduce all-cause mortality in children under-five by around 20%, lower the risk of clinical malaria illness by around 50%, reduce parasitemia by 13% and reduce the risk of high-density parasitemia by 20-29%.(17) ITNs have also been shown to affect a number of other malariometric indices, including reductions in severe anemia and splenomegaly. A more limited body of evidence also suggests that ITNs improve anthropometric outcomes in children.(18) In addition to the protection afforded to individual users, ITNs suppress the vector population and reduce their ability to transmit malaria. Thus the presence of ITNs in households and communities offers protection even to individuals who are not using nets.(19-21)

In high transmission settings, the protective effect of ITNs is most marked in children under the age of two years, during the vulnerable period when they have yet to develop partial immunity to malaria. The other high-risk group for whom ITNs provide substantial protection is pregnant women whose immunity to malaria is compromised. Insecticide-treated net use by women during pregnancy has been shown to reduce placental parasitemia, improve birth weight and reduce fetal loss and stillbirth. The protective effect is even greater during first/second pregnancies and for women with HIV infection.(22)

ITN Implementation

Early experience with ITNs in Tanzania began with the Muheza trial (Tanga Region) in the late 1980s. During the 1990s, three large sub-national ITN projects commenced (Bagamoyo, KINET, SMITN) covering areas ranging from single districts to four regions.(23, 24) In 2004 the first *national* ITN strategy began, with a focus on scaling-up the social marketing of ITNs and home-treatment kits across all of Mainland Tanzania (see Figure 6).

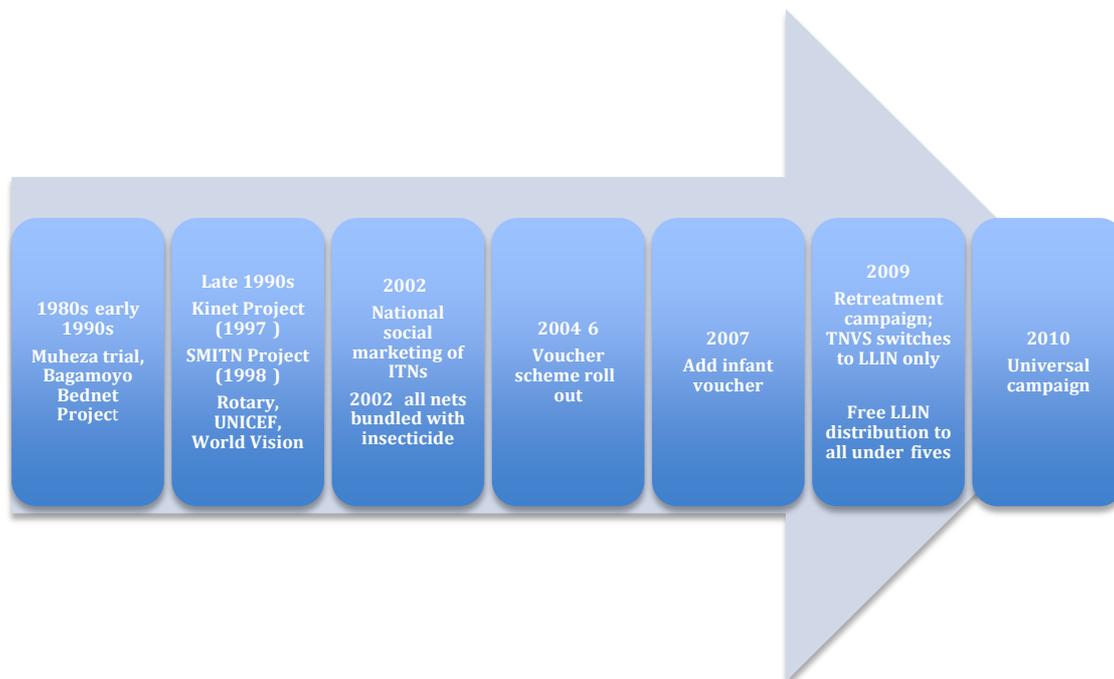
In 2004, Mainland Tanzania began an ITN voucher scheme on the basis of the model developed by the KINET project(25) and funded initially by Global Fund, and later by additional partners (including PMI). The original voucher, aimed at pregnant women, provided a discount of \$2.50 on the purchase of an ITN from a local retailer, with the client providing an average a top-up payment of \$0.80

(depending on the size of the net purchased). The Tanzania National Voucher Scheme (TNVS) was launched in October 2004 and expanded in phases to reach the whole country by May 2006. An additional voucher, targeted at infants and distributed at the time of measles vaccination (nine months of age) was added to the scheme in 2006. In 2009 the value of the voucher was increased and the beneficiary top-up was capped at \$0.30. At the same time the scheme switched to providing long-lasting insecticidal nets (LLINs) rather than nets bundled with a home-treatment insecticide kit.

To accelerate coverage and address the equity gap, the NMCP undertook an “under-five catch-up campaign-U5CC” in 2009-10 that distributed LLINs free of charge to all children under five years of age. In total, 8.7 million LLINs were distributed at a cost of \$69 million. Concurrent with the free distribution of LLINs, a behavior change campaign encouraged people to use their ITNs more consistently and a “retreatment campaign” sought to treat all existing polyester nets with longer-lasting insecticide. Actual retreatment of nets lagged behind both the original timeline and the numerical target of 6.5 million. The retreatment campaign was completed in July 2010 with a total of 3.7 million nets having been treated.

In 2008 Mainland Tanzania formally adopted a strategic goal of providing universal access to ITNs for the entire population. With financial support from the Global Fund, 18.2 million free LLINs were scheduled in the frame of the “Universal Catch-up Campaign-UCC” to be distributed between October 2010 and November 2011 to achieve the objective of providing one LLIN for every sleeping space not already protected.

Figure 6: Evolution of ITN implementation in Mainland Tanzania

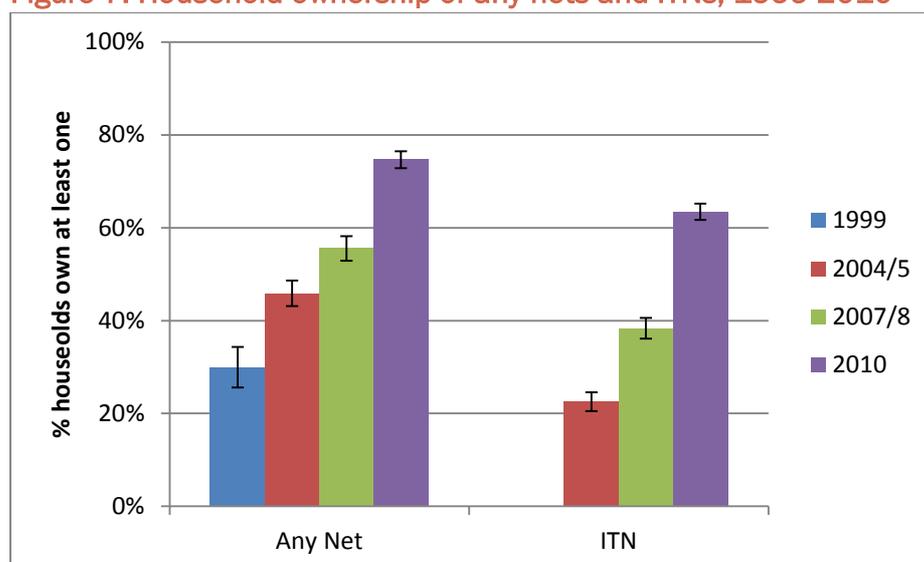


ITN Coverage Trends

ITN coverage trends are described below using two main indicators: household ownership and use by target groups. All data are from the DHS surveys.

The proportion of households that owned at least one net (treated or untreated) rose from 30% in 1999 to 75% in 2010. Ownership of treated nets (not measured in 1999 but likely to be below 1%) rose from 23% in 2004/5 to 63% in 2010 (Figure 7).

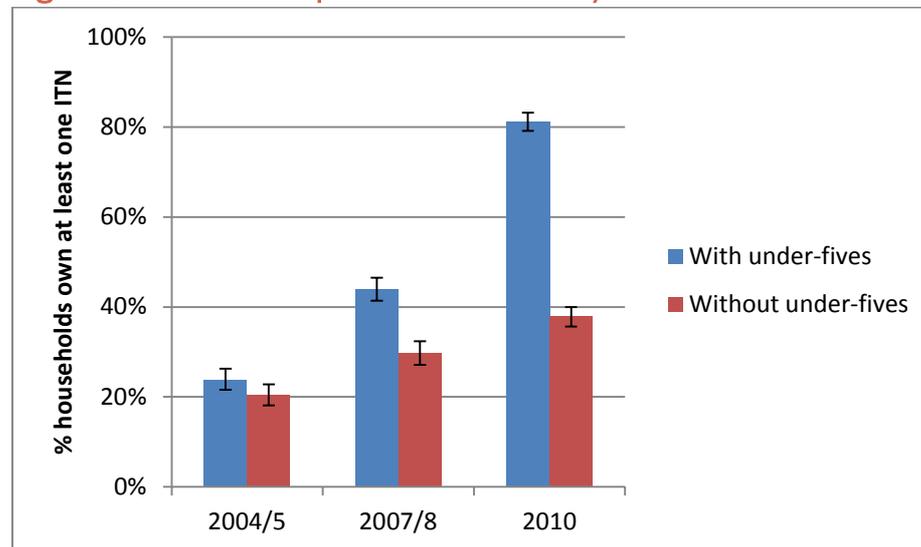
Figure 7: Household ownership of any nets and ITNs, 1999-2010



Note: The ITN ownership was around 1% in 1999.

Because the ITN strategy targeted pregnant women, infants and (later) all under-fives, it is not surprising that ownership rose much more rapidly between 2004/5 and 2010 in households with children under-five years of age than in other households (Figure 8). Over the same period, the mean number of ITNs per household in Mainland Tanzania rose from 0.43 to 1.23 nets.

Figure 8: ITN ownership in households with/without under-fives

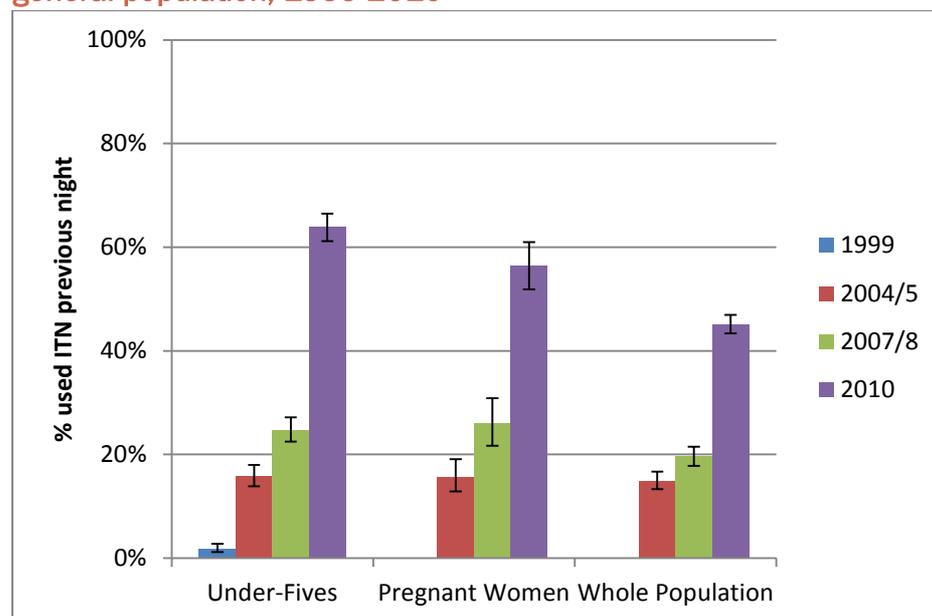


Use of ITNs followed a similar trajectory, with the greatest increase occurring between 2007/8 and 2010 (Figure 9). Among under-fives, use of ITNs the night before the survey rose from close to zero in 1999 to 64% in 2010. For pregnant women, ITN use rose from 16% (2004/5) to 56% (2010), while for the population as a whole, ITN use rose threefold from 15% in 2004/5 to 45% in 2010. It should be noted that in four regions, fieldwork for the 2010 survey either preceded¹, or overlapped², the mass distribution of LLINs to under-fives. The coverage attained at the end of the campaign is therefore expected to be marginally higher than the estimates at the time of survey. In all settings these measures preceded the universal coverage campaign.

¹ Dar es Salaam and Morogoro

² Coast, Dodoma and Arusha

Figure 9: ITN use among children under five years, pregnant women and the general population, 1999-2010



Equity in ITN Use

Table 4 presents data on equity of ITN use by under-fives and pregnant women by residence, wealth quintiles and mother’s education. Up until 2007/8, ITN use by under-fives in urban households was significantly higher than in rural households. An equity gap was also evident according to household wealth quintile and mother’s educational level. These differences disappeared completely in the 2010 survey results, reflecting a dramatic “catch up” by previously-disadvantaged groups. In all survey years, there was no significant difference in under-five ITN use between the sexes. Among pregnant women, there were similar disparities in ITN use according to residence, wealth and education in 2004/5 and 2007/8. As with under-fives, these equity gaps were no longer evident in the 2010 survey results.

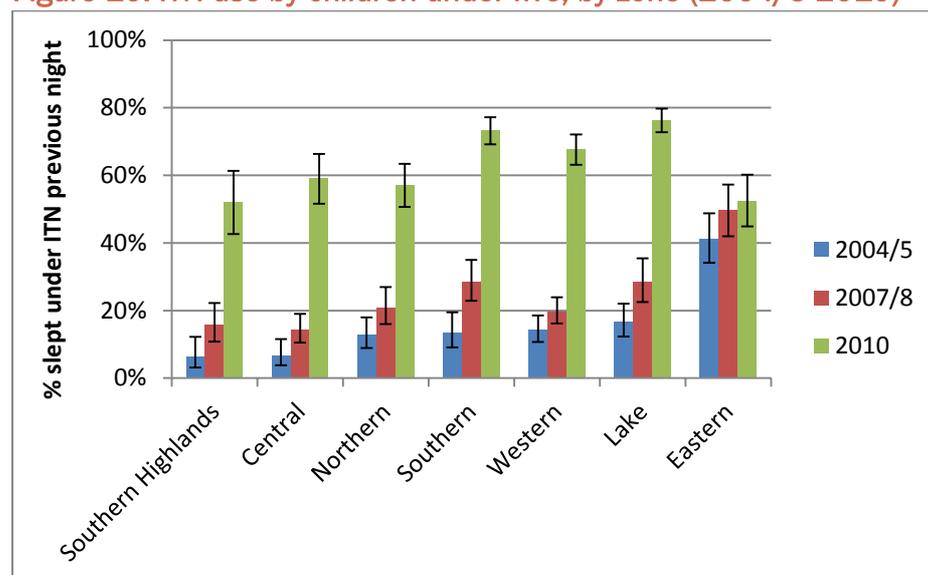
Table 4: Equity of ITN use by under-fives and pregnant women

	Under-fives			Pregnant Women		
	2004/5	2007/8	2010	2004/5	2007/8	2010
Sex						
Male	16%	25%	64%			
Female	16%	24%	64%			
Ratio Male:Female	1.0	1.0	1.0			
Residence						
Urban	41%	49%	65%	40%	48%	47%
Rural	10%	20%	64%	10%	21%	59%
Ratio Urban:Rural	4.2	2.5	1.0	4.0	2.3	0.8
Wealth						
Quintile 1 (Poorest)	4%	13%	61%	4%	13%	56%
Quintile 2	6%	16%	64%	7%	21%	63%
Quintile 3	12%	23%	62%	13%	26%	57%
Quintile 4	19%	28%	67%	16%	22%	58%
Quintile 5 (Least Poor)	50%	55%	67%	48%	19%	52%
Ratio Least Poor:Poorest	14.0	4.3	1.1	13.7	1.4	0.9
Mother's Education						
None	7%	17%	62%	6%	20%	54%
Primary Incomplete	9%	22%	64%	10%	21%	66%
Primary Complete	20%	29%	66%	21%	29%	58%
Secondary +	50%	49%	66%	48%	42%	46%
Ratio Secondary +:None	7.3	2.9	1.1	8.4	2.2	0.9

Geographic Variation in ITN Use

Across the seven (DHS) zones of Mainland Tanzania, there were considerable disparities in use of ITNs by under-fives (Figure 10). Eastern zone, which includes Dar es Salaam, had ITN use that was significantly higher than other zones in 2004/5 and 2007/8. In the 2010 survey, coverage in Eastern Zone was no longer higher than Southern Highlands, Northern and Central; and was lower than in Western, Southern and Lake. The comparatively small coverage increment in Eastern Zone between the last two surveys is most likely because 2010 DHS fieldwork in most of the zone preceded the under-five campaign.

Figure 10: ITN use by children under five, by zone (2004/5-2010)



Other Factors Associated with ITN Use

We examined a range of other household and individual factors associated with ITN use by under-fives in 2010 using a multivariate model, restricted to households with at least one ITN and controlling for sex, residence and wealth. Because of clustering, the model was restricted to the youngest child within each household. The results are presented in Annex 4.2.

No consistent relationship was seen with regard to mother's education. Insecticide-treated net use was lower in Southern Highlands compared to all other regions. Greater likelihood of ITN use was associated with smaller household size and a greater number of ITNs in the household.

ITN Summary

The various ITN campaigns over the past ten years have resulted in an increase in household ITN ownership from around 1% in 1999 to 63% in 2010. Following the free "under-five catch-up campaign" to distribute ITNs to children under-five years, ITN ownership in households with under-fives increased to about 80%. Accompanying the rise in ownership has been an increase in ITN use by children under-five years of age from about 2% in 1999 to 64% in 2010, while ITN use by pregnant women attained 56% in 2010. Inequities in ITN use by children under-five and pregnant women that were present earlier in the decade, disappeared by 2010. Given the large increase in ITN ownership between 1999 and 2010, it is plausible to expect a reduction in malaria-related morbidity and all-cause mortality among under-fives over this period.

Malaria Treatment

Background

Prompt and effective treatment of clinical malaria illness is one of the key malaria control strategies recommended by the World Health Organization.(26) In this section we begin with background on the evolution and implementation of treatment policies in Mainland Tanzania. Trends in prompt and effective treatment in children under five years of age are presented, together with analysis of factors underlying this indicator – such as treatment-seeking, timing, and choice of antimalarial.

Drug Policy

In the three decades up to 2001, the recommended first-line treatment for uncomplicated malaria in Mainland Tanzania was chloroquine (CQ) monotherapy. The first confirmed cases of chloroquine-resistant *Plasmodium falciparum* malaria acquired in Africa were reported in Tanzania in 1978. The increasing failure of CQ may lie behind an increase in the proportion of infective mosquitoes in Tanzania during the 1980s and 1990s(14) as well as the resurgence of malaria across Sub-Saharan Africa more generally.(27) In Mainland Tanzania, between 1997 and 1999, 52% (28%-72%) of children treated with CQ had treatment failure at day 14.(28, 29)

In 2001, Mainland Tanzania formally adopted sulphadoxine-pyrimethamine (SP) as first-line treatment for uncomplicated malaria, amodiaquine as the second-line drug and intravenous quinine for severe malaria. CQ was withdrawn from public sector health facilities and was banned from sale at private drug shops. This removal was actually quite effective in practice.(30)

However, it was recognized that resistance to SP would probably emerge rapidly and that SP represented an interim treatment policy. In 2001, 14% of children treated with SP had treatment failure at day 14.(31) Two years later, treatment failure rates were 15% at day 14 and 42% at day 28.(32)

Growing SP resistance,(33) WHO policy guidance and the prospect of Global Fund support prompted the Government of Tanzania to adopt new treatment policies in November 2006: artemisinin-based combination therapy (ACT) using artemether-lumefantrine (ALu) as first-line therapy and quinine as second-line therapy. Implementation of the policy commenced in early 2007. In clinical trials, the new first-line drug had treatment efficacy greater than 95%,(34-36) far surpassing SP. Surveillance of drug resistance has found no evidence of *P. falciparum* resistance to ALu in Mainland Tanzania to date.

Treatment Implementation

Stocks of SP were plentiful at the national and zonal levels throughout the period 2002-2004, mainly because of initial over-ordering of the drug in 2001. The drug was widely available at an affordable price in private health clinics and over-the-counter in drug shops, even though it was not government policy for SP to be

sold in ordinary shops or in lower-level pharmacies. However, dwindling national stocks and changes to the national drug distribution led to increasingly common stock-outs at health facilities during 2005 (F. Molteni, personal communication). In 2006 the shortages became more acute because anticipation of the imminent transition to ACT meant that stocks of SP were not replenished.

In the first two years after the change to ALu, no national level drug stock-outs occurred. However, procurement delays in 2009 led to diminishing inventory that soon filtered down to zonal medical stores, districts and health facilities. Widespread stock-outs of ALu at the health facility level became common in late 2009 and persisted through much of 2010. By mid-2010, most ALu in the country had been obtained through a series of emergency procurements funded by PMI. The shortage of ALu in the public sector was compounded by its inaccessibility due to cost (~\$10 per dose) in pharmacies.(37) At the same time, SP and other antimalarials remained widely available in drug shops.(37)

Historically, laboratory confirmation of malaria by microscopy in Mainland Tanzania has been restricted to hospitals, while clinicians in dispensaries and health centers have relied upon clinical diagnosis without confirmation. The introduction of rapid diagnostic tests (RDT) began in three regions (Coast, Iringa, Kagera) in 2009, a further two regions (Arusha, Manyara) in early 2010, and six more regions in late 2010.

Coverage of Prompt and Effective Treatment

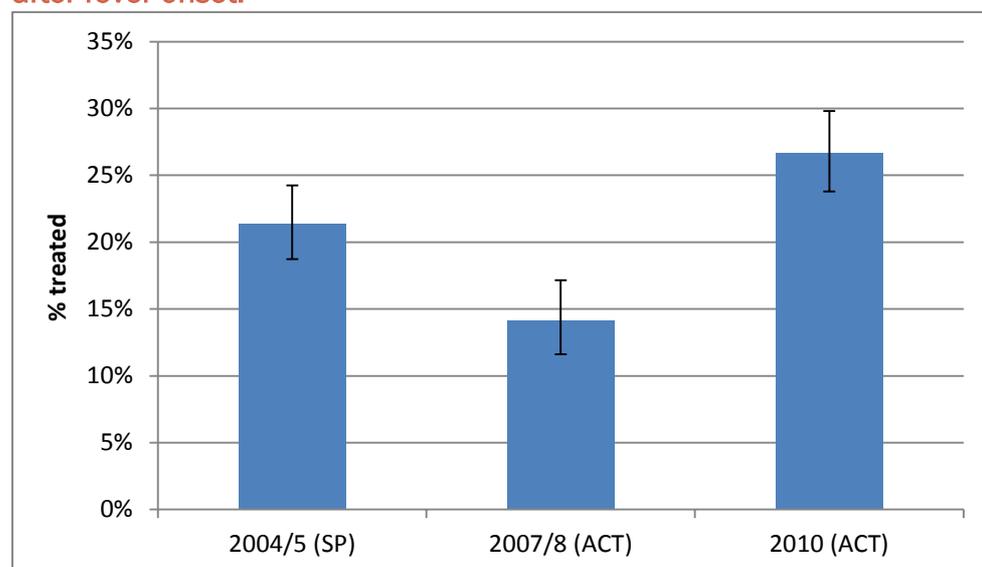
The DHS surveys ask mothers to report incidence of fever in children under-five years of age during the two weeks prior to the survey. Of children who experienced fever, a series of further questions³ are asked about treatment – including the provider, the timing of treatment and type of anti-malarial used.

The comparability over time of this indicator may be affected by the introduction of RDTs, which should lead to more selective diagnosis and treatment of children presenting with fever. For this evaluation, this bias is thought to be minimal because RDTs had been implemented in less than a quarter of regions in Mainland Tanzania by the time of the 2010 survey.

Figure 11, presents trends over the period of 2004/5 to 2010 in prompt treatment of children under the age of five years five with a first-line antimalarial.

³ The 1999 survey did not include questions on the type of antimalarial used for treatment and is therefore excluded from this time series analysis.

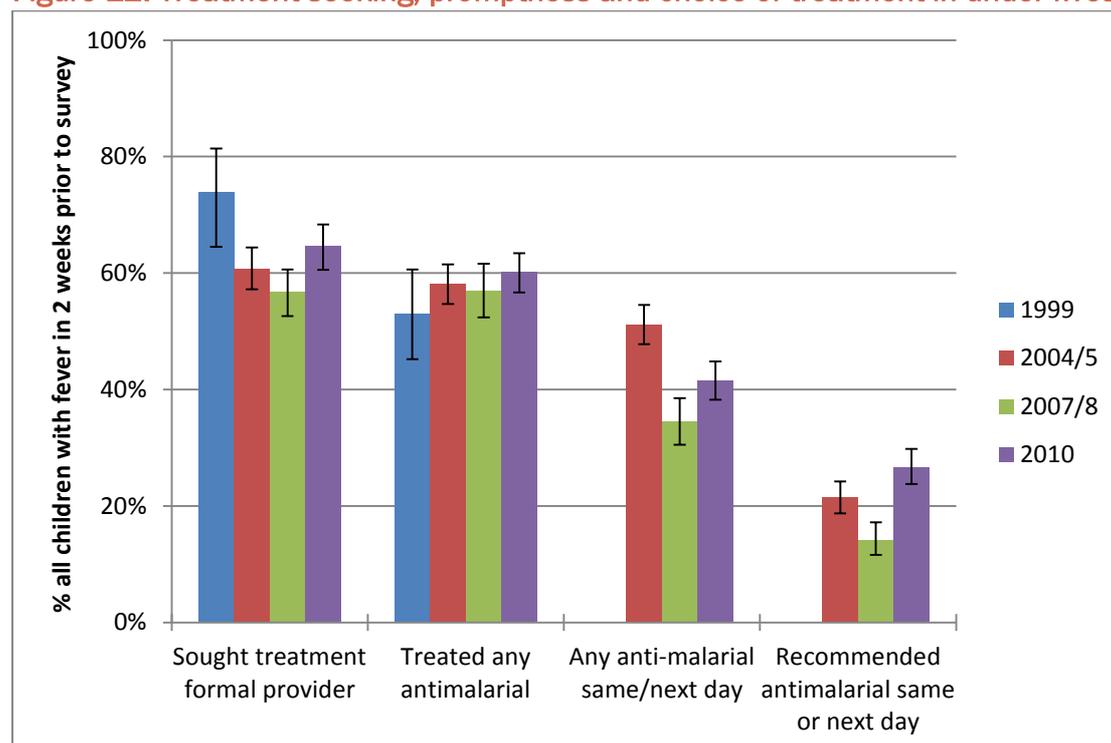
Figure 11: Percentage of children 0-59 months with fever during two weeks prior to survey who were treated with recommended antimalarial same or next day after fever onset.



Of all children who experienced fever in the two weeks prior to the survey, the proportion treated with recommended (first-line) anti-malarial the same day, or the day following fever onset, first fell (from 21% in 2004/5 to 14% in 2007/8), then rose again to 27% in 2010.

A number of underlying factors contribute to this indicator, including the likelihood of seeking treatment of any sort, likelihood of treatment with any antimalarial, the timing of treatment, and the likelihood of using first-line recommended treatment. Trends in these related indicators are depicted in Figure 12.

Figure 12: Treatment seeking, promptness and choice of treatment in under-fives



Apart from 1999, all surveys found that around 60% of children who had fever in the previous two weeks were reportedly taken to a formal health care provider, and almost all of these were treated with an antimalarial. However, the proportion of children treated promptly with any antimalarial dipped slightly in 2007/8 before rising again in 2010. The same trend pattern pertains in the final, compound indicator (prompt treatment with first-line therapy), suggesting that the trend observed is driven in part by the timing of treatment. However, among children treated with any antimalarial, there was also a change in the likelihood of treatment with recommended (first-line) therapy, from 24% in 2004/5 and 22% in 2007/8 to 35% in 2010 (Table 5). This change is offset by a reduction of corresponding magnitude in the proportion treated with amodiaquine.

Table 5: Percentage of children under five with fever in two weeks prior to survey, by type of anti-malarial used for treatment

Antimalarial	2004/5	2007/8	2010
ACT	n/a	22%§	35%§
SP	24%§	5%	3%
Quinine	12%	12%	10%
Amodiaquine	22%	18%	7%
Other	<1%	2%	1%
Total “any anti-malarial”	58%	57%	60%

§ - first-line treatment in respective survey years

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

Equity and Factors Associated with Treatment Access

A detailed description of equity by residence, wealth and other background characteristics is omitted because sample sizes for this indicator are too small, and confidence intervals too wide to observe significant differences across strata. However, it should be noted that there was no significant difference between the sexes in the likelihood of prompt treatment with recommended first line treatment in each of the last three surveys (data not shown).

Malaria Treatment Summary

In summary, prompt access to first-line anti-malarial treatment in children with fever has increased only slightly from 2004/5 to 2010. At 27%, the indicator falls well short of the national target of 60%. Nonetheless, it is noteworthy that 60% of children with fever are taken to a formal health provider for treatment, and more than two-thirds of these received an anti-malarial either same day, or the day following, fever onset.

During the period of 1999 to 2010, the change with the most public health significance was the transition from CQ to more effective drugs. In the late 1990s, more than one in two children with malaria who were treated with the recommended CQ therapy would experience treatment failure by day 14. After the introduction of SP in 2001-2, this proportion fell to 1 in 7. Following the introduction of ACT in 2007, treatment failure rates are now less than 1 in 20 at day 14.(32) It is plausible to anticipate that these dramatic improvements in treatment efficacy will have resulted in higher rates of parasite clearance, fewer chronic infections and better treatment outcomes.(38, 39)

Although the impact at the individual level of the new therapies is well known, the public health impact, especially of ACTs, is not yet well documented. Artemisinin rapidly reduce gametocyte carriage and consequently the transmissibility of malaria—possibly reducing malaria incidence. This transmission effect and its impact on malaria incidence is only now being quantified and further evidence is needed to appropriately account for ACT use.

Intermittent Preventive Treatment in Pregnancy (IPTp)

Background

Malaria prevention and control during pregnancy has a three-pronged approach, including IPTp, ITN use and case-management of clinical illness. This section focuses on IPTp.

Risks associated with malaria in pregnancy are greatest in the first and second pregnancies, during the second and third trimesters of each pregnancy, and in all pregnancies for women who are HIV positive. Malaria in pregnancy significantly raises the risk of severe illness in the pregnant woman and her baby, with serious adverse consequences, including severe anemia, miscarriage, intra-uterine growth retardation, pre-term birth and low birth weight.(40, 41) In high transmission settings, malaria is a significant indirect contributor to maternal death.(42) Malaria in pregnancy is thought to affect neonatal mortality risk via low birth weight and anemia in the newborn.(43, 44)

In 2002, WHO recommended(45) IPTp using SP as a prevention policy for countries with endemic malaria. The recommended regimen is at least two treatment courses of SP (three tablets each containing 500mg of sulfadoxine and 25mg of pyrimethamine), from the second trimester onwards, at least four weeks apart.

IPTp Implementation

Policy guidelines for introduction of IPTp in Mainland Tanzania were developed in 2001 and the launch of the program was announced in April 2002. Prior to the adoption of the IPTp policy, there already existed in Mainland Tanzania a common practice of CQ chemoprophylaxis during pregnancy.

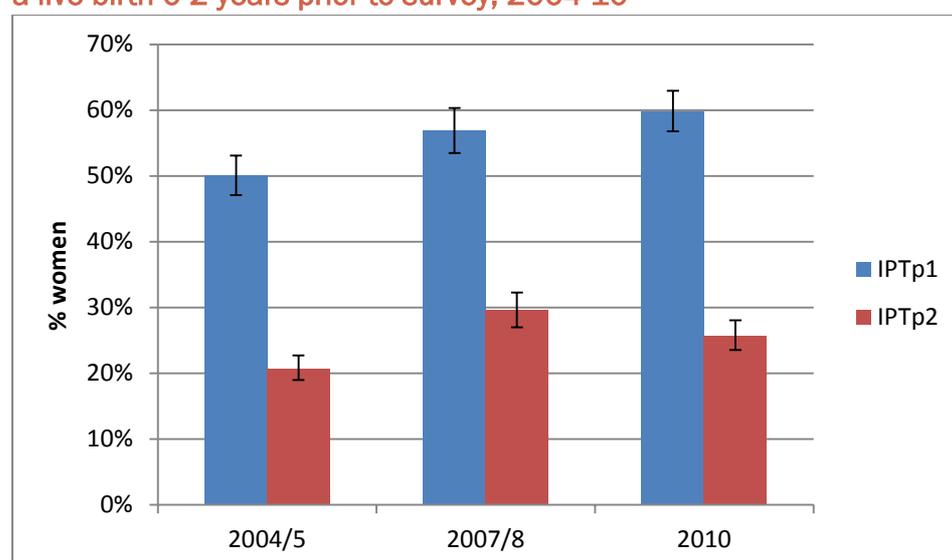
As described in the previous section, there were national shortages of SP in 2006-7 during the transition of malaria treatment policy to ALu. Moreover, districts initially had to purchase SP (from Medical Stores Department) using their drug budget, but policy prohibited charging women for IPT. In an effort to encourage facilities to order adequate SP stocks, the drug was “zero priced” by Medical Stores Department from 2009. In a non-random group of health facilities supported under the JHPIEGO program, 48% out of 29 health facilities in 2007 experienced SP stock-out, averaging 155/365 days out of stock. In 2009, 47% out of 38 facilities experienced stock-out, averaging 90/365 days out of stock.(46)

IPTp Coverage

The 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.

In 2010 IPTp coverage reached 26% (Figure 13). This was marginally higher than in 2004/5 (21%) but was not significantly different ($p>0.05$) from the 2007/8 estimate (30%). Thus, coverage of IPTp remains much lower than the national target of 80%. In all survey years, the coverage of IPTp first dose was higher than complete (two or more) doses.

Figure 13: Intermittent preventive treatment for malaria prevention, with at least two therapeutic doses of sulfadoxine-pyrimethamine in women (15-49 years) with a live birth 0-2 years prior to survey, 2004-10



Equity in IPTp

Changes in the equity of IPTp coverage with respect to residence, wealth and women's education are presented in Table 6.

Table 6: Equity of IPTp 2004/5-2010

	2004/5	2007/8	2010
Residence			
Urban	28%	42%	30%
Rural	19%	27%	25%
Ratio urban:rural	1.5	1.6	1.2
Household Wealth			
Quintile 1 (Poorest)	17%	24%	24%
Quintile 2	20%	26%	23%
Quintile 3	17%	27%	26%
Quintile 4	24%	30%	27%
Quintile 5 (Least Poor)	30%	47%	31%
Ratio Least Poor:Poorest	1.7	2.0	1.3
Woman's Education			
None	15%	21%	22%
Primary	23%	31%	26%
Secondary	31%	45%	35%
Higher	34%	69%	40%
Ratio Secondary+: None	2.1	2.1	1.6

In 2004/05 and 2007/08, IPTp coverage was significantly higher in urban areas than in rural areas (nine and 15 percentage points difference, respectively). In 2010, this difference had diminished to five percentage points and was no longer statistically significant. Similarly, there was a significant wealth gradient in IPTp coverage in 2004/5 and 2007/8, with coverage in women from the highest wealth quintile having coverage that was roughly double that of the lowest quintile. In 2010, there were no significant differences in coverage by wealth quintile. Women with secondary education or more had higher IPT coverage than those with primary education or less education in all survey years, but the gap in 2010 was smaller than in preceding surveys.

IPTp Summary

Following the introduction of IPTp in 2002, Mainland Tanzania attained coverage of 26% in 2010 - well short of the 80% target, and only five percentage points higher than in 2004/5. IPTp coverage remains very low considering that over 90% of women in Mainland Tanzania attend antenatal care (ANC) clinics, and coverage of other ANC interventions such as tetanus toxoid vaccination (48% in 2010) are much higher.

On a more positive note, equity of IPTp coverage has improved. There are no longer significant disparities between urban and rural areas, or wealth quintiles, and inequity by mothers' educational status has also diminished.

By the end of the evaluation period a higher proportion of women received their first dose of IPTp. Studies in Tanzania suggest that the lag in receiving the second dose cannot simply be attributed to delays in first ANC attendance.(47, 48) Instead, it would appear that inconsistencies between the ANC guidelines and the malaria guidelines led to confusion among health workers on the gestational age for IPT eligibility and the spacing of doses. Gross *et al.* conclude that adherence to the simplified WHO guideline in their study area would have raised IPTp coverage by 20% points.(49)

Other Interventions

Indoor Residual Spraying (IRS)⁴

IRS was introduced in Mainland Tanzania in 2007 following a request from the MOHSW to PMI/Tanzania to control malaria outbreaks in selected areas of Karagwe and Muleba Districts in Kagera Region in northwest Tanzania. In 2007 and 2008, 40,000 and 100,000 houses were targeted respectively in these two districts and 93% coverage was achieved. Due to the success in IRS implementation in these two districts, in 2009 the MOHSW requested that IRS operations in Kagera be scaled up from selective spraying in unstable malaria transmission areas to blanket spray in the remaining stable and high transmission areas of Kagera Region, adding approximately 340,000 additional houses. The scale up was implemented in the original two districts, Karagwe and Muleba, between January and June 2009 and an additional five districts (Chato, Biharamulo, Ngara, Bukoba and Missenyi) between August and October 2009. In 2009 the overall spray coverage in Kagera Region was 94% with 440,000 households sprayed and 2.2 million people protected. In 2010 another IRS round was successfully conducted in the seven districts of Kagera. In September 2010 IRS operations started in two additional regions, Mara and Mwanza. Cumulatively over 1.2 million house structures were targeted in the three regions of Lake Zone, to protect a population of over 6 million people. Surveillance by NMCP/WHO across 14 sites in Tanzania in 2009 found that mortality in *An. gambiae* mosquitoes exposed to lambda-cyhalothrin (0.05%), the insecticide used for IRS, was 71.3%-94.7%.

The Tanzania 2010 DHS survey results found that 1% of households in Mainland Tanzania had been sprayed in the past 12 months by the government or a private company. However, survey fieldwork preceded the expansion of the spraying program described above. If the programmatic targets for 2010 described above are achieved, IRS will have reached approximately 15% of the total Mainland population at the end of 2010.

Environmental Control and Larvicides

In Dar es Salaam, the Government of Tanzania launched an integrated malaria program which was supported by the Japan International Cooperation Agency (JICA) between 1988 and 1996, incorporating several vector control techniques, including IRS, ITNs, larviciding and environmental management. The latter included drain cleaning and reconstruction and “was considered as one of the most effective measures implemented by the program and led to significant reductions in the density of both *An. Gambiae* and *An. Funestus* in affected areas.”(50) The urban malaria program continued beyond the period of JICA support. Starting in 2004, a community-based system for surveillance of breeding sites and application of larvicide was scaled up to cover 15 out of 73 wards of Dar es Salaam, covering an area of 56 square kilometers and a combined population of over 600,000, approximately 1.5% of the population of

⁴ Information on IRS implementation comes from RTI program reports to PMI.

Tanzania.(51) Studies conducted at various stages of implementation of the urban malaria program documented a decline in parasitemia among school children,(52) a decline in the proportion of slide-positivity in inpatients and outpatients(53) and a reduction in the entomological inoculation rate (EIR).(54, 55) However, the concurrent implementation of multiple malaria control measures makes it difficult to attribute specific impact to individual interventions. The larviciding program in Dar es Salaam is still ongoing at the time of writing.

Intermittent Preventive Treatment in Infancy (IPTi)

A large-scale trial of IPTi was carried out in half of all wards within six districts in southern Tanzania between April 2005 and 2007. The trial formed part of a broader international research effort to gather evidence on the acceptability, feasibility, safety, effectiveness and cost-effectiveness of the strategy. IPTi was delivered as a single curative dose of SP during the first year of life during routine vaccination clinic contacts. A follow-up survey in 2006 found that 76% of eligible infants were reported to have received at least one dose of IPTi. The trial found some evidence that the intervention was associated with reduced malaria parasitemia and higher mean hemoglobin. A major decline in mortality in both case and control areas occurred in the IPTi trial area following distribution of LLINs to all under-fives in 2006 (described further in the case study). This left the trial sample size under-powered to detect mortality change associated with the IPTi intervention.(56) Subsequent to the trial, routine implementation of IPTi has not been scaled up in Tanzania, so this intervention was limited to the six districts in Lindi and Mtwara Regions between 2005 and 2007.

MALARIA MORBIDITY

Morbidity Indicators and Data

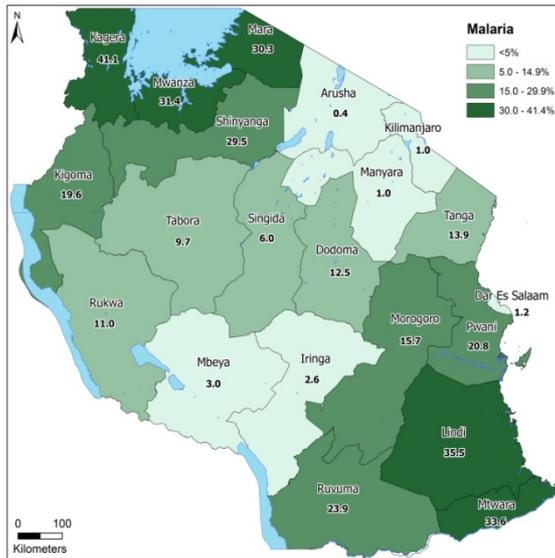
In this section we examine changes in malaria parasitemia, anemia and fever in children under-five years of age. We focus primarily on population-based data from the DHS survey series representative of Mainland Tanzania. In children 6-59 months of age malaria parasitemia was measured in only one survey (2007/8) and anemia in three surveys (2004/5, 2007/8 and 2010). Fever, in children under-five, during the two weeks prior to survey was measured in all survey years.

Separate large-scale surveys on anemia and parasitemia in under-fives in sentinel sites were conducted by the NMCP in 2006 and 2008. These provide some insight on changes over a very short time period, but are not directly comparable to the DHS estimates because of differences in the sampling frame and methodologies. Repeat cross-sectional survey data that are comparable over time are available also for the Ifakara Demographic Surveillance System (DSS) area (2001-2010) and from the intermittent preventive treatment in infants (IPTi) trial (control arm) in Lindi and Mtwara. We will also present malaria morbidity data from two hospitals for which quality-assured data is available on the proportion of inpatient admissions of children under-five who tested positive for malaria.

Figures 14a-c below provide a spatial representation of our three malaria morbidity measures (parasitemia, severe anemia and fever). There is a clear spatial congruence across the three indicators, supporting the implicit assumption that anemia and fever prevalence are associated with malaria endemicity.

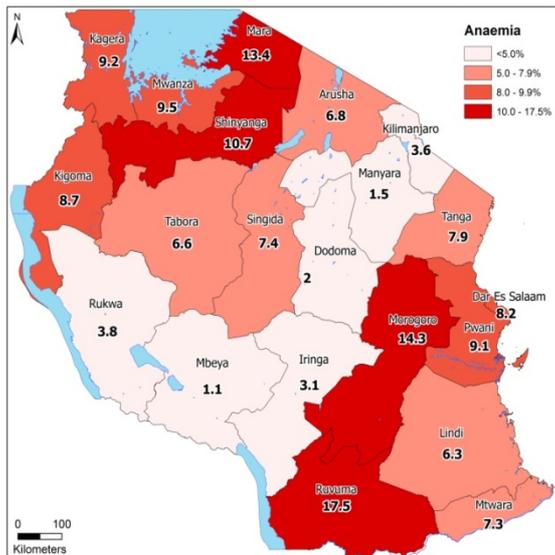
Figure 14: Malaria morbidity (parasitemia, severe anemia and fever), Mainland Tanzania, 2007/8

a.) Parasitemia (6-59 months), 2007/8



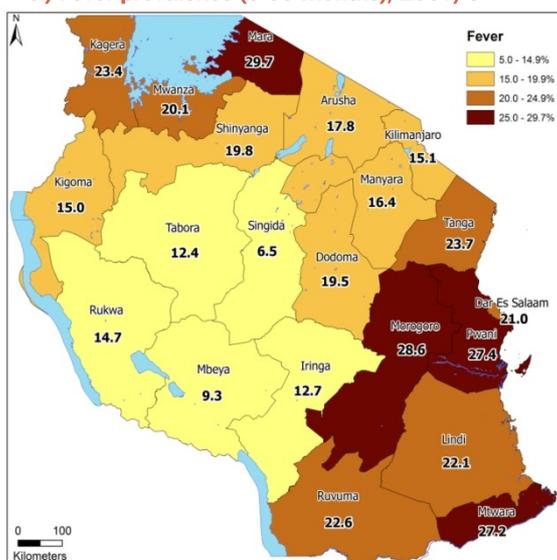
Regional variation in *P. falciparum* parasitemia, measured by RDT, Mainland Tanzania 2007-08.

b.) Anemia prevalence (6-59 months), 2007/8



Regional variation in severe anemia (Hb < 8.0 g/dL) prevalence, Mainland Tanzania, 2007-08.

c.) Fever prevalence (0-59 months), 2007/8



Regional variation in fever (previous two weeks) prevalence, Mainland Tanzania, 2007-08.

Malaria Parasitemia

Malaria Parasitemia in Mainland Tanzania in 2007/8

The 2007/8 Tanzania HIV and Malaria Indicator Survey (THMIS) tested children aged 6-59 months for the presence of *P. falciparum* parasites using RDTs (Paracheck Pf™ test). Timing of the survey was October 2007 to March 2008, which was predominantly in the dry season. Table 7 presents malaria parasitemia among children aged 6-59 months, stratified by age.

Table 7: Malaria parasitemia in children 6-59 months, by age, Mainland Tanzania, 2007/8

Age in months	Percentage of children with malaria parasitemia	95% CI	Weighted sample size
6-11	9%	6.8-12.7	743
12-23	15%	12.2-17.7	1415
24-35	20%	17.1-23.6	1372
36-47	20%	16.9-23.6	1273
48-59	23%	19.0-26.3	1408
Total	18%	15.9-20.5	6211

For Mainland Tanzania as a whole, 18% of children aged 6-59 months tested positive for malaria in 2007/8. Parasitemia increased with age over the first two years of life, reaching a plateau of around 20% among children aged 2-4 years.

Table 8 examines variations in malaria parasitemia among children aged 6-59 months, stratified by various individual and household characteristics. Estimates are rounded to the nearest whole percentage.

Table 8: Malaria parasitemia in children 6-59 months, by background characteristics, Mainland Tanzania, 2007/8

Background characteristics	Percentage of children with malaria parasitemia	95% CI	Weighted Sample Size
Sex			
Male	18%	16.0-21.0	3,100
Female	18%	15.4-20.7	3,111
Residence			
Urban	7%	3.3-14.4	1,126
Rural	20%	17.9-23.0	5,085
Zone			
Western	22%	17.9-25.9	1,398
Northern	4%	2.7-6.9	875
Central	10%	5.2-18.7	411
Southern Highlands	5%	3.3-8.3	987
Lake	34%	27.6-41.6	1,338
Eastern	10%	6.7-16.1	645
Southern	30%	24.5-36.2	558
Household Wealth			
Poorest	23%	19.4-28.1	1,442
Second quintile	22%	18.3-25.9	1,382
Third quintile	21%	16.3-26.1	1,359
Fourth quintile	15%	11.2-18.8	1,140
Least Poor	4%	2.8-6.3	888
Mother's Education			
None	23%	18.1-28.0	642
Primary Incomplete	21%	17.4-24.1	2,170
Primary Complete	16%	14.1-19.1	3,201
Secondary+	4%	1.6-10.6	198
Altitude			
<1000	18%	15.7-21.4	4,562
1000m+	18%	14.6-21.2	1,632
ITN Use			
No	18%	15.9-20.7	4,750
Yes	18%	14.8-21.7	1,461
Total	18%	15.9-20.5	6,211

Malaria parasitemia was nearly three times as high in rural (20%) than in urban areas (7%). Parasitemia was also higher among children from poorer households, and those whose mothers had less than a secondary level education. Somewhat surprisingly, there was no difference in malaria parasitemia by altitude (above/below 1000m), nor by ITN use the night before the survey. As already depicted in Figure 14, parasitemia was highest in the Southern and Lake zones, lowest in the Northern and Southern Highlands zones, and intermediate in the Central and Eastern zones.

Parasitemia Trend – NMCP Surveys 2006-2008

For an indication of trend directions, we must turn to other data sources that have repeat measurements over time. National-scale surveys were carried out by the NMCP in 2006 and 2008 across 21 districts with a purposive sample methodology⁵ and malaria detection using microscopy. Fieldwork for both surveys was conducted in June-July. Although survey methodology differed from the THMIS, these two NMCP surveys are at least comparable with each other. The results (Table 9) showed a statistically significant decline of 3.3 percentage points in malaria parasitemia among under-fives between 2006 and 2008, a relative reduction of 17%.

Table 9: Malaria parasitemia in children under-five years of age, Mainland Tanzania, 2006-2008

2006			2008		
Percentage of children with malaria parasitemia	95% CI	Sample size	Percentage of children with malaria parasitemia	95% CI	Sample size
19.4%	18.6-20.3	8249	16.1%	15.2-17.2	5,341

Source: NMCP, in Lottner & Lengeler, June 2010

In the absence of corroborating data it would not be reasonable to reach a conclusion on trends from these data because they comprise only two point estimates, temporally too close, and the magnitude of difference might be explainable by chance climatic differences between surveys.

Parasitemia Trend, Lindi and Mtwara, 2004-2007

In 12 divisions of Lindi and Mtwara Regions, three large scale cross-sectional household surveys were carried out in 2004, 2006 and 2007 in the context of a community-randomized study of an IPTi trial. To exclude any potential bias from the IPTi intervention, the results reported here are drawn from the control arm of the study. Malaria parasite prevalence data was collected from 8,706 people in 2004, 2,962 people in 2006, and 1,680 people in 2007. Infants aged 2-11 months contributed 3% to the sample each survey year after adjustment for the different sampling fractions for the total survey population. The presence of *P. falciparum* malaria parasitemia was tested using RDTs (Paracheck Pf™).

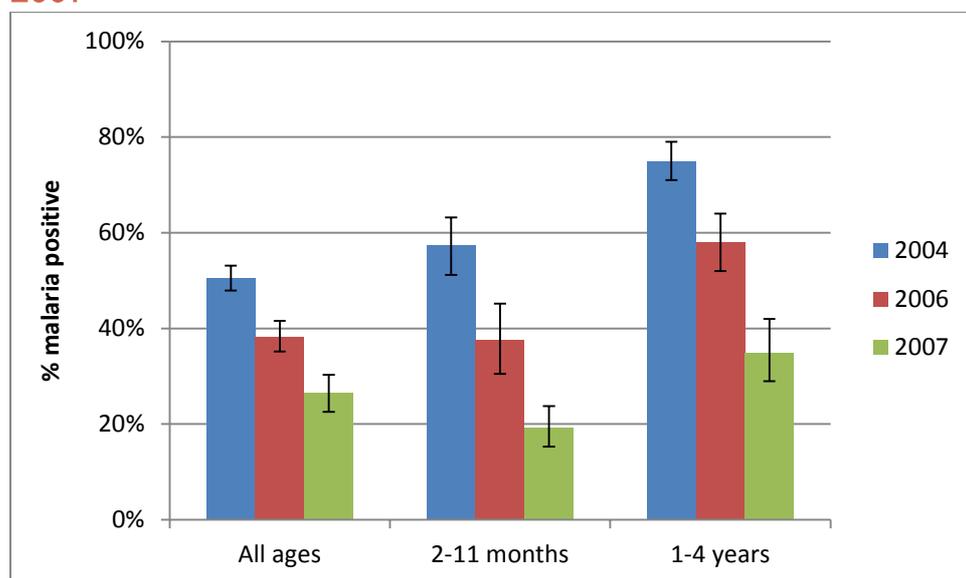
For the total population, a 12 percentage point reduction in malaria parasitemia was observed each survey year leading to a halving of overall malaria parasite prevalence during the study period from 50.5% (47.9-53.1) in 2004 to 38.3% (35.2-41.6) in 2006 and 26.5% (22.6-30.3) in 2007 (chi² test for trend p<0.001). Among infants aged 2-11 months, malaria parasite prevalence declined by almost 20 percentage points each survey year leading to a reduction in

⁵ One district for each of 21 regions; two villages in each district – one close and the other distant from – a health facility. Under-fives were randomly sampled within villages.

prevalence by two-thirds between 2004 and 2007, from 57.3% (51.2-63.2) in 2004, to 37.6% (30.5-45.2) in 2006, and 19.2% (15.3-23.8) in 2007 (chi² test for trend p<0.001). Similarly, in children 1-4 years of age, malaria parasite prevalence halved during the study period from 75% (71-79) in 2004, to 58% (52-64) in 2006, and 35% (29-42) in 2007 (chi² test for trend p<0.001), (Figure 15).

Lindi and Mtwara Regions are atypical in that they had the highest under-five mortality rates in the country(57) and relatively high malaria endemicity (based on climatic suitability for transmission).(8) These regions are also relatively poorer than other regions of Mainland Tanzania. The major decline in malaria parasitemia occurred after the distribution of ITNs targeting all under-fives in these regions in 2005. Changes in ITN ownership and use, parasitemia and other malariometric indices from this area are explored in further detail in the case study later in this report.

Figure 15: Malaria parasitemia, in Lindi and Mtwara, Southern Tanzania, 2004-2007

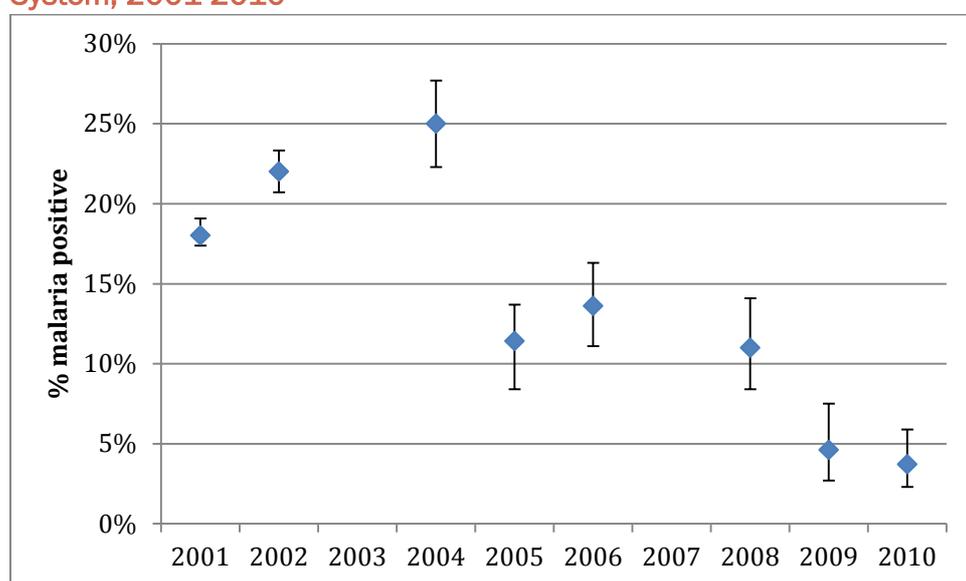


Malaria Parasitemia Trend, Ifakara Demographic Surveillance System, 2001-2010

Malaria epidemiology and transmission have been studied for over twenty years in the Ifakara DSS area located in the Kilombero Valley in Morogoro Region. Periodic surveys of all-age malaria parasitemia [2001-2006 determined by microscopy and from 2008 and beyond by RDT (Paracheck Pf™)] in a random sample of households within the DSS area have been undertaken for eight out of the last ten years. The timing of fieldwork was similar for all surveys and followed the long rains (2001-2006, June-September; 2008-2010 May-September). Sampling methodology, sample sizes, confidence intervals and measurement methods are described more fully in Annex 1.8.

During the period of 2001 to 2004, all-age malaria parasite prevalence ranged between 17% and 25% (Figure 16). Between 2005 and 2008, prevalence was substantially lower, ranging from 11% to 14%. Malaria parasite prevalence results for the latest two years are lower still: 4.6% in 2009 and 3.7% in 2010. Like the Lindi/Mtwara area, the Ifakara DSS area is situated in an area of unusually high initial malaria transmission (EIR was 349 infective bites per person per year between 2001-3 and recently was determined to be 81). The area was one of the first in Tanzania to begin the social marketing of ITNs (KINET 1996-2000) so that the rise in ITN coverage in this area began several years earlier than the rest of the country. The relationship between ITN scale-up and other malaria-related variables in this area is described in more detail as a case study later in this report.

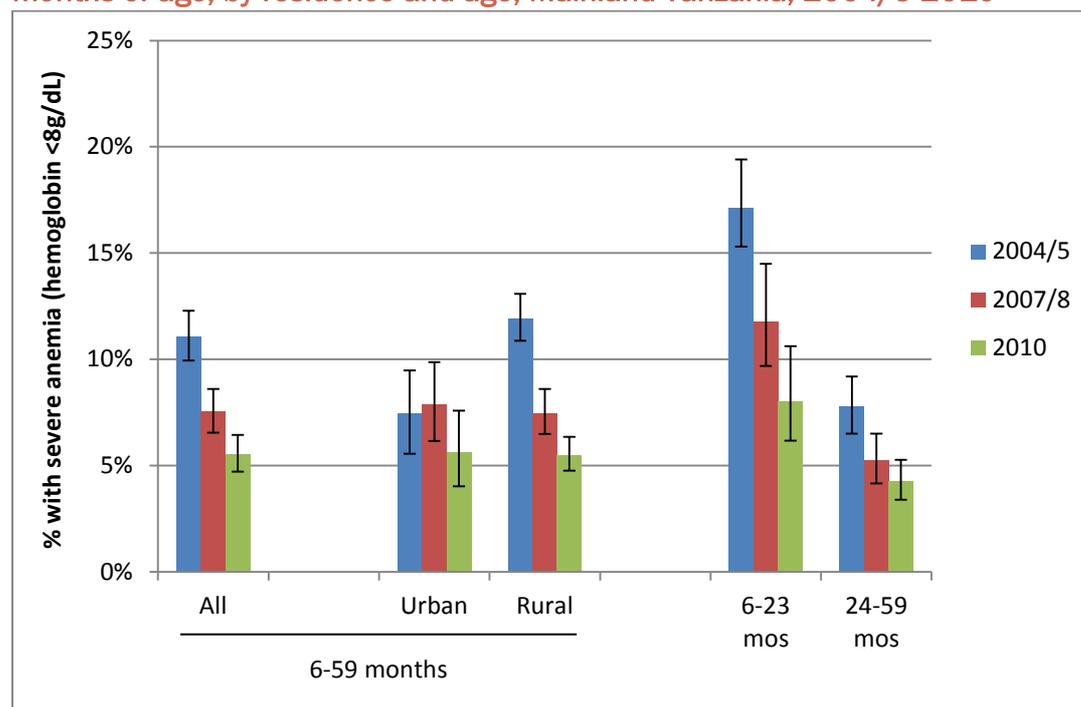
Figure 16: Malaria Parasitemia (All Age) in Ifakara Demographic Surveillance System, 2001-2010



Severe Anemia Trends

National estimates of the prevalence of severe anemia (Hb <8 g/dL blood) in children aged 6-59 months are available from the last three DHS surveys. The results are shown in Figure 17.

Figure 17: Trends in severe anemia (Hb< 8g/dL) prevalence in children 6-59 months of age, by residence and age, Mainland Tanzania, 2004/5-2010



Between 2004/5 and 2010 the prevalence of severe anemia among children aged 6-59 months halved, declining from 11.1% (10.0%-12.3%) to 5.5% (4.7%-6.4%). In all survey years, prevalence of severe anemia was higher among children younger than 2-5 years (Figure 17). The reduction in severe anemia in children aged 12-23 months was greater than in other age groups when comparing either the 2004/5 or 2007/8 survey to 2010 (Table 10).

Table 10: Relative reduction in severe anemia, 2004-2010 by age group (months)

Age	2004/5	2007/8	2010	Relative change 2004/5-2007/8	Relative change 2004/5-2010	Relative change 2007/8-2010
6-11 mos.	16.0%	11.2%	9.6%	-30.3%	-40.1%	-14.2%
12-23 mos.	17.7%	12.1%	7.3%	-31.8%	-59.0%	-39.9%
24-35 mos.	10.7%	8.1%	5.5%	-24.8%	-48.7%	-31.8%
36-47 mos.	8.1%	5.0%	4.5%	-38.6%	-44.4%	-9.5%
48-59 mos.	4.2%	2.8%	2.8%	-34.0%	-34.5%	-0.7%

Gender and Socio-Economic Disparities

Disparities in the prevalence of anemia by gender and socio-economic characteristics are shown in Table 11. No significant difference in anemia prevalence was evident in any of the three surveys. Anemia prevalence in rural areas (11.9%, CI 10.6-13.3%) exceeded that of urban areas (7.4%, CI 5.6-9.7%) in 2004/5, but there was no difference by residence in 2007/8 or 2010 (equity ratio 1.1 and 1.0, respectively). Disparities by household wealth quintile were significant in 2004/5, but in neither of the two subsequent surveys,

while disparities by mother's educational status did not reach statistical significance in any survey year.

Table 11: Severe Anemia (Hb<8g/dL) prevalence in children 6-59 months of age, by background characteristics, Mainland Tanzania, 2004/5-2010

Characteristic	2004/5	2007/8	2010
Sex			
Male	11.1%	8.4%	5.0%
Female	11.1%	6.6%	6.1%
Ratio Male:Female	1.0	1.3	0.8
Residence			
Urban	7.4%	7.9%	5.6%
Rural	11.9%	7.4%	5.5%
Ratio Urban:Rural	0.6	1.1	1.0
Wealth			
Poorest	14.0%	8.8%	7.1%
Second Quintile	12.1%	7.5%	5.0%
Third Quintile	12.1%	7.4%	5.1%
Fourth Quintile	8.5%	5.6%	4.8%
Least poor	7.0%	8.1%	5.5%
Ratio Least Poor: Poorest	0.5	0.9	0.8
Education (Mother)			
None	14.3%	9.6%	6.8%
Primary Incomplete	11.1%	6.6%	6.4%
Primary Complete	10.0%	7.2%	4.9%
Secondary+	8.1%	8.6%	6.7%
Ratio Secondary+:None	0.6	0.9	1.0
Total	11.1%	7.5%	5.5%

Severe Anemia Trends and Malaria Risk

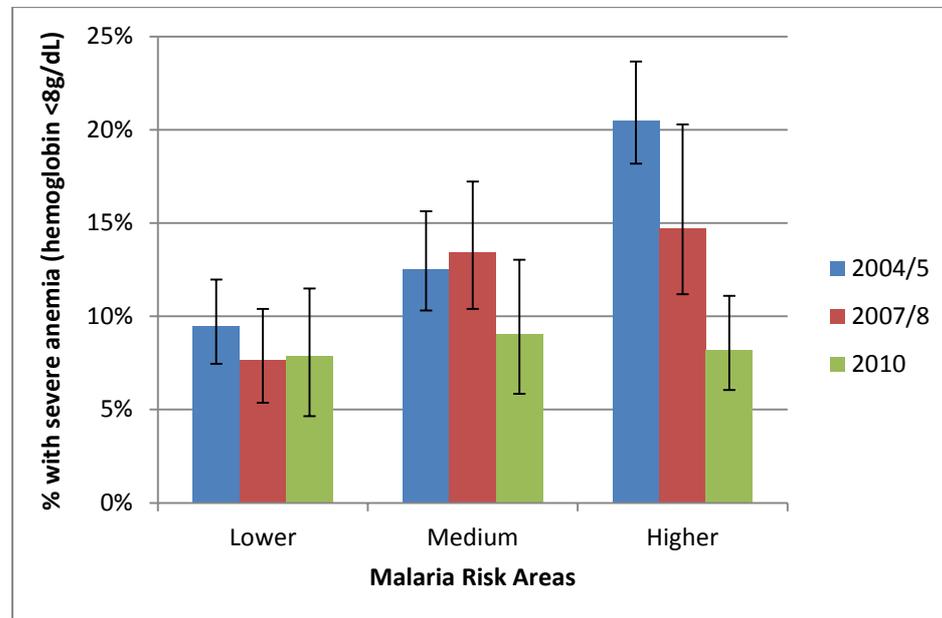
If the anemia reduction is associated with malaria decline, one would expect to see a higher baseline and greater reduction in anemia prevalence in areas with relatively higher risk of malaria.

Three risk "terciles", each comprising six or seven regions, were constructed using regional malaria parasitemia (6-59 months) prevalence in 2007/8 as a proxy measure of relative malaria risk. Respective malaria parasitemia for the three categories in 2007/8 was: 0.8%-9.7% (lower); 9.9%-23.5% (medium); and 29.7%-40.4% (higher). Trends over time for anemia prevalence (6-23 months) in these three categories are shown in Figure 18.

In 2004/5, anemia prevalence was significantly higher among children (6-23 months) living in "higher risk" regions (20.5%, CI 17.3-24.1%) than in medium (12.6%, CI 10.3-15.3%) or lower risk (9.5%, CI 7.5-12.0%) regions. Substantial reductions in severe anemia were seen in higher malaria risk areas between 2004/5 and 2010, but not in medium or lower risk areas. As a result, by 2010,

severe anemia prevalence in higher, medium and lower malaria risk areas was comparable.

Figure 18: Trends in severe anemia (Hb <8g/dL) prevalence in children 6-23 months of age, by malaria risk areas, Mainland Tanzania, 2004/05, 2007/08 and 2010



Fever Prevalence

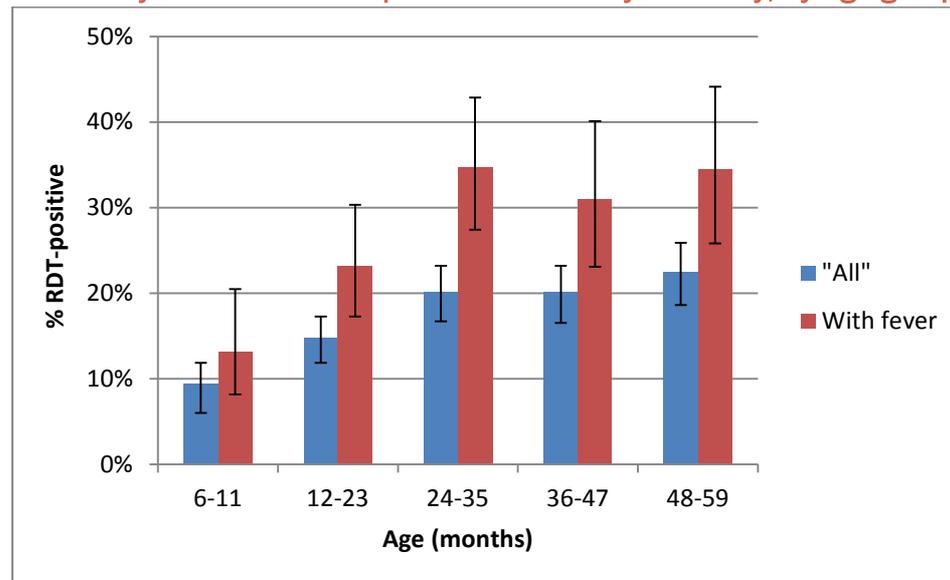
In Mainland Tanzania, good quality facility-based morbidity data are not available. However, population-based estimates of fever in children under-five years of age have been collected in every DHS survey going back to 1991/2.

In addition to the RBM-MERG morbidity indicators, this report includes a description of trends in fever, defined as the proportion of children under five years of age who had a fever within a two week period preceding the survey, as reported by their mother or caregiver. This indicator is included because an association between fever prevalence and malaria control is biologically plausible, and national trend data are available, but reliable national facility-based measures of “presumed malaria” are not available in Mainland Tanzania.

The DHS questionnaire requested mothers to report any incidence of fever among children under-five years of age, during the two-week period preceding the survey. However, it should be noted that fever is an imperfect proxy of the burden of malaria disease because malaria is not the sole cause of fever. A systematic review(11) of 39 studies across 16 countries in sub-Saharan Africa between 2001 and 2009 found that just 22% of children (of various age groups) presenting with fever tested positive for malaria. In the 2007/8 THMIS, 27% of children (6-59 months) who had experienced fever in the two weeks prior to the

survey also tested positive for malaria on the day of the survey⁶ and this proportion rose with age. Compared to the “background” malaria positivity (all children under-five), children with fever in the 24-59 month age group had malaria parasite prevalence that was 11-15 percentage points higher (Figure 19). For those children (6-59 months) that were febrile on the day of the survey and were tested, 40.4% (33.0%-48.2%, n=355) were RDT-positive.

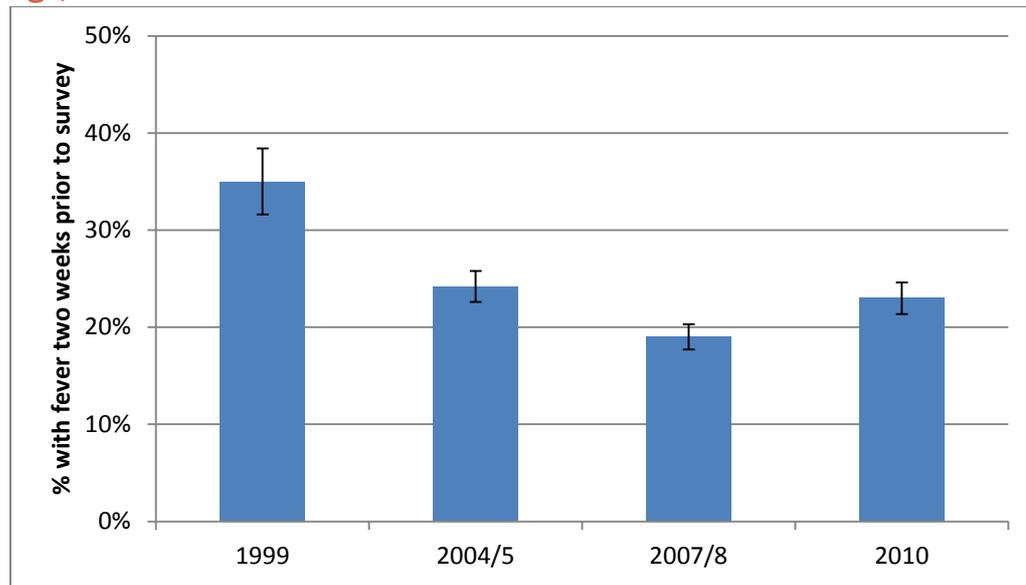
Figure 19: Proportion of all children and those with fever in the two weeks prior to the survey who tested RDT-positive on the day of survey, by age group, 2007/8



During the 1990s, DHS surveys found that roughly a third of under-fives had suffered from fever in the two weeks prior to the survey, and there was no significant change across the three surveys (1991/2, 1996, 1999 – data not shown). Between 1999 and 2007/8, a statistically significant decline in fever prevalence occurred between each successive survey (Figure 20). The estimate for 2010 is marginally higher than in 2007/8, but it should be noted that fieldwork in 2010 included both rainy and dry seasons, while earlier surveys were predominantly “dry season.”

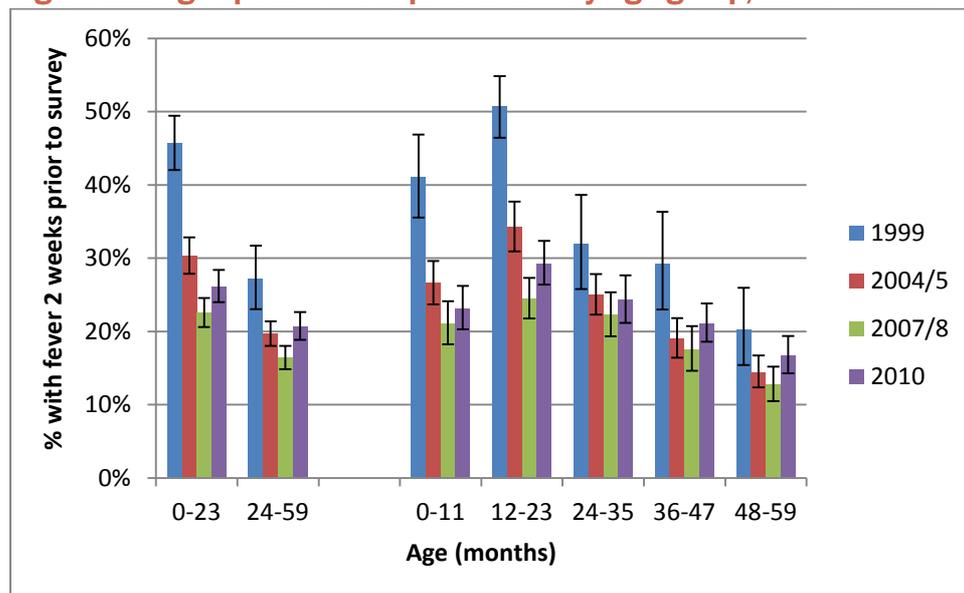
⁶ Note that the HRP2 based RDT tests positive for two weeks after treatment with an antimalarial because of the persistence of the antibody markers detected by the test.

Figure 20: Fever during the two weeks prior to survey, children under-five years of age, 1999-2010



Trends in fever prevalence show a distinctive age-related pattern. Prevalence was significantly higher in children under-two than in older children for all survey years, with 45.7% (42.0-49.4) of children 0-23 months with a fever compared to 27.2% (23.0-31.7) of children 24-59 months in 1999 and 26.1% (24.0-28.4) of 0-23 month olds vs. 20.7% (18.9-22.7) of 24-59 month olds in 2010. Among under-twos, fever halved between 1999 and 2007/8, while for children over two years of age the relative decline was by one-third (Figure 21). The result is a much “flatter” distribution of fever across age groups in recent years, compared to the marked elevation in fever rates among under-twos reported in 1999.

Figure 21: Age-specific fever prevalence by age group, 1999 - 2010

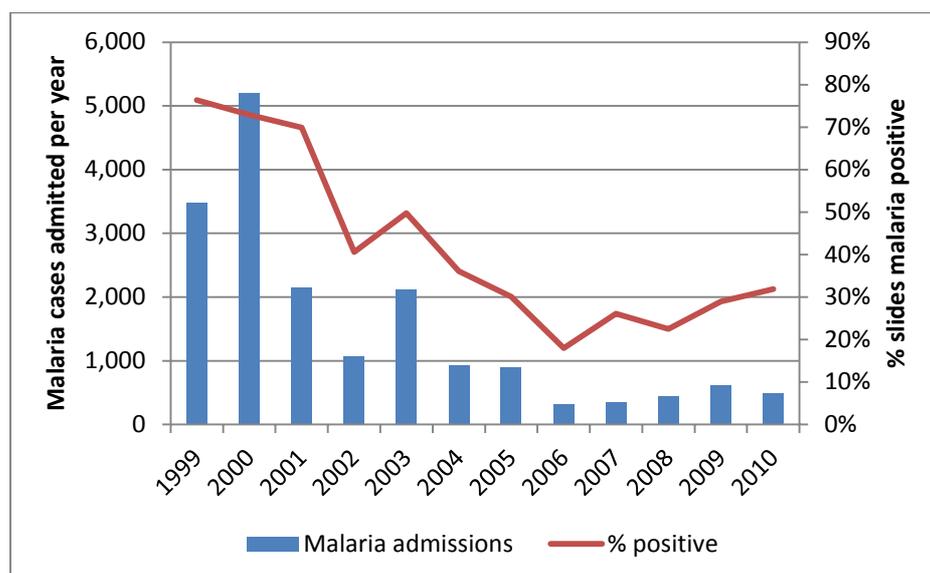


Facility-Based Morbidity

Routine health statistics for much of Mainland Tanzania are either unavailable, of unknown completeness, or report malaria cases based only on clinical diagnosis rather than laboratory confirmation. The analysis below is therefore restricted to two hospitals where facility data has been collected and quality-assured on a prospective basis, through Ifakara Health Institute's clinical surveillance system. In both cases, the figures refer to inpatient admissions of children under five years of age.

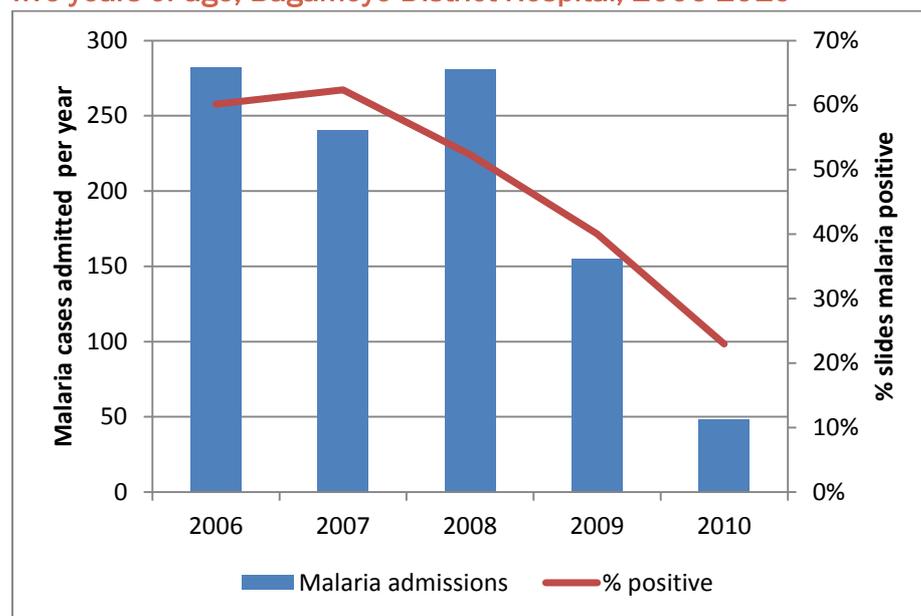
The results for Ifakara District Designated Hospital are shown in Figure 22. Both the slide positivity rate (proportion of slides from admitted patients with suspected malaria that tested positive) and the absolute number of malaria admissions (confirmed cases) for children under five years of age exhibit a decline between 1999-2001 and 2005/6, after which the slide positivity rate remained in the range 18%-32%. Expressed as multi-year averages, the 1999-2000 cases had slide positivity of 57%, compared to 46% and 25% for the 2001-5 and 2006-10 periods respectively.

Figure 22: Malaria admissions and blood slide-positivity, in children under-five years of age, Ifakara District Designated Hospital, 1999-2010



At Bagamoyo District Hospital, inpatient data collection began in 2005 (part year). Figure 23 below shows the trend in malaria admissions (confirmed cases) and slide-positivity among children under-five years of age between 2006 and 2010. Over this period, the number of under-five malaria admissions declined from 282 to 48 per year, while the slide positivity rate fell from 60% (2006) to 23% (2010).

Figure 23: Malaria admissions and blood slide positivity among children under-five years of age, Bagamoyo District Hospital, 2006-2010



Morbidity Summary

In this section we have reviewed the available data on malaria-related morbidity indicators.

Repeat cross-sectional surveys for various sub-national samples all indicate that a marked decline in malaria parasitemia has occurred in recent years. The NMCP survey conducted in 21 districts found a decline from 19.4% in 2006 to 16.1% in 2008. The Lindi/Mtwara data describe a 50% relative decline in all-age malaria parasite prevalence and a 66% decline in prevalence in infants aged 2-11 months from 2004 to 2007. All-age malaria parasitemia in the Ifakara DSS area fell from 25% in 2004 to less than 5% in 2010.

Health facility data for under-five malaria admissions and slide-positivity also exhibit a decline in two reference hospitals. At Ifakara District Designated Hospital the five-year average slide positivity rate fell from 66% (1996-2000) to 46% (2001-05) and 25% in 2006-2010. At Bagamoyo District Designated Hospital inpatient under-five data exhibit a decline of similar magnitude, from more than 60% in 2006 and 2007, to 23% in 2010.

For Mainland Tanzania as a whole, severe anemia in children aged 6-59 months halved during the five year period from 11% in 2004/5 to 5.5% in 2010. The decline in severe anemia was greatest in the age group traditionally most affected by malarial anemia, children aged 6-23 months, and was also greater in high malaria risk areas as compared to “medium or low risk” areas. Inequities in anemia prevalence by residence, wealth and mother’s education narrowed or disappeared entirely between 2004/5 and 2010.

The prevalence of fever in children under five years of age, which showed no significant change between 1992, 1996 and 1999, has since declined. Between 1999 and 2007/8, the proportion of children with fever in the two weeks before survey fell by more than a third, from 35% to 19%. The latest survey (where fieldwork was conducted during a mixed dry/rainy season), estimated fever prevalence was four percentage points higher than in 2007/8 (fieldwork predominantly in dry season). Fever prevalence exhibited a marked age pattern in 1999, peaking in the 12-23 month age group. Over successive surveys, this age-peak in prevalence has diminished, and the distribution of fever prevalence by age group has become much flatter.

In conclusion, all available time-series data on malaria-related morbidity point towards a significant decline over the recent decade. While the absence of historic national baseline estimates make it difficult to estimate the time frame over which this decline has taken place, anemia data suggest that it had already commenced before 2007, and fever estimates suggest that it began between 1999 and 2004.

MORTALITY

Mortality

Background

All-cause under-five mortality is the principal measure of impact employed in this evaluation. This impact measure, recommended by the RBM-MERG(58) is preferable to malaria-attributable mortality for a number of reasons. Malaria-attributable mortality rates are only available for a small number of demographic sentinel surveillance sites which are not nationally representative. Measurement of cause-specific mortality depends upon verbal autopsy and the assignation of “probable cause,” but this method has limitations of both sensitivity and specificity.(2) More importantly, the narrow malaria-attributable estimate omits the substantial indirect contribution of malaria to all-cause mortality. The magnitude of “indirect” malaria mortality has been estimated to be equivalent to 50% - 100% of mortality that is directly attributable to the disease.(59, 60)

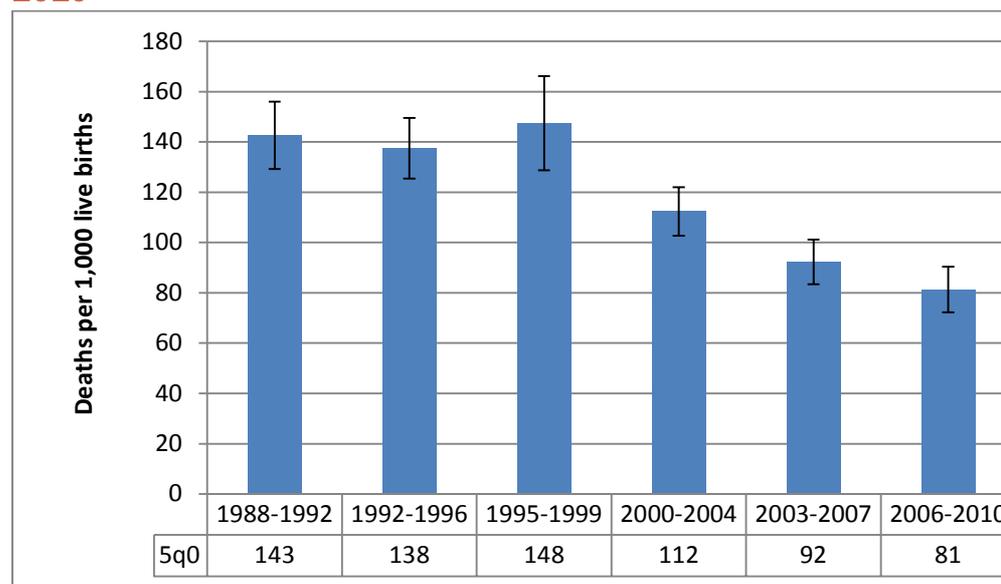
Every aspect of mortality analysis presented in this section (timing, age-pattern and residence differentials) is consistent with reduction in mortality due to a decrease in malaria between 1999-- 2010. This section also includes an ecological analysis examining changes in mortality with respect to malaria risk. Mortality estimates from the 1992 and 1996 surveys are described to put recent trends in a longer-term context. All mortality figures represent direct estimates, and unless otherwise stated, they represent the period 0-4 years before each survey. Thus the 1999 estimate reflects the approximate calendar period 1995-99; 2004/5 reflects 2000-04 and 2010 reflects 2006-10.

Mortality estimates presented in this evaluation are derived from multiple Demographic and Health Survey datasets 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.

Trend in All-Cause Under-Five Mortality

Estimates of all-cause under-five mortality from successive DHS surveys conducted between 1992 and 2010 are presented in Figure 24. Mortality estimates are shown for the period 0-4 years prior to the survey.

Figure 24: Trend in all-cause under-five mortality ($5q_0$), Mainland Tanzania, 1992-2010



The results show no significant change between the three surveys (1992, 1996, 1999) conducted during the 1990s since 95% confidence intervals overlap in all cases. Moreover, the 1999 estimate (representing the period 1995-99) had a slightly higher point estimate than either of the preceding surveys.

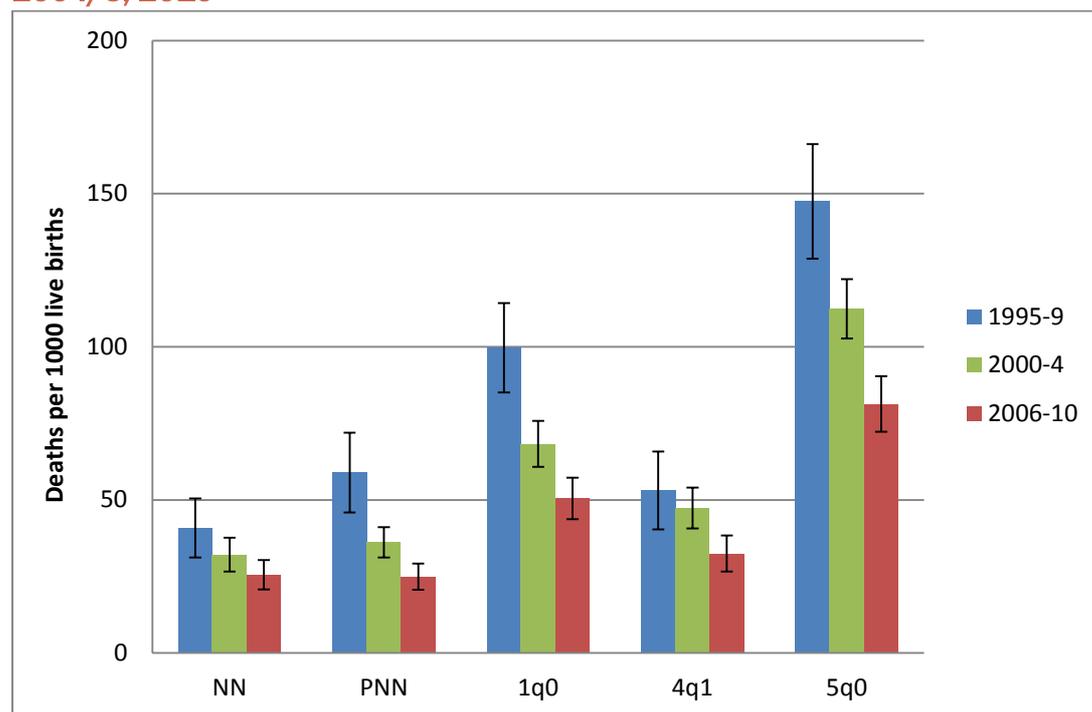
By contrast, between the 1999 and 2004/5 survey, an absolute decline in under-five mortality of 36 deaths per 1000 live births occurred. A further decline of 20 deaths per 1,000 live births occurred between the 2004/5 and 2007/8 surveys. In both cases, the changes were significant at the 95% level of confidence. Over the whole period from 1995-9 to 2006-10, all cause under-five mortality declined by 67 deaths per 1,000 live births, a relative reduction of 45% over eleven years.

Disaggregation of data from all surveys up to 2004/5 into annual estimates of $5q_0$ revealed that the change in trend seems to have commenced around 1999/2000 and continued through to 2005,(61) broadly corresponding to when Tanzania entered a period of unprecedented economic growth and during which malaria control interventions first began scaling up.

Age-Specific Mortality

Trends in age-specific mortality across the last three surveys are presented in Figure 25.

Figure 25: Trends in age-specific childhood mortality, Mainland Tanzania, 1999, 2004/5, 2010



Key: NN = neonatal mortality (first month), per 1,000 live births; PNN = postneonatal 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 estimates show a mortality decline between 1995-9 and 2006-10 in all age categories. However, the change in under-five mortality is largely due to changes in mortality before exact age one, while mortality decline in the 1-4 years age group is smaller and exhibited no change between 1995-9 and 2000-4.

The mortality estimates and relative change by age category are shown in Table 12. The analysis includes three additional age categories: 6-23 months (where malaria-related mortality would be expected to be concentrated)(62, 63) and 1-5 months and 24-59 months (for comparison).

Table 12: Age-specific mortality (deaths per 1000 live births)^a and relative change in age-specific mortality, 0-4 years prior to the survey

Age Category	Mortality (0-4 years prior to the survey)			Relative change 1995/9-2000/4	Relative change 1995/9-2006/10	Relative change 2000/4-2006/10
	1995-9	2000-4	2006-10			
Neonatal (NN)	41	32	26	-21.3%	-37.4%	-20.5%
Post-neonatal (PNN)	59	36	25	-38.6%	-57.7%	-31.1%
Infant ($1q_0$)	100	68	50	-31.5%	-49.4%	-26.1%
Child ($4q_1$)	53	47	32	-11.0%	-38.9%	-31.3%
Under-five ($5q_0$)	148	112	81	-23.8%	-44.9%	-27.7%
1-5 months	32	19	11	-40.0%	-65.6%	-42.6%
6-23 months	55	39	28	-29.1%	-48.6%	-27.4%
24-59 months	28	27	19	-5.2%	-33.5%	-29.9%

^aChild mortality ($4q_1$) is per 1,000 children surviving to 12 months of age

Within the infant mortality category, 34 points (deaths per 1,000 live births) out of the 50-point absolute change are attributable to a reduction in post-neonatal mortality, comparing the 1995-9 period to the 2006-10 period. The relative mortality decline between the 1995-9 and 2006-10 periods was greater for the post-neonatal age group than any other category (except the 1-5 month age group) and was 19 percentage points greater than the decline in child mortality (58% vs. 39%). Relative mortality decline in the 6-23 month age group (49%) was larger than the decline (34%) in the 24-59 month age group (between the 1995-9 – 2006-10 periods). A large decline in mortality (66%) in the 1-5 month age group was seen between the 1995-9 period and 2006-10 period, possibly reflecting the increased coverage of other child health interventions during this timeframe.

Mortality Change by Residence

Figures 26 and 27 show mortality rates (0-4 years prior to survey) from the 1999 and 2010 surveys for rural and urban areas respectively, stratified by age group.

Figure 26: Age-specific mortality, rural areas of Mainland Tanzania, 1999 and 2010

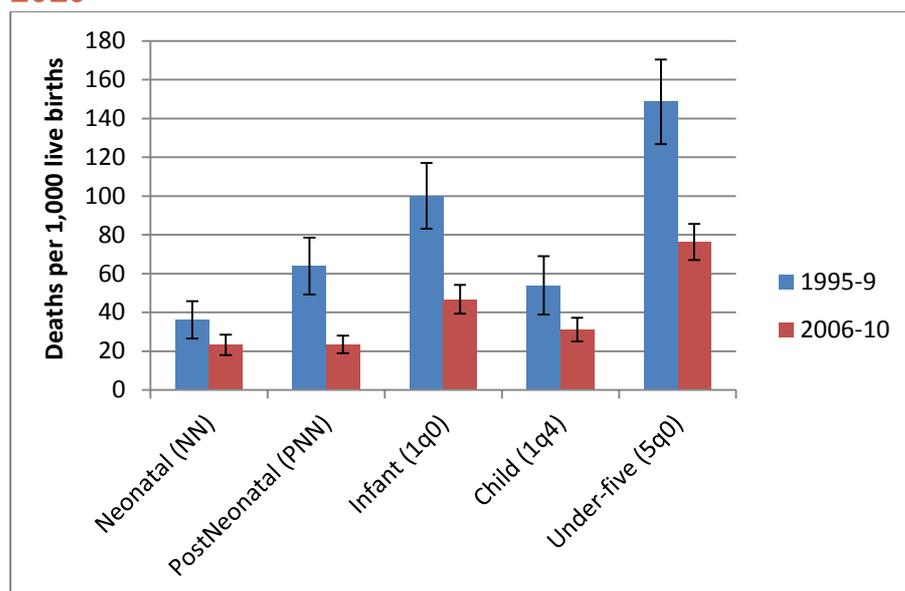
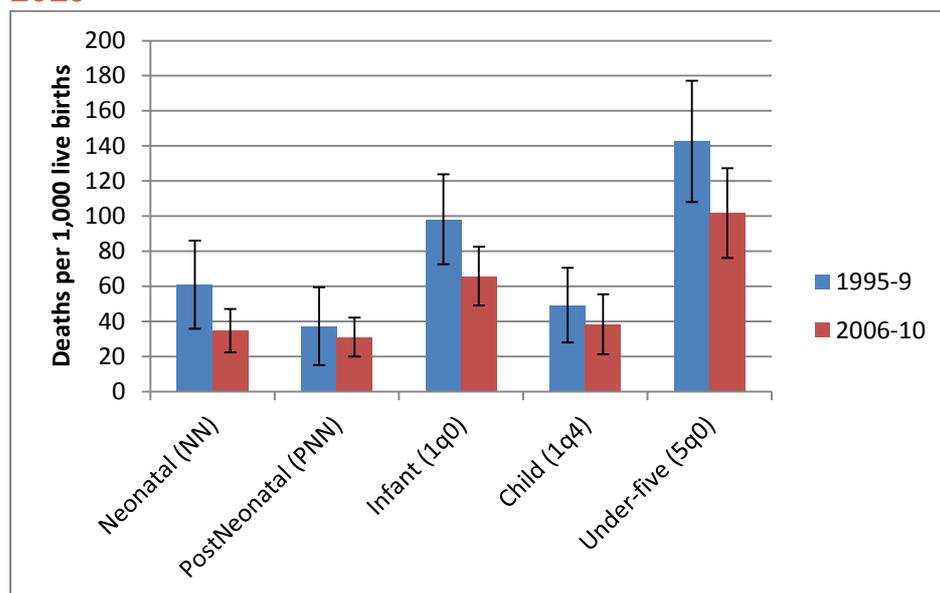


Figure 27: Age-specific mortality, urban areas of Mainland Tanzania, 1999 and 2010



Under-five mortality in rural areas declined from 147.6 (126.8-170.4) in 1995-9 to 76.3 (67.1-85.7) in 2006-10; representing an absolute decline of 72 deaths per 1,000 live births and a relative decline of 49%. In urban areas, the absolute and relative differences (41 and 29% respectively) between estimates were much smaller and did not reach statistical significance going from 142.7 (108.1-177.2) deaths per 1,000 live births in 1995-9 to 101.7 (76.2-127.3) in 2006-10.

The age-pattern of mortality also appears to differ between rural and urban areas. In the former, post-neonatal mortality exhibited a larger relative change (64%) than either neonatal (36%) or child mortality (42%). By contrast, in urban areas neonatal mortality declined more (43%) than either post-neonatal (17%) or child mortality (22%). None of the urban mortality changes were statistically significant at the 95% level of confidence, although confidence intervals are much wider than in rural areas due to smaller sample sizes.

Under-Five Mortality Change and Malaria Risk

If a major part of the under-five mortality decline was malaria-related, we would expect to see a greater decline in mortality among children living in areas of greater malaria risk, which has a higher baseline, as compared to areas of lower malaria risk. (64, 65)

To test this hypothesis, we divided the country into three categories, using regional malaria parasite prevalence (6-59 months) in 2007/8 as a proxy measure of relative malaria endemicity. Each category comprises six or seven regions, with respective parasitemia of 0%-9.2% (lower); 10.4%-21.9% (medium) and 28.7%-38.6% (higher) respectively. Infant and under-five mortality rates were then calculated for each category using the 1999 and 2010 survey data. Trends in infant and under-five mortality, stratified by our proxy of malaria risk, are shown in Figures 28 and 29.

Figure 28: Trends in infant mortality in higher, medium and lower malaria risk areas, Mainland Tanzania 1999 and 2010

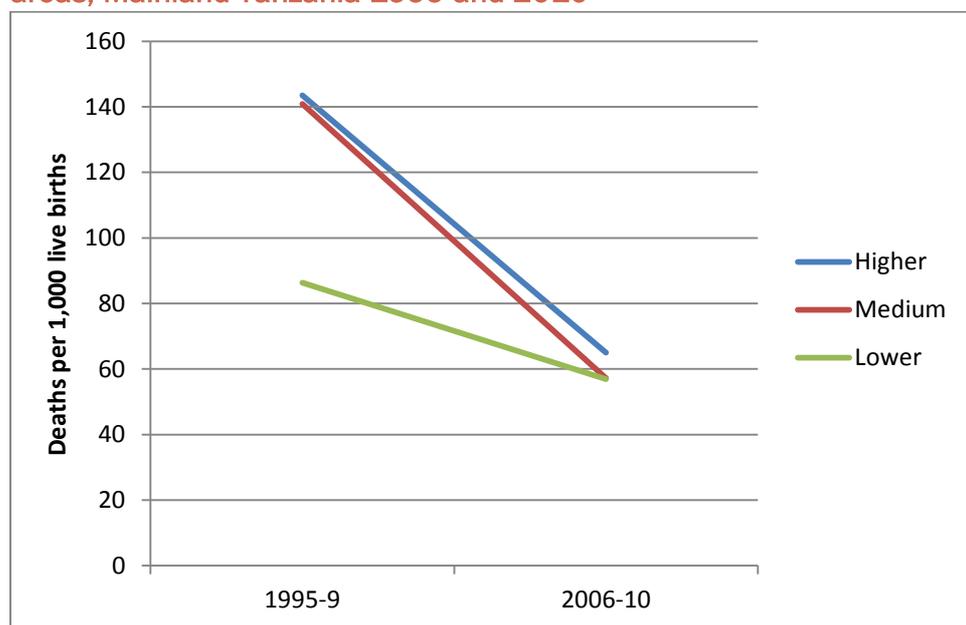
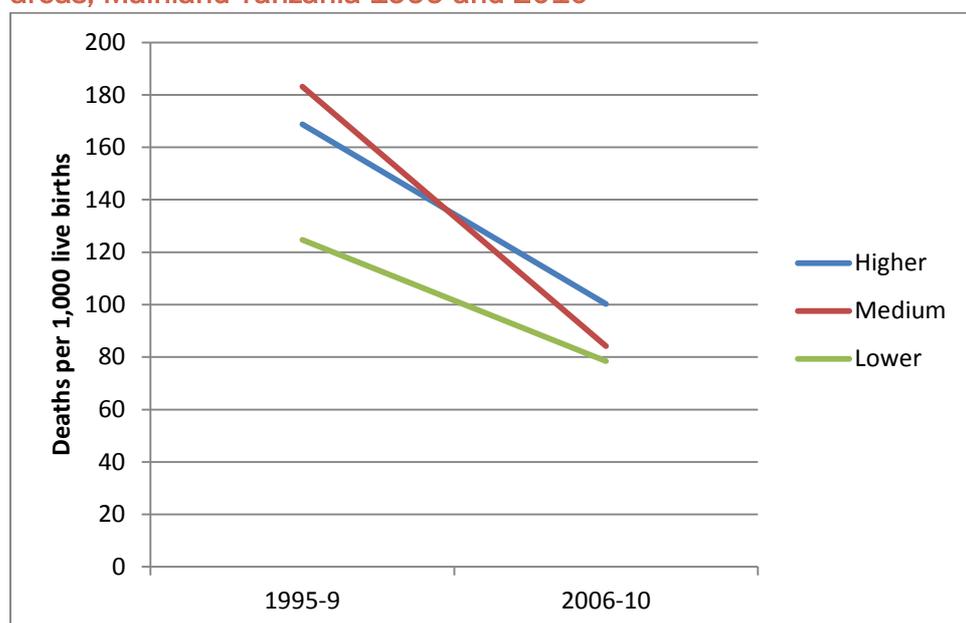


Figure 29: Trends in under-five mortality in higher, medium and lower malaria risk areas, Mainland Tanzania 1999 and 2010



In the 1999 survey (representing mortality between 1995-1999) infant mortality rates were 144, 141 and 86 deaths per 1,000 live births respectively in the higher, medium and lower risk categories. A difference of similar magnitude is apparent across the categories for under-five mortality (169, 183 and 125, respectively for higher, medium and lower risk categories).

By the time of the 2010 survey (representing mortality between 2006-2010), infant mortality rates in the three risk categories had converged (65, 57 and 57

deaths per 1,000 live births respectively). A similar, though less complete, convergence is evident with under-five mortality (100, 84 and 79 deaths per 1,000 live births respectively).

In addition, to examine the mortality changes in the age-group expected to be most affected by changes in malaria-related mortality, trends in mortality in 6-23 month olds (and 24-59 month olds for comparison) were stratified by the proxy for malaria risk in Figures 30 and 31.

Figure 30: Trends in mortality in 6-23 month olds in higher, medium and lower malaria risk areas, Mainland Tanzania 1999 and 2010

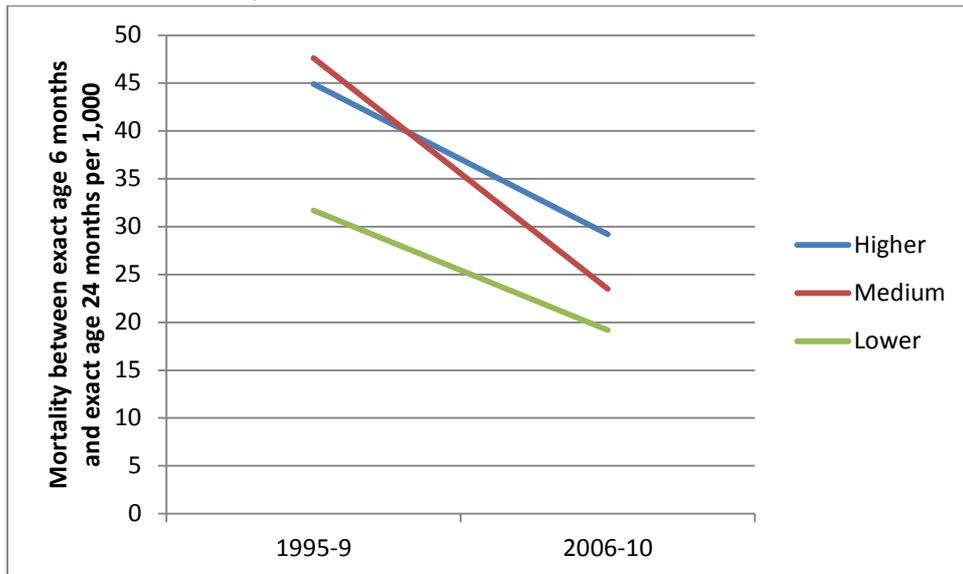
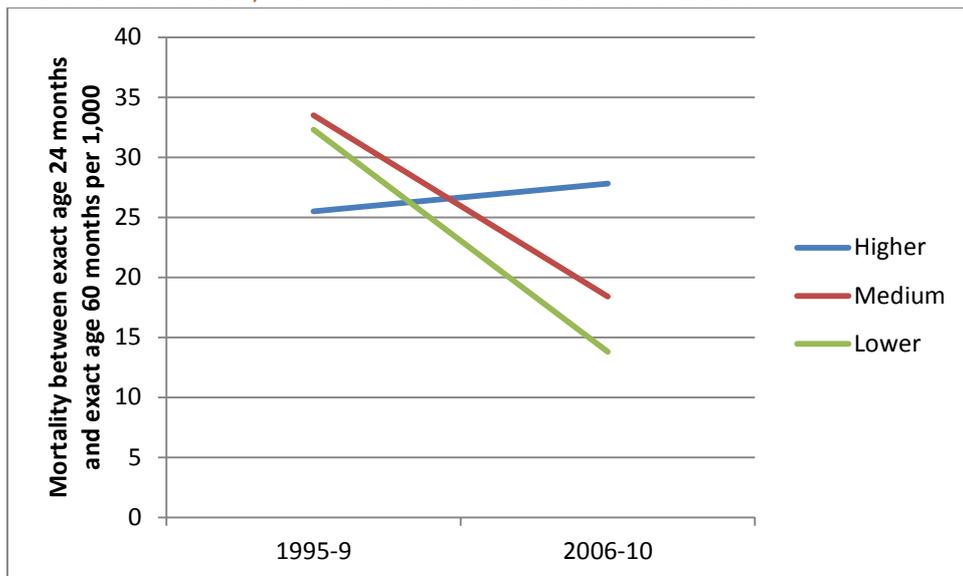


Figure 31: Trends in mortality in 24-59 month olds in higher, medium and lower malaria risk areas, Mainland Tanzania 1999 and 2010



For the 6-23 month olds, the mortality rates from the 1999 survey (1995-9) were 45, 48 and 32 deaths per 1,000 live births respectively in the higher,

medium and lower risk categories. By the 2010 survey (2006-10), the mortality rates had dropped to 29, 24, and 19 per 1,000 live births respectively in the higher, medium and lower risk categories.

For the 24-59 month old reference age group, mortality rates in the three risk categories in the 1999 survey were 26, 34 and 32, respectively. These had changed to 28, 18 and 14 by the 2010 survey. In this age group, there is no difference between the trends in the medium and low risk categories. We are unable to explain the trend for the high risk category, but it may in part be due to a small sample size.

The results are consistent with our hypothesis that mortality rates would show a greater (absolute) decline from a higher baseline in areas with greater malaria risk than those with lower malaria risk for age groups (infants, 6-23 months and overall under-fives) expected to be most affected by changes in malaria mortality.

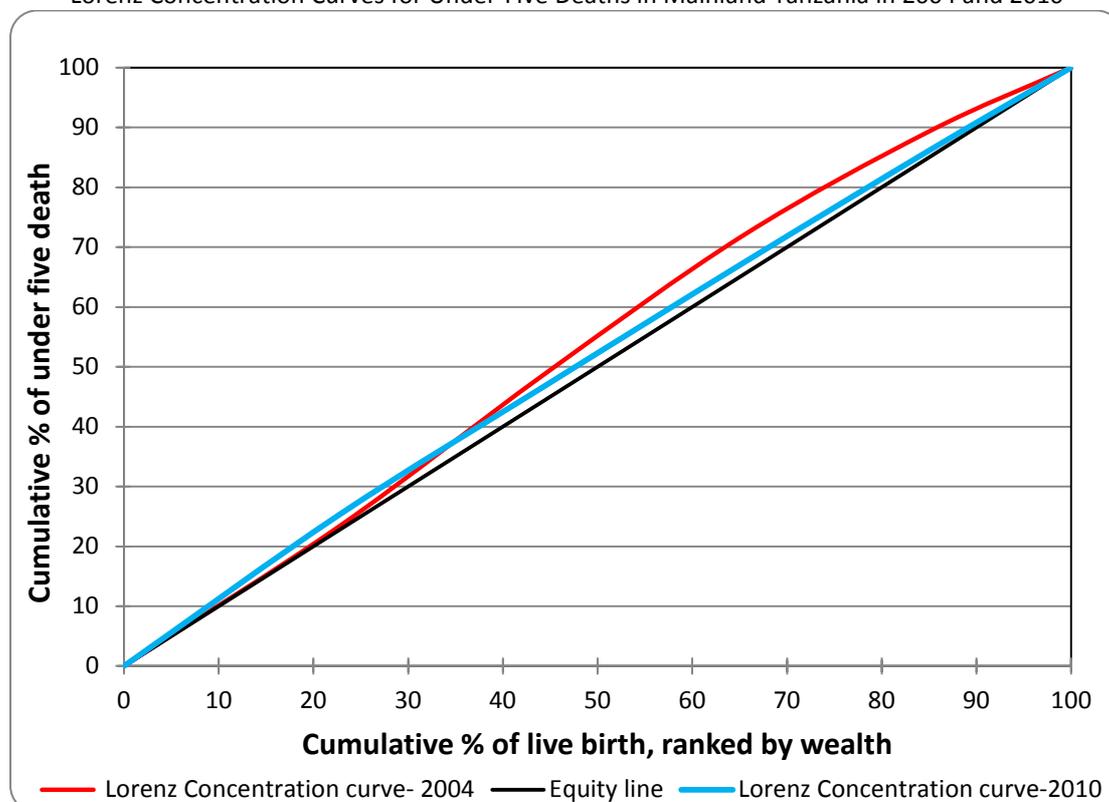
This analysis has a number of limitations. Regional malaria parasitemia in 2007/8 may include an upward bias in the bimodal rainfall areas because fieldwork was carried out partially in the rainy season, whereas in unimodal rainfall areas it was predominantly dry. Parasitemia in 2007/8 may already have been impacted by malaria control measures in prior years, and thus may not reflect inherent or historic relativities in malaria transmission intensity. Regional parasitemia rates may obscure considerable intra-regional variation in malaria risk because of inclusion of both urban and rural areas as well as ecological variation in transmission risk. It would have been preferable to use a finer spatial resolution of malaria risk than “whole regions” for assigning populations to malaria risk categories.

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. Inequalities in mortality are presented here using concentration curves – where the straight line represents perfect equality (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 32: Inequalities in under-five mortality 2004/5 - 2010

Lorenz Concentration Curves for Under-Five Deaths in Mainland Tanzania in 2004 and 2010



Concentration Index

2004/05: Concentration Index (CI): -0.0631; 95% CI (-0.1419; 0.0157)

2010: Concentration Index (CI): -0.0335; 95% CI (-0.0554; -0.0115)

Figure 32 shows the results of this analysis for under-five mortality estimates for 10 years in 2004/5 (1994-2004) and 2010 (2000-2010). The concentration index in 2010 (-0.0335) was closer to “equality” than in the 2004/5 survey (-0.0631), indicating that equity of mortality improved between these two survey periods. Under-five mortality rates by wealth quintiles from the 2004/5 and 2010 surveys are included in Annex A.3.21.

Mortality Summary

In summary, the data show that a significant decline in under-five mortality occurred in Mainland Tanzania between 1995-9 and 2006-10, following a decade in which no significant change took place. The mortality decline that began in the first half of the period from 1995-9 to 2006-10, continued in the second half of the period, coinciding with the scale up of malaria control interventions.

The mortality decline over the last decade was largest in the post-neonatal age group and in rural areas. Within rural areas, the post-neonatal mortality reduction was especially pronounced, whereas this was not the case in urban areas. Stratification of infant and under-five mortality by malaria risk showed a

larger absolute decline, from a higher baseline, in areas with medium/higher risk than in areas of lower malaria risk over the period 1995-9 to 2006-10.

Every aspect of mortality analysis presented in this section (timing, age-pattern, residence differentials, and relationship to malaria risk) is consistent with the results that we would expect to see if malaria were a major factor underlying the mortality change in Mainland Tanzania.

CASE STUDIES

Case Studies

Thus far, the report has documented, at the national level, a significant scale up of malaria interventions, a decline in malaria-related morbidity, and a reduction in all-cause under-five mortality. However, we also noted that nationally-representative time-series data were lacking for some of the parameters of interest. The purpose of this section is to present case studies that have a more complete record of intervention coverage and associated changes in morbidity and/or mortality. Data availability for the respective case studies is summarized in Table 13. Further detail on the data sets referred to here can be found in Annexes 1 and 3.

Table 13: Case study summary

Case Study	Location	Remarks	Data availability
Ifakara DSS Area	Kilombero valley, Morogoro Region, SE Tanzania	ITN coverage rose earlier and more rapidly than TZ average	ITN use, malaria parasitemia, EIR, slide positivity of hospital admissions, infant/under-five mortality, rainfall
Lindi/Mtwara	Southern Tanzania	Mass distribution of LLINs to all under-fives in 2006	ITN use, malaria parasitemia
Kagera	North-west Tanzania	IRS carried out in specific districts 2009/10	Malaria slide positivity proportion among suspected malaria cases in hospitals

Ifakara DSS Area

This case study focuses on the Ifakara DSS area in the Kilombero valley in south-eastern Tanzania where the epidemiology and transmission of malaria has been studied intensively over a period of more than 20 years. Since 1997, the Ifakara DSS area has tracked all households within a defined geographic area consisting of 13 villages in Kilombero District and 12 villages in Ulunga District, both located in Morogoro Region. These are predominantly rural areas with subsistence farming as the main source of income. Social marketing of ITNs began in this area in 1997, three years before nation-wide implementation commenced.

Figures 33-38 below describe trends in ITN use, malaria parasitemia, hospital slide-positivity, infant and under-five mortality, entomological inoculation rate (EIR) and annual rainfall over a period from the 1990s to the present. ITN use in this case study area rose from less than 10% (all ages) in 2001-2002 to over 40% in 2009-10. Over a similar period, malaria parasitemia (all ages) fell from ~20% (2001-2003) to less than 5% in 2009-10. Slide positivity among under-

fives admitted with suspected malaria to St. Francis District Hospital fell from over 70% (1999-2001) to between 18% and 32% (2006-2010). Under-five mortality declined from 141 deaths per 1,000 live births in 1998 to 88 in 2009. Infant mortality declined from 115 to 60 over the same period. Between the early 1990s and 2008, there was an eighteen-fold reduction in the EIR for unprotected people in entomological surveillance sites in the Kilombero Valley, decreasing from 1481 infectious bites per person per year in 1990-94 to 81 in 2008. Rainfall over this period showed major year-to-year variations (Figure 38), but no systematic downward trend that could explain the change in malaria transmission.

Figure 33: ITN and any net use (all ages)

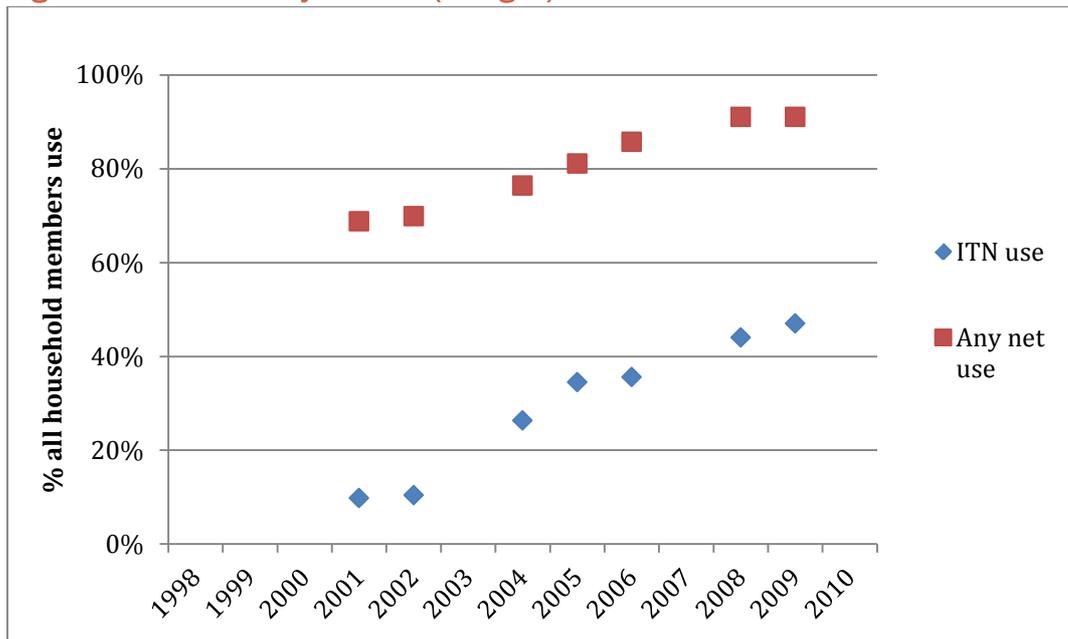


Figure 34: Malaria parasitemia (all ages)

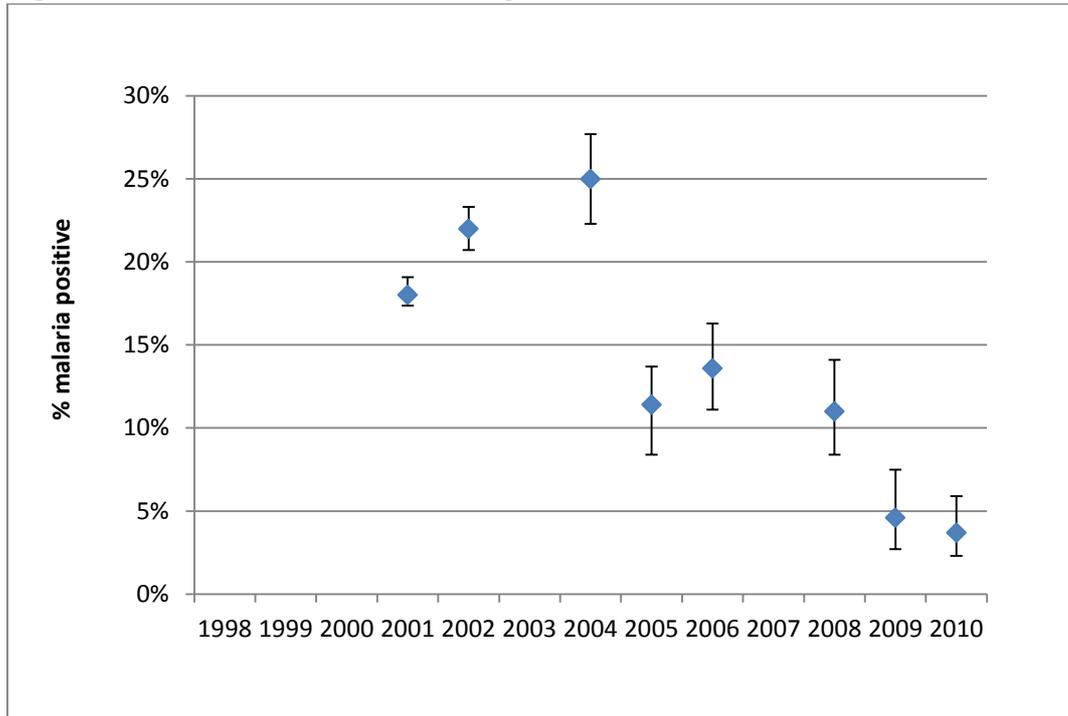


Figure 35: Slide positivity, under five patients

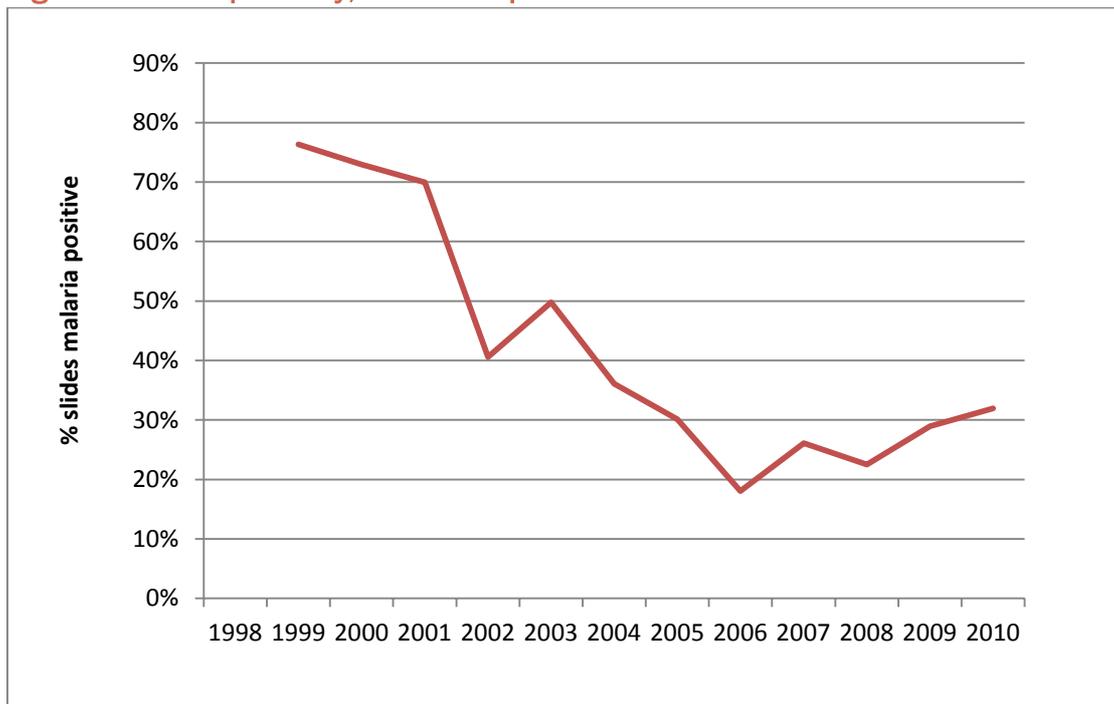


Figure 36: Infant and under-five mortality rates

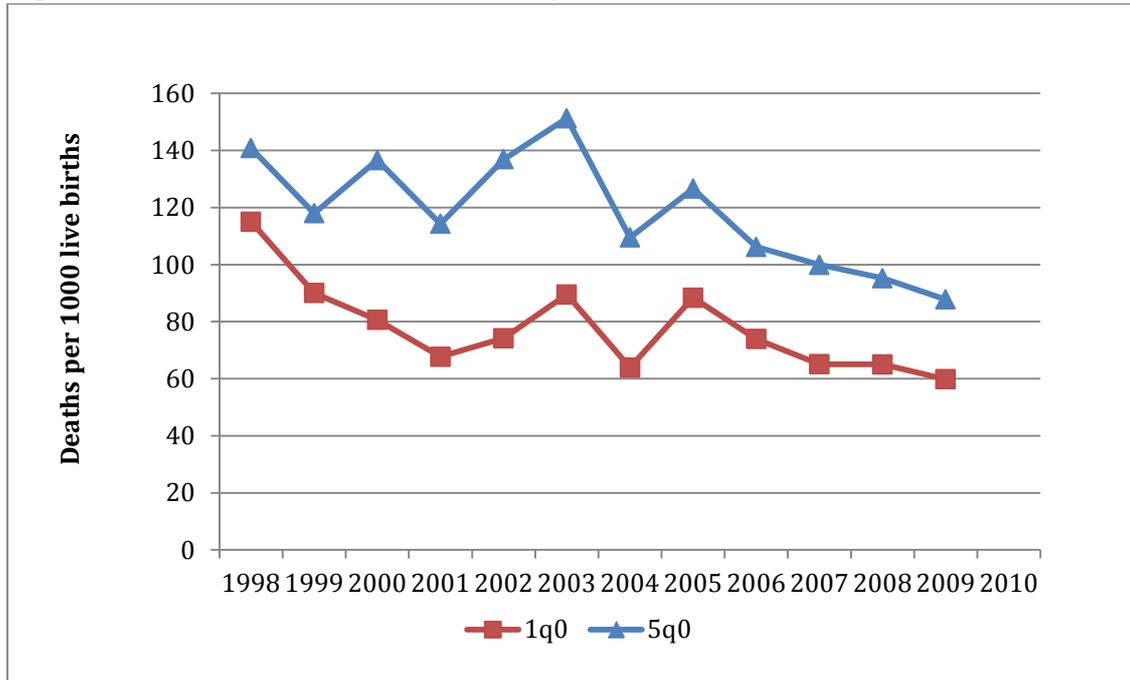


Figure 37: Entomological inoculation rate

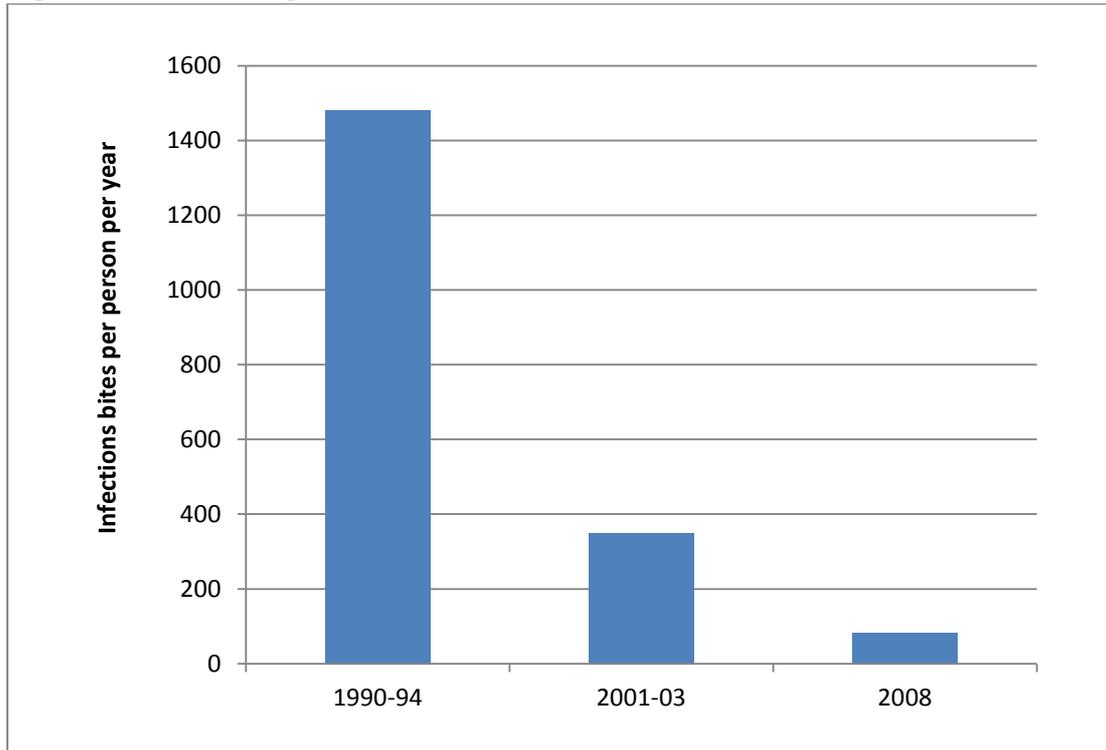
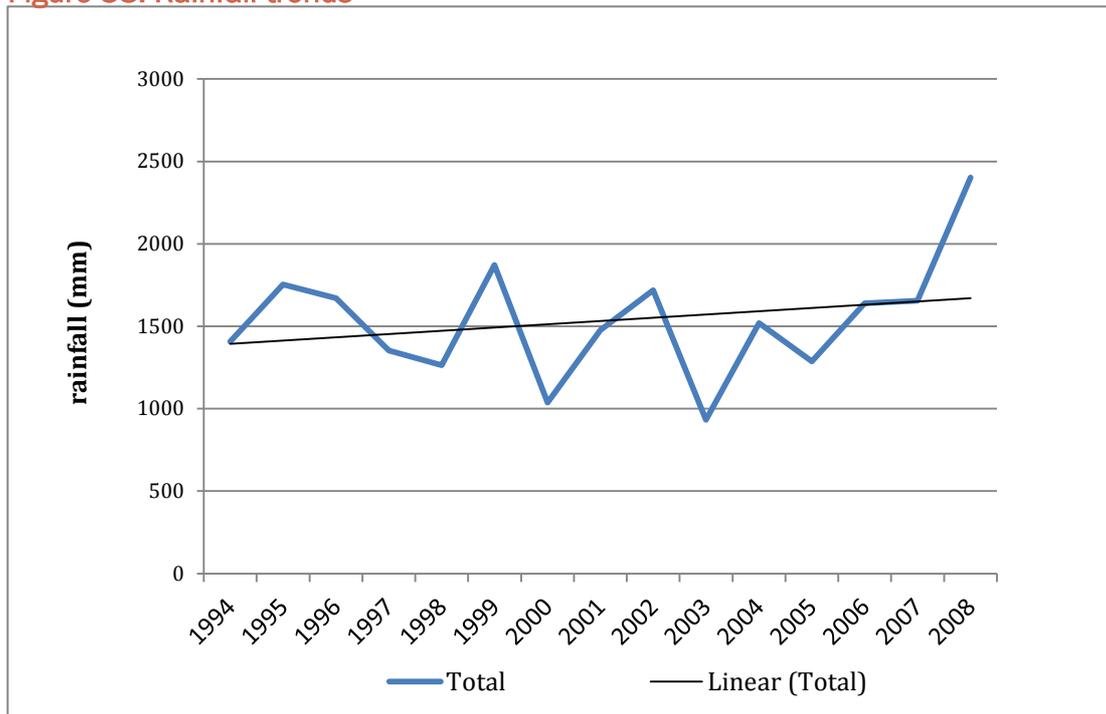


Figure 38: Rainfall trends

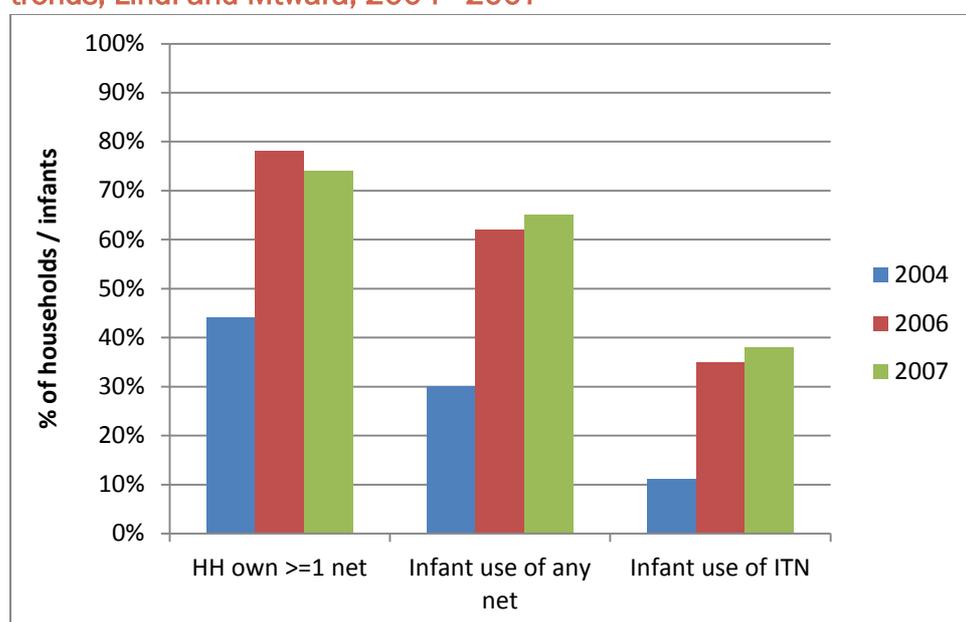


Lindi and Mtwara

Lindi and Mtwara Regions are situated in Southern Tanzania where the Government of Tanzania undertook a mass distribution of nets bundled with insecticide in 2005, targeting all under-fives. This program was part of an integrated child health campaign that also included administration of measles vaccination, mebendazole treatment and Vitamin A supplementation. The campaign in Lindi and its effect on net/ITN ownership and use has previously been described.(66)

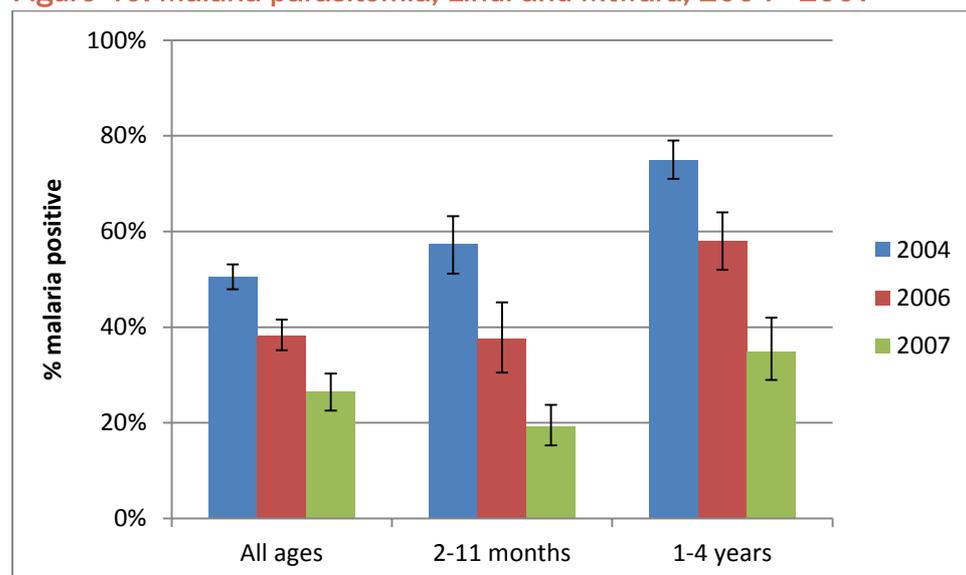
These two regions were also the site of an IPTi trial that has been extensively described in the literature.(56) A range of malaria-related indicators (including parasitemia and anemia) were collected through large-scale, representative, randomly-selected household surveys in 2004, 2006 and 2007 in 24 divisions (12 intervention, 12 comparison) across five districts. Data presented in this case study come from a re-analysis of selected indices from the comparison arm of the study (Marchant *et al.*, manuscript in preparation). The surveys included 10,800, 2,880 and 125,000 households for the three respective years, and the survey aimed to test all children aged 2-11 months for malaria parasitemia and anemia, producing sample sizes of 232, 274 and 640 for the respective survey years.

Figure 39: Household net ownership and infant (2-11 months) net/ITN use trends, Lindi and Mtwara, 2004 - 2007



Household ownership of at least one net (irrespective of treatment) rose from 44% in 2004 to 78% in 2006 and 74% of households in 2007. Use of “any net” the night prior to survey by infants aged 2-11 months (rose from 30% to 62% and 65% respectively; while use of ITNs rose from 11% to 35% and 38% across the respective survey years (Figure 39).

Figure 40: Malaria parasitemia, Lindi and Mtwara, 2004 - 2007



Across the three surveys, malaria parasitemia in the whole population (all age groups) declined from 51% (48-53) in 2004 to 38% (35-42) in 2006 and 27% (23-30) in 2007. Among infants aged 2-11 months, malaria parasitemia fell by two-thirds, from 57% (51-63) in 2004 to 38% (31-45) in 2006 and 19% (15-24) in 2007. Similarly, in children 1-4 years of age, malaria parasite prevalence halved during the study period from 75% (71-79) in 2004 to 58% (52-64) in 2006 and 35% (29-42) in 2007 (Figure 40).

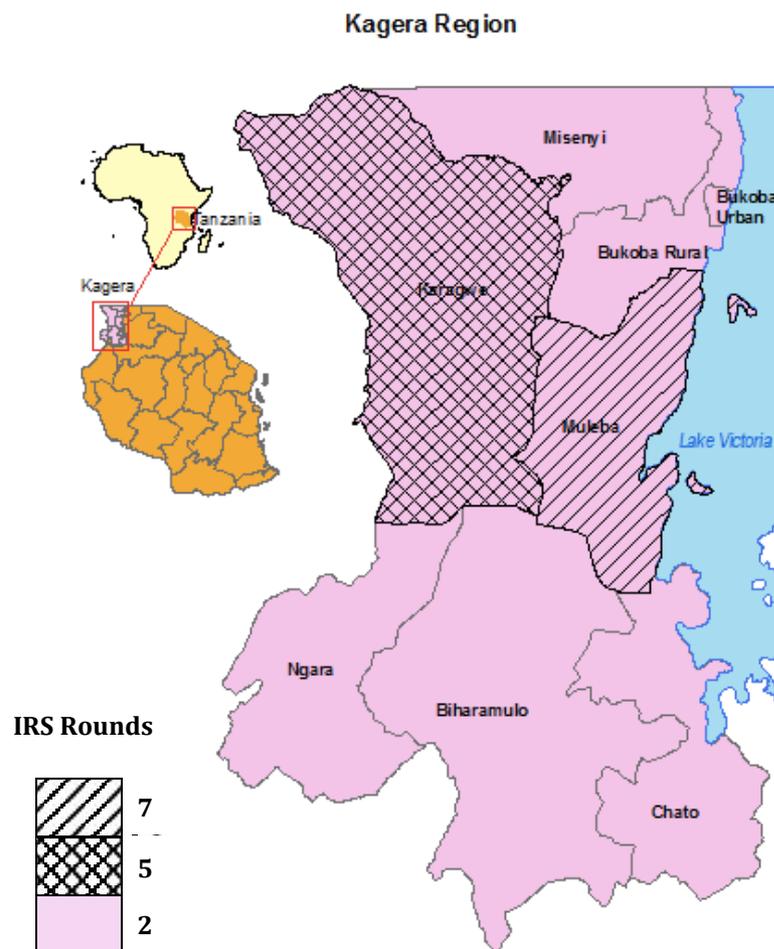
Anemia prevalence data from the same surveys were previously reported for 2004 and 2006. In the control group, the proportion of infants aged 2-11 months with severe anemia (hemoglobin <8g/dL) nearly halved, from 29% (69/238) in 2004 to 16% (44/276) in 2006.

In an exploration of potential confounding variables that might explain the reduction in malaria parasite prevalence, the re-analysis of the comparison arm of the IPTi study (Marchant *et al.*, manuscript in preparation) found no major change in rainfall, health care-seeking, population level use of SP, nor indicators of household wealth. An ecological analysis across 12 divisions and three years of data explored the relationship between malaria parasite prevalence and ITN coverage, SP detection and average household socio-economic status. Only ITN coverage showed evidence of an association with reduced malaria parasite prevalence. At the individual level, multivariate analysis showed that the (adjusted) odds ratio for malaria infection was 50% lower for infants who slept under any net on the night before the survey (compared to not using a net) and 20% lower for all-age groups who lived in a house with at least one net (compared to those with no net).

IRS in Kagera Region

As described earlier, IRS began in 2007/8 in selected areas of Karagwe and Muleba Districts in Kagera Region (Figure 41). IRS was scaled-up to include all remaining areas of Karagwe and Muleba during the first half of 2009, plus a further five districts (Chato, Biharamulo, Ngara, Bukoba and Missenyi) between August and October 2009. This case study examines the temporal relationship between successive IRS spraying rounds and blood slide malaria positivity at local hospitals in the respective districts. The denominator for this indicator is all blood slides (all ages) that were read for malaria whether for inpatients or outpatients. The numerator is the number of blood slides that were positive for malaria parasites by microscopy. All data are as reported by district hospitals to RTI/PMI and data prior to 2008 were recovered retrospectively from laboratory registers and hospital reports.

Figure 41: Map of Kagera Region showing districts with number of IRS rounds since inception



The results, shown in Figures 42-44 below indicate a close temporal relationship between the introduction of IRS and the proportion of blood slides that were malaria positive at the district hospitals in the respective districts. Also notable is the suppression of seasonal peaks in blood slide positivity that were apparent in years prior to IRS implementation.

Figure 42: Number and % blood smears positive for malaria, Nyakahanga District Hospital, Karagwe District (2003-2010)

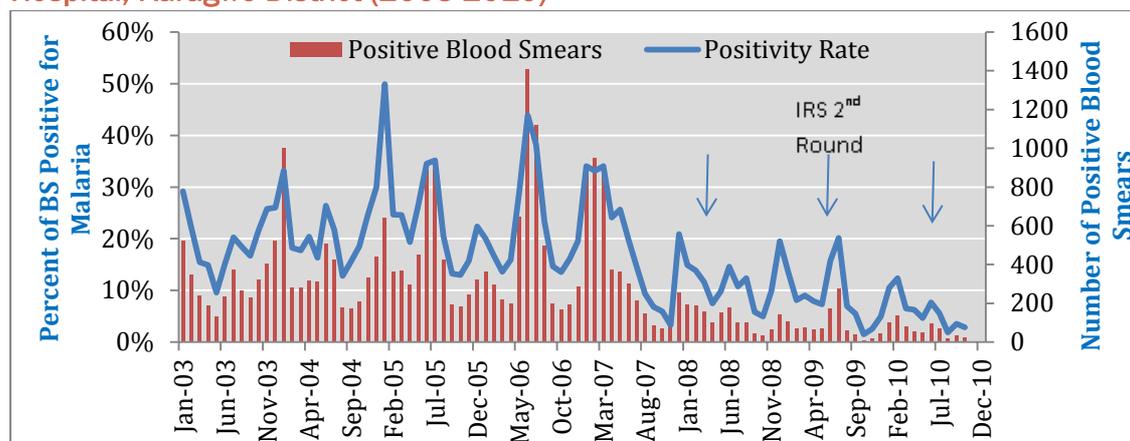


Figure 43: Malaria positivity, Chato District Hospital, Chato District

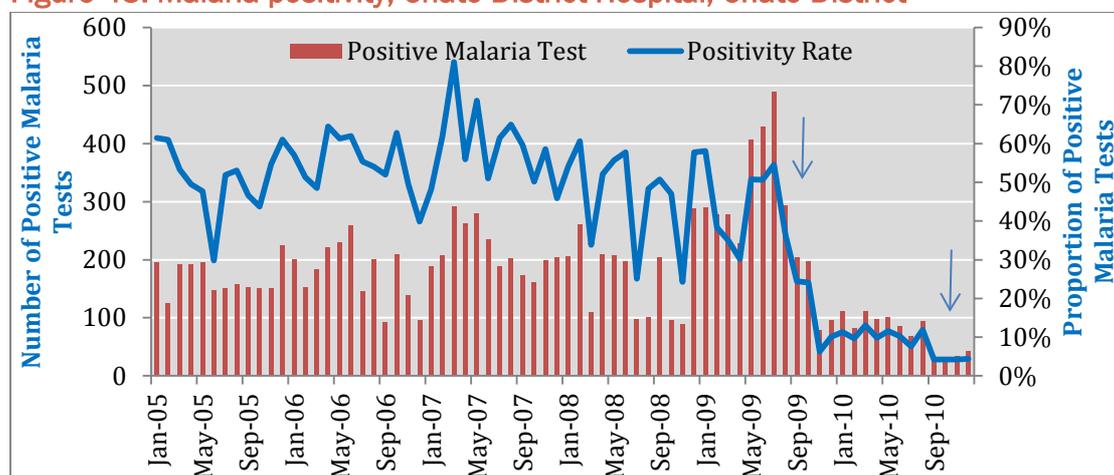
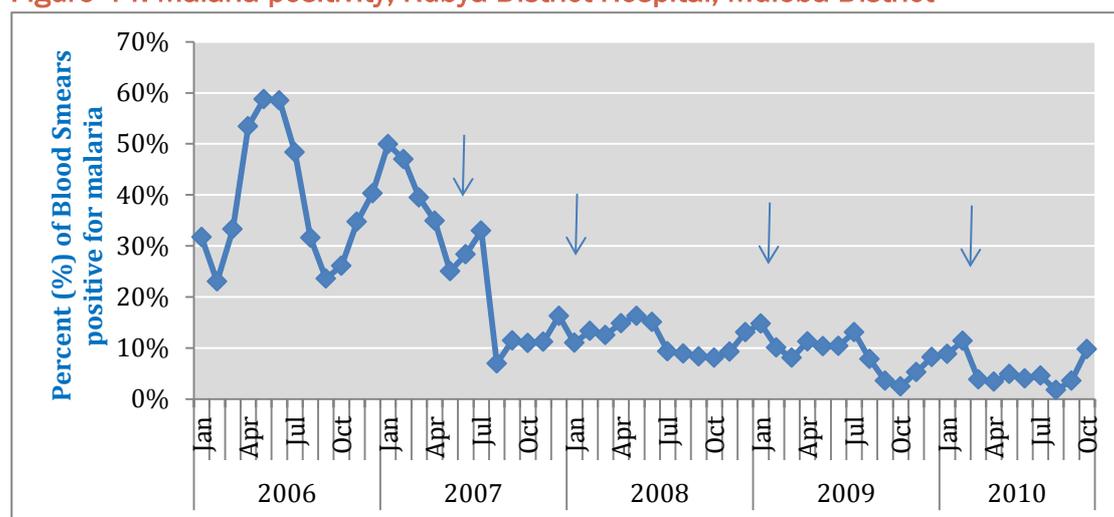


Figure 44: Malaria positivity, Rubya District Hospital, Muleba District



In Karagwe district (Figure 42), three rounds of IRS started in January 2008 (unstable transmission areas) and two rounds of blanket IRS were implemented

beginning in January 2009. At Nyakahanga (Figure 42) District Designated Hospital in Karagwe, blood slide positivity fell from an annual average of 23% (2003-2007) to 10% (2008-2009) and 5% in 2010 (January-September).

In Chato district (Figure 43), where IRS began in September/October 2009, the mean slide positivity rate during the high transmission season (November-March) fell from 52% (range: 24-61) in the five years prior to IRS to 10% (range: 6-13%) between November 2009 and March 2010.

In Muleba district (Figure 44), mean annual blood slide positivity at the hospital dropped from about 40% prior to IRS to about 10% in the two years following, and about 5% in 2010 (January-September, not including start of high transmission period). Seasonal peaks in slide positivity (previously 50-60%) were greatly diminished (10%-20%) following successive rounds of IRS.

In all cases, the introduction of IRS has been followed by at least a four-fold reduction in malaria blood slide positivity at district hospitals in the respective areas, compared to pre-IRS levels.

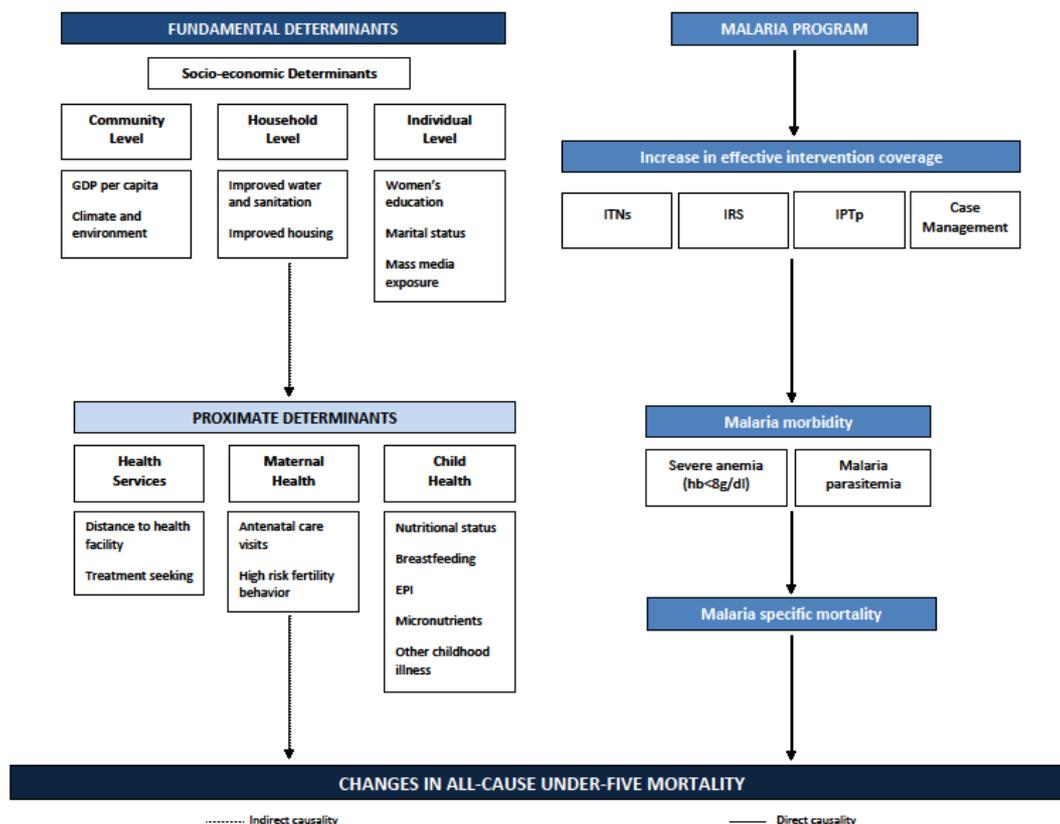
CONTEXTUAL FACTORS and PLAUSIBILITY ANALYSIS

Accounting for Contextual Factors

The plausibility design for the impact evaluation in Mainland Tanzania requires collecting data on non-malaria programs and other factors, collectively referred to as contextual factors, that might offer alternate explanations for the observed changes in malaria transmission, morbidity, and mortality.(67) Appropriate considerations of these contextual factors are essential for ensuring the internal and external validity of evaluations of large-scale health programs,(68) particularly for evaluations that are conducted when rapid changes are under way in other aspects of health services because of political, economic, and structural reforms.(69)

Contextual factors associated with childhood mortality and illness, including malaria, can be broadly categorized into the **fundamental** and **proximate** determinants of disease.(70-77) Fundamental determinants are the social and economic conditions under which people live, while proximate determinants are biological risks. The “impact model”(69, 78-80) conceptualized for the evaluation design in Mainland Tanzania, Figure 45, 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 on 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, Malaria Indicator Surveys), as well as other sources.

Figure 45: Impact model for the evaluation of the malaria control program, Mainland Tanzania, 1999 to 2010



Fundamental Determinants

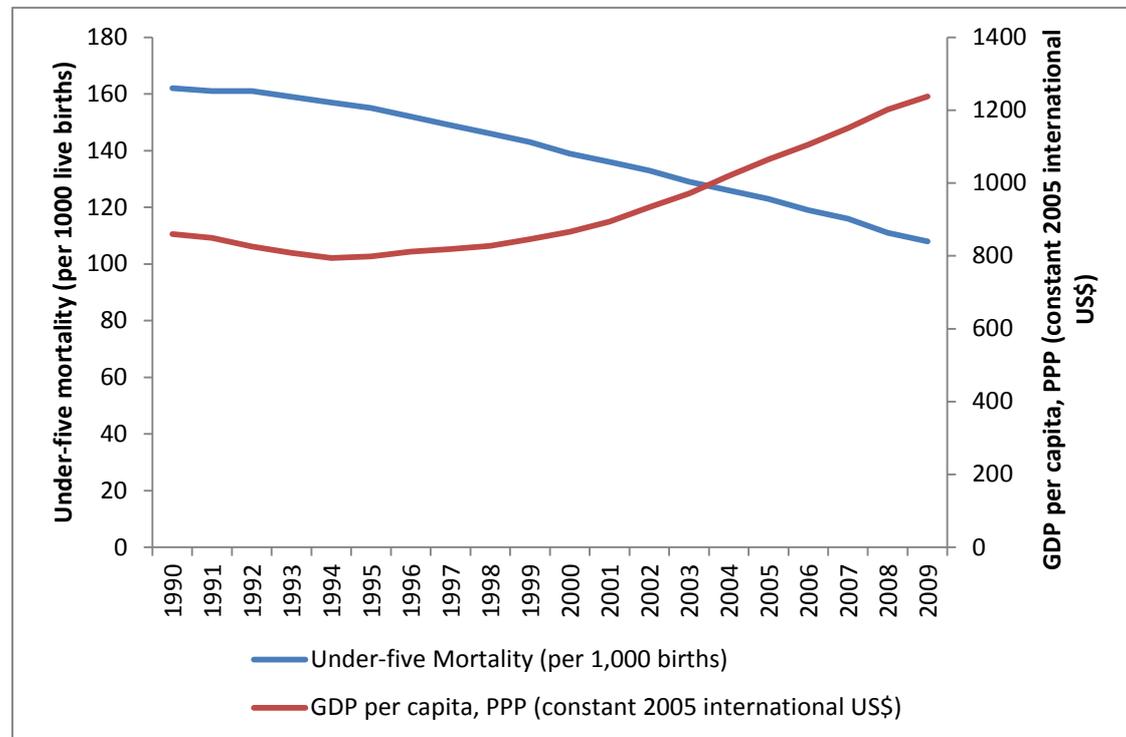
Socioeconomic Factors

A range of socioeconomic determinants at the community, household, and individual level are associated with child survival,(75, 81, 82) as shown in the impact model in Figure 45.

Economic poverty, either at the country or individual level, strongly correlates with poorer health outcomes,(83) hence GDP per capita income, a measure of population wealth in a country, is a typical macroeconomic determinant of health.(81) The relationship between GDP per capita and under-five mortality shows that a 1% annual increase in GDP per capita is associated with an estimated 0.4-0.6% reduction in under-five mortality.(84) In Mainland Tanzania, the GDP per capita (current US\$) was \$503 in 2009, up from \$300 in 1999.(85) Trends in GDP per capita and growth in Tanzania are shown in Figure 46. Between 1999 and 2009, Tanzania, experienced a compound growth of GDP per capita amounting to 44% in constant prices. Applying the upper and lower estimates of the relationship between growth and mortality reduction, we would expect that economic growth between 2000 and 2009 should deliver a reduction of under-five mortality ranging between 18% and 27%. Since the actual

reduction in under-five mortality observed over the period is 45%, this would imply that economic growth could explain between one-third and one-half of the mortality change that has occurred over the ten-year period.

Figure 46: Trends in gross domestic product (GDP) per capita and under-five mortality, Tanzania, 1990 - 2009



Household and microeconomic factors are important determinants of child health and malaria risk.(82, 86) Socio-economic differentials⁷ at the household level are associated with access to malaria interventions, increasing the vulnerability of the poorest.(87) Levels and trends in household attributes and other proxies of socio-economic status are summarized in Table 14.

Safe water and sanitary facilities contribute to improved child health and survival.(88) In 2010, 57% of households surveyed reported an improved water source (i.e., protected, borehole, piped), as compared to 66% in 1999. Having a water source within 15 minutes of household was 37% in 2010, as compared to 34% in 1999. Twelve percent of households had improved, unshared toilet facilities in 2010, as compared to 2%in 1999. During 1999 to 2010, access to improved water and sanitation did not change (Table 14).

Housing construction, such as flooring and roofing material, are associated with malaria risk.(89, 90) The Tanzanian Household Budget Surveys show housing conditions improved considerably in Mainland Tanzania in recent years.(4) From 2001/2 to 2007, households with an improved roof (i.e., not thatch, grass,

⁷ Socioeconomic status of households can be measured using asset index. The index is constructed using simple weighted average of proportion of households that own individual durable goods, such as such as, radio, TV, and cell phones, as well as access to electricity, piped water and improved toilet facilities. These are considered validated microeconomic proxies of household income. (Günther et al., 2011; Gamage-Mendis et al., 1991; Ye et al., 2006)

or mud) increased from 51% to 62%, while the fraction with modern floor materials (i.e., not earth, sand, or dung) increased from 21 to 32%. 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.

Table 14: Household attributes and asset ownership, Mainland Tanzania, 1999-2010

Survey year	1999			2010			% change	Sig.
	%	95% CI	n	%	95% CI	n		
Improved water source, (% households)	65.8	(59.1-71.8)	3526	56.9	(53.3-60.4)	9377	-13.5	ns
Time to water source <15 min, (% households)	34.3	(29.6-39.4)	3526	36.5	(33.8-39.4)	9377	6.4	ns
Improved toilet facilities (not shared), (% households)	1.5	(1.0-2.3)	3526	12.1	(10.5-14.0)	9377	7.1	*
Improved roof (not thatch/grass/mud), (% households) §	50.6	(47.3-53.8)	9483	61.9	(58.9-64.9)	9377	22.3	*
Modern floor material (not earth/sand/dung), (% households)	20.9	(17.0-25.4)	3526	31.8	(28.7-35.0)	9377	52.2	*
Electricity, (% households)	7.7	(5.5-10.7)	3526	14.2	(11.9-17.0)	9377	84.4	*
Telephone, (% households) §	8.9	(7.6-10.5)	9483	45.5	(42.9-48.0)	9377	411.2	*
Often/always had problems satisfying food needs in last yr. (% households) §	22.6	(21.2-24.1)	9483	23.3	(21.6-25.1)	9377	3.1	ns

*protected, borehole, piped; § signifies 2004/5 DHS source

Sig.= Statistical significance. Statistics with non-overlapping 95% confidence intervals are considered significantly different change. NS denotes no statistically significant change and * denotes statistically significant change

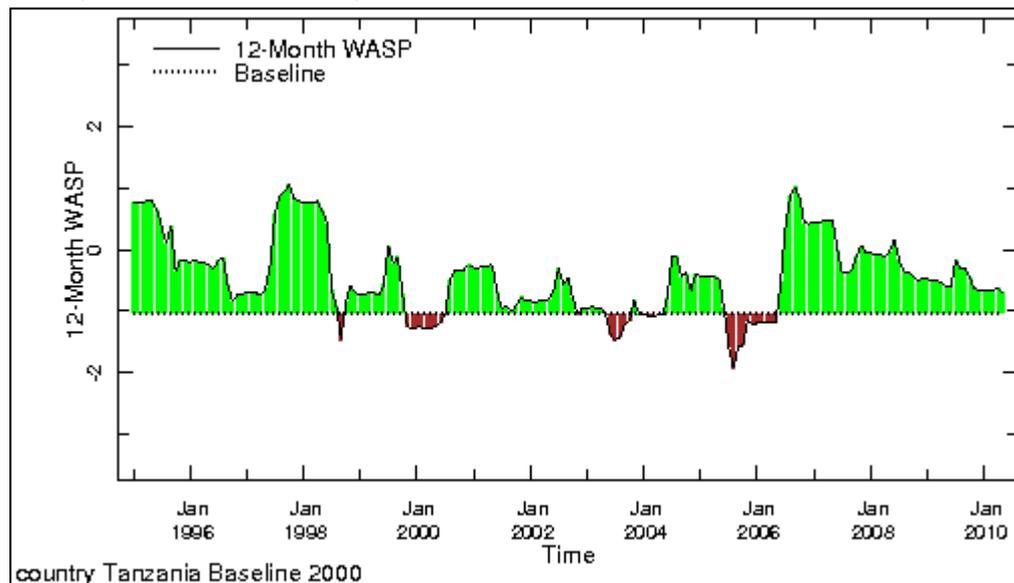
Climatic variability, particularly rainfall variations, can modify malaria transmission patterns.(91) Monthly rainfall data from 23 recording stations in Mainland Tanzania, provided by the Tanzania Meteorological Agency, were reviewed for the period 1999-2009. Data completeness was 99.8%, and values for missing months were interpolated using mean monthly rainfall for relevant stations from other years. The annual and monthly rainfall patterns, depicted in Annex A.3.23 and A.3.24, show substantial variations in annual and monthly rainfall patterns during 1999-2009, but with clear seasonal rainfall patterns (summary statistics for rainfall recorded in all the 23 stations are available in Annex A.3.25). The average annual rainfall recorded in Bukoba (1941 mm ± SD) and Mahenge (1877mm ± SD) was higher than other stations.

The 12-month Weighted Anomaly Standardized Precipitation (WASP)⁸ data between January 1995 and January 2010 with the year 2000 as baseline, was

⁸ Weighted Anomaly Standardized Precipitation (WASP) index is an estimate of the relative deficit or surplus of precipitation for different time intervals ranging from 1 to 12 months and is based solely on monthly precipitation data. To compute the index, monthly precipitation

reviewed to assess variations in rainfall in Mainland Tanzania. As shown in Figure 47, rainfall was generally above the WASP baseline during 1995-2010. Thus, rainfall patterns suitable for malaria transmission persisted throughout the evaluation period, and it is unlikely that any variations in rainfall could have altered malaria transmission during the evaluation period.

Figure 47: The 12-month Weighted Anomaly Standardized Precipitation (WASP) index, Mainland Tanzania, 1995-2010



At an individual level, maternal education is an important determinant of reproductive behavior, as well as maternal and child health.(81, 92-97) In Mainland Tanzania, 66% of women completed primary education in 2010, up from 52% in 1999, and women’s literacy was 70% in 2010, as compared to 64% in 1999 (Table 15).

Survivorship and health outcomes of children under-five are better among married women. In 1999, 66% of women reported being married at the time of survey as compared to 64% in 2010.

Exposure to mass media can influence women’s reproductive health behavior as well as illness recognition and health care seeking for their children. In Mainland Tanzania, the proportion of women who reported exposure to mass media was 78% in 2010, as compared to 65% in 1999.

departures from the long-term average are obtained and then standardized by dividing by the standard deviation of monthly precipitation. The standardized monthly anomalies are then weighted by multiplying by the fraction of the average annual precipitation for the given month. These weighted anomalies are then summed over varying time periods - here, 3, 6, 9 and 12 months. On the plots, the value of the given WASP index has itself been standardized. For the WASP index, shading starts at +/- 1.0 with green shades indicating unusually wet conditions and brown unusually dry, respectively. Regions with an annual average precipitation of less than 0.2 mm/day have been "masked" from the plot. Source: http://ccnmtl.columbia.edu/projects/iri/responding/tutorial_frame_t3p2.html

Table 15: Women's* education and marital status in Mainland Tanzania, 1999-2010

Indicator	1999			2010			% change	Sig.
	%	95% CI	N	%	95% CI	n		
Mean years of education	4.7	(4.4-5.0)	3929	5.7	(5.5-5.9)	9813	22.0	*
Completed primary education (%)	51.7	(47.8-55.5)	3929	66.2	(63.7-68.5)	9813	28.0	*
Literacy (%)	63.8	(59.5-67.9)	3929	70.1	(67.9-72.3)	9813	9.9	ns
Married (%)	65.9	(63.3-68.5)	3929	63.5	(62.1-64.9)	9813	-3.6	ns

*Women aged 15-49 years

Sig.= Statistical significance. Statistics with non-overlapping 95% confidence intervals are considered significantly different change. NS denotes no statistically significant change and * denotes statistically significant change

Proximate Determinants

Maternal and Child Health

Antenatal care visits are considered a key entry point for a continuum of care during and after pregnancy. They offer timely opportunities for receiving health promotions, as well as preventive and therapeutic interventions aimed at improving maternal, fetal, and newborn survival and wellbeing. 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 Mainland Tanzania, in 1999 70% of women attended the WHO-recommended four or more antenatal care (ANC4+) visits compared to 43% in 2010. During the same period, women who had their most recent births (within the last two years) protected against neonatal tetanus, using two doses of tetanus toxoid vaccine, was 62% in 1999 and 48% in 2010.

Child birth at health facilities, usually by skilled attendants, can reduce the chances of maternal and newborn complications. In 2010, 50% of live births occurred in health facilities, compared with 44% in 1999. Births in women with high-risk fertility behavior⁹ can increase the risk of early childhood mortality. From 1999 to 2010, births in any high-risk fertility category (57% in 1999 vs. 57% in 2010) or with avoidable fertility risk (17% in 1999 vs. 15% in 2010) did not change. Live births, with low-birth weight (< 2500 grams) were 8.4% in 1999 and 6.1% in 2010 (Table 16).

⁹ Births, in women who are relatively younger (less than 18 years of age) or older (after 34 years of age), too close together (less than 24 months apart), and multiple births (birth order more than 3).

The WHO Expanded Program on Immunization (EPI) offers vaccinations against common childhood communicable diseases and is considered one of the most cost-effective child survival interventions.(98, 99) Effective coverage of these vaccinations could lead to reductions in under-five mortality. In Mainland Tanzania, the recommended EPI schedule for children includes one dose each of BCG (to protect against tuberculosis) at birth or first clinic contact, and measles at nine months of age; three doses each of oral polio vaccine (OPV) and diphtheria, pertussis and tetanus vaccine (DPT), at 4, 8, and 12 weeks of age.(100). The hepatitis B and *Haemophilus influenzae (b)* (Hib) antigens were added to the DPT vaccine in 2001/2 and 2009, respectively. Table 16 reports coverage of each of these childhood vaccinations from 1999 to 2010, according to vaccination cards or mother's report during household surveys. In 2010, 75% of children aged 12-23 months received all of the vaccinations recommended in the EPI schedule, up from 68% in 1999. Measles vaccination, in children aged 12-23 months, was 85% in 2010 and 78% in 1999. Vaccination against Hib, given as DPTw-HB-Hib at birth, was 88% in 2010.

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, both globally and in Tanzania. 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. The prevalence and treatment seeking practices of these two conditions in Mainland Tanzania from 1999 to 2010 are shown in Table 16. These data were collected during household surveys by asking mothers whether their children under-five years of age had been ill with a cough accompanied by short, rapid breathing in the two weeks preceding the survey.

In the two weeks before the surveys in 2010, 4% of children under-five were ill with symptoms of ARI, cough and rapid breathing, as compared to 8% in 2004/5 (The case definition of ARI in the 1999 Tanzania Reproductive Child Health Survey was different from what was used in the 2010 Tanzania DHS; 2004/5 and 2010 survey definitions are comparable). Eighty-five percent of children under-five with symptoms of ARI sought treatment at a health facility in 2010, as compared to 81% in 2004/5.

During the two weeks preceding the survey, 15% of children under-five had diarrhea in 2010, as compared to 13% in 1999. Sixty-four percent of children with diarrhea were taken to a health provider in 2010, as compared to 65% in 1999.

Table 16: Maternal and child health in Mainland Tanzania, 1999-2010

Indicators	1999			2010			% change	Sig
	%	95% CI	N	%	95% CI	n		
ANC visits 4+ (% women, most recent live birth, 0-2yrs)	69.9	(63.8-75.4)	2131	42.7	(40.6-44.8)	5378	-38.9	*
Tetanus toxoid 2+ (% women, most recent live births, 0-2yrs)	61.5	(55.9-66.8)	2131	47.9	(45.8-50.1)	5378	-22.1	*
Delivery at a health facility (% women, live births 0-4yrs)	43.7	(37.6-50.0)	3196	50.2	(46.9-53.4)	7955	14.9	ns
Births in any high-risk fertility category (%)	56.9	(53.6-60.2)	3196	57.1	(55.2-58.9)	7955	0.4	ns
Births with avoidable fertility risk (%)	17.3	(15.4-19.5)	3196	14.9	(13.9-16.0)	7955	-13.9	ns
Low birth weight <2500g (%)	8.4	(6.3-11.2)	772	6.1	(5.0-7.4)	2786	-27.4	ns
Small/very small size at birth (mother's estimate) (%)	10.8	(8.9-13.1)	3196	8.3	(7.5-9.3)	7955	-23.1	ns
EPI Vaccination coverage								
BCG	92.6	(89.7-95.5)	578	95.4	(93.5-96.8)	1533	3.0	ns
DPT3 / DPT3-HB-Hib	80.9	(73.2-86.9)	578	87.8	(84.8-90.3)	1533	8.5	ns
Polio3	79.9	(73.9-84.8)	578	84.9	(81.7-87.6)	1533	6.3	ns
Measles	78.2	(72.0-84.4)	578	84.5	(81.6-86.9)	1533	8.1	ns
All (BCG, measles, DPT3, polio3)	68.3	(61.1-74.7)	578	75.1	(71.6-78.3)	1533	10.0	ns
Children 0-4yrs with ARI sought treatment	81.1	(72.1-87.7)	388	84.6	(78.3-89.4)	319	4.3	ns
Children 0-4yrs with diarrhoea sought treatment	63.6	(56.5-70.2)	349	52.6	(48.2-56.9)	1086	-17.3	ns
Sig.= Statistical significance. Statistics with non-overlapping 95% confidence intervals are considered significantly different change. NS denotes no statistically significant change and * denotes statistically significant change								

Breastfeeding Practices and Under-nutrition 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, two of the leading causes of under-five mortality.(72, 101) Early and exclusive breastfeeding is an important child survival intervention that reduces neonatal, infant, and child mortality,(102) and as much as 13% of all cause under-five mortality could be prevented by promotional strategies to increase breastfeeding rates.(72) Currently the WHO recommends early and exclusive breastfeeding for the first six months following birth.(103, 104) Sixty percent of children under-six months were exclusively breastfed in 2010, as compared to 30% in 1999. The percentage of children still breastfeeding by 23 months was 48% in 2010, as compared to 49% in 1999.

Under-nutrition 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.(105) The continuum of maternal, fetal, and child under-nutrition is estimated to result in 3.5 million preventable child and maternal deaths annually.(106)

In children under-five, the standardized anthropometric measures of under-nutrition(107) are a) low birth weight due to intrauterine growth restriction ; 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, indicated by a low weight-for-height.

In Mainland Tanzania, under-nutrition prevalence in children under-five was determined during a series of household survey conducted during 1999 to 2010 (Table 17). Those household surveys conducted in 2004/5 and 2010, found 23% of households “often” or “always” had problems satisfying food needs in the past year (Table 14). In the 2010 survey, 8.4% children were reported to be born with a low birth weight, as compared to 6.1% in 1999. Underweight, stunting, and wasting prevalence in children under five, was 21%, 36% and 5% respectively in 2010, as compared to 30%, 44%, and 5%, respectively, in 1999.

Among micronutrient deficiencies, vitamin A deficiency has been implicated in increased morbidity and mortality from infectious diseases prevalent in children-under five, such as, measles, diarrhea, and ARI, and globally result in an estimated 600,000 under-five deaths annually.(106) 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 pre-existing vitamin A deficiency has been shown to replenish vitamin A stores needed for essential physiological functions and decrease under-five mortality by up to 23%.(108, 109) In Mainland Tanzania, biannual vitamin A supplementation campaigns began in 2002, to complement routine supplementation after birth at health care facilities.(110) Progress on reducing vitamin A deficiency is measured using coverage of micronutrient supplementation campaigns. A 1996 survey by the Tanzania Food and Nutrition Center found that 23% of children under-five had retinol deficiency, placing Tanzania in the “retinol deficient” category. In Mainland Tanzania, 60% of

children age 6–59 months received a vitamin A supplement in the six months prior to the survey, in 2010 well above the 13% in 1999.

Table 17: Breastfeeding and under-nutrition in children and women in Mainland Tanzania, 1999-2010

Indicator	1999			2010			% change	Sig.
	%	95% CI	n	%	95% CI	n		
Early and exclusive breastfeeding (%)	32.9	(24.4-42.5)	317	58.7	(54.1-63.2)	849	78.4	*
Under-fives stunted (%) **	48.4	(44.7-52.1)	2,509	42.3	(40.6-44.0)	7292	-12.6	*
Under-fives underweight (%) **	24.5	(21.4-27.8)	2,509	15.7	(14.4-17.0)	7292	-35.9	*
Vitamin A supplementation within past 6 mo. (% children 6-59 mo)	13.3	(10.3-16.9)	2,503	59.8	(57.4-62.2)	6638	349.6	*

** 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 * 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.(111) Child survival stagnated and even reversed in many countries in sub-Saharan Africa(112) and HIV/AIDS was found to be an increasingly important cause of under-five mortality in sub-Saharan Africa.(113)

In Mainland Tanzania, where the first cases of HIV infection were reported in 1983, the disease rapidly spread. Population trends in prevalence of HIV infection in Tanzania were monitored through the HIV/AIDS Indicator Surveys of 2003/4 and 2007/8. Nationally representative estimates of HIV prevalence in Mainland Tanzania in women of reproductive age was 7.7% in 2003 and 6.6% in 2007. Data from repeat surveys of women attending antenatal clinics showed HIV prevalence of 9.6% (95% CI 8.9-10.2) in 2001/2 and 7.0% (95% CI 6.7-7.2) in 2007/8.

Population based estimates of HIV infection and mortality 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 1000 live births (corrected for other competing causes of mortality) was around 5% in 2010 as compared to 15.6 % in 1999.(113, 114)

Plausibility Argument

To determine whether it is plausible to conclude that scale-up of malaria control interventions could have contributed to the observed 45% 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 (Figure 45).

Assessment of the evidence from the direct causal pathway (Figure 45) supporting lower mortality: Evidence from the current evaluation supporting a causal role of malaria control interventions on reducing malaria-specific mortality are summarized in Table 18.

During the period 1999 to 2010, mortality in children under-five declined from 148 to 81 deaths per 1000 live births. 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 decline was larger in rural areas (49%), where the burden of malaria is expected to be much larger, as compared to urban areas (29%). During the same period, the relative decline in mortality in children 6-23 months, who are at higher risk of severe malaria and mortality, was 49%, as compared to 34% in children 24-59 months. From 2004 to 2010, the relative decline in severe anemia (Hb<8g/dL) in children 6-59 was larger in rural areas (54%) as compared to urban areas (24%). Severe anemia in children 6-23 months, who are at a higher risk of severe malaria syndromes and mortality, (62, 63) declined by 60% in high malaria risk areas, as compared to medium (28%) and low risk areas (17%). It is therefore plausible that reductions in severe anemia could have led to reductions in malaria-specific mortality.

During 1999-2010, the relative increase in household ownership¹⁰ and use of ITN among children under-five was 34-fold and, considering the proven protective efficacy of ITNs (55%)(115) and sustained insecticide susceptibility of the local malaria vectors, reduced malaria-attributable mortality in children 1-59 months by 35%.

Care-seeking for fever at formal health providers and fever treated with any antimalarial did not significantly change during the evaluation period. Although in 2010, only 27% of children under-five received an ACT on or the next day following fever onset, the superior therapeutic efficacy of ACTs,(39) compared to both CQ and SP,(32) the first-line antimalarial drugs prior to introduction of ACTs in 2007, would be expected to result in higher rates of parasite clearance, fewer chronic infections, and better treatment outcomes. However, because ACT use was only 27%, at a population level, the high (86-99%) protective efficacy of ACT treatment of uncomplicated *P. falciparum* malaria(116) compared to 70-80% for SP at the time of drug change may not have contributed substantially in reducing malaria mortality in children 1-59 months.

¹⁰ Household ITN ownership in 1999 estimated based on ITN use in children under-five

Intermittent preventive treatment for malaria prevention during pregnancy with at least two therapeutic doses of SP (IPTp2+) was 26% in 2010, and did not significantly increase during the evaluation period from 21% in 2004/5; thus, it is unlikely that IPTp coverage would have contributed to any decline in neonatal mortality.

Table 18: Summary of evidence of changes in under-five mortality in Mainland Tanzania, 1999-2010

	Evidence supporting lower mortality	No evidence suggesting change in mortality	Evidence supporting higher mortality
Malaria control interventions	<ul style="list-style-type: none"> • Household Ownership of ITNs • ITN use by children under-five • IRS (in selected areas) 	<ul style="list-style-type: none"> • ACT within the same or next day after fever onset • IPTp2+ 	
Other contextual determinants	<ul style="list-style-type: none"> • Fundamental determinates <ul style="list-style-type: none"> ○ GDP per capita growth ○ Maternal education • Proximate determinants <ul style="list-style-type: none"> ○ Nutritional status ○ Early and exclusive breastfeeding ○ Vitamin A supplementation ○ Hib vaccination ○ HB vaccination ○ ARI prevalence ○ PMTCT, ART 	<ul style="list-style-type: none"> • Birth at health facility • DPT3, measles, BCG & polio vaccination • Diarrhea prevalence • Diarrhea treatment (oral rehydration solution/extra fluids) • ARI care seeking • HIV prevalence (female 15-49 years) 	<ul style="list-style-type: none"> • Antenatal Care attendances 4+ • Neonates protected from Tetanus

Assessment of the evidence from the indirect causal pathway (Figure 45) supporting lower mortality

The fundamental and proximate determinants of child health and mortality that were not in the direct causal pathways of the impact model (Figure 45) were examined to assess alternate explanations, other than malaria program factors, that might account for the mortality reduction.

In 2010, two important fundamental determinants, not in the direct causal pathway – GDP per capita and maternal education – changed favoring lower mortality following scale-up of malaria control interventions (Table 18) (Figure 45). Improvements in socioeconomic status and maternal education in Mainland Tanzania from 1999 to 2010 are considered significant contributors to mortality decline in children under-five. However, the dynamics of socio-economic determinants on population health is often complex (117, 118) and these determinants, arguably, (119) must operate through the proximate determinants, which are typically the biological risk factors, to affect child survival. (75)

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. An in-depth analysis needs to be undertaken to understand if and how climatic variability could have influenced malaria transmission in Mainland Tanzania from 1999 to 2010. Review of data from 23 rainfall station suggests rainfall patterns suitable for malaria transmission persisted throughout the evaluation period and it is unlikely that any variations in rainfall could have altered malaria transmission during the evaluation period.

During the evaluation period, several proximate determinants changed favoring lower mortality. As shown from nationally representative household surveys (Table 17), the 350% relative increase in vitamin A supplementation in children 6-59 months favors lower mortality. However, data from WHO/UNICEF, which provides annual trends and accounts for supplemental immunization activities, suggests that the proportion of children under-five fully protected by two doses of Vitamin A was sustained above 80% since 2000, but has not increased significantly. It is therefore considered unlikely that the relative contribution of Vitamin A supplementation resulted in additional reduction in under-five mortality.

Haemophilus influenzae (b) vaccination coverage, as a component of the pentavalent vaccine DPTw-HB-Hib, in children under-five increased to 88% in 2010 following its introduction in the EPI schedule in 2009. However, the length of time between vaccines introduction in 2009 to mortality decline measured in 2010, is much too soon for Hib to have lowered under-five mortality. Although the increase in Hepatitis B vaccine coverage, as part of the DPTw-HB-Hib vaccine, could have lowered the burden of transmission and infections, it is unlikely to have contributed substantially to the reduction in under-five mortality as the hepatitis B mortality burden, typically falls on the older age groups. (120) Sustained high coverage of other vaccinations in the EPI schedule-- BCG, measles, and OPV-- were observed during the evaluation period, but no significant increases in sustained high coverage of these vaccinations were observed during 1999 to 2010. It is therefore possible that there was little or no relative increase in the contributions of these interventions on the observed reductions in under-five mortality.

Stunting, underweight, and wasting in children under five significantly declined by eight percentage points, nine percentage points and 0.7 percentage points, respectively between 1999 and 2010. Models derived from international data

estimate that a 5% reduction in the prevalence of underweight is associated with a 13% reduction in under-five mortality and a 31% reduction in child mortality, independent of socio-economic improvement. Applying these coefficients to the Mainland Tanzania data, nutritional improvement between 1999 and 2010 would be expected to result in a decline of 23% in under-five mortality and a 56% reduction in child mortality (age 1-4 years). 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 interventions are associated with improved anthropometric indices. It is also worth noting that the age-pattern of mortality decline observed in this evaluation was much greater in the post-neonatal category than among children aged 1-4; the opposite of what would be expected if nutrition improvement were the dominant driver of mortality change. It is therefore unlikely that improved nutrition could have independently and substantially contributed to lower mortality.

In summary, the 45% decline in under-five-mortality in Mainland Tanzania from 1999 to 2010 was observed following a 36-fold relative increase in ITN use among children under-five and 50% decline in severe anemia prevalence in children 6-59 months. Larger declines in under-five mortality and severe anemia were observed in rural areas, where the risk of malaria is higher compared to urban areas. The decline in mortality and severe anemia was also larger in children 6-23 months, who are at a higher risk of severe malaria syndromes and mortality, as compared to children 24-59 months. During the evaluation period, climatic conditions favorable for malaria transmission persisted, and no additional sustained increase in other child survival interventions were observed. It is therefore plausible to conclude that reductions in under-five mortality in Mainland Tanzania during the period 1999 to 2010 were at least in part due to reductions in malaria-specific mortality.

LiST Model: Estimating Lives Saved

Estimating the number of deaths prevented due to the scale-up of any one particular intervention is complicated by the fact that other health interventions are likely to be introduced or scaled up simultaneously (as seen in the improvements in health indicators in Table 18). The Lives Saved Tool (LiST) is one method of assessing lives saved (deaths prevented) in the context of a complex set of health interventions. The LiST model was created by the child health community and has recently been used by the malaria community to estimate the number of lives saved due to ITN scale-up in 34 countries in sub-Saharan Africa and due to IPTp scale-up in 27 countries in sub-Saharan Africa.(121) It was also used by Global Fund to assess the number of lives saved by ART, directly-observed treatment, short-course for tuberculosis and ITNs.(122)

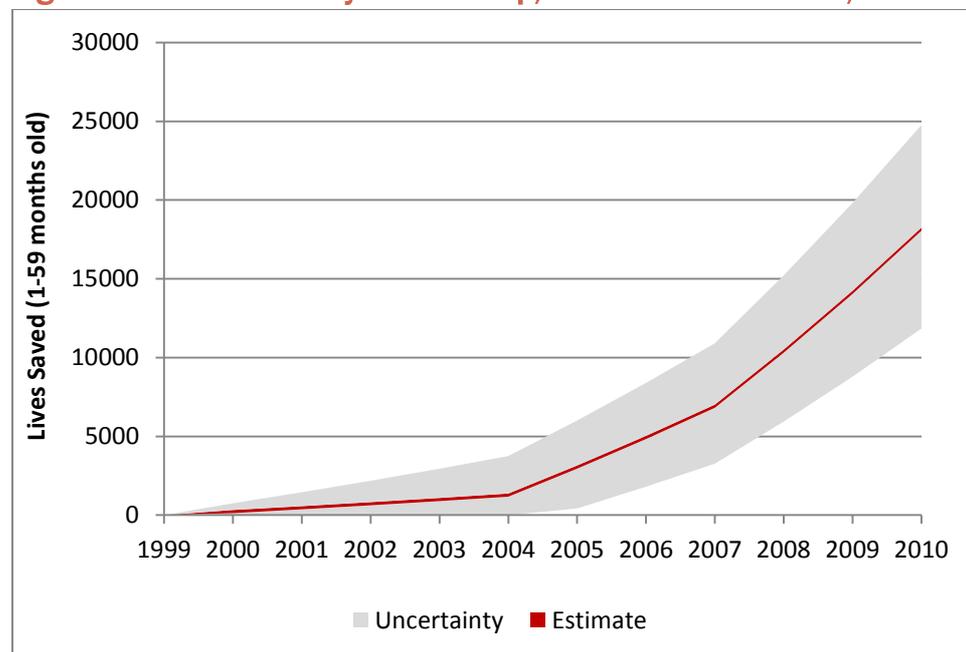
Studies have shown that LiST-modeled estimates of mortality reductions are similar to measured mortality reductions. A validation study, performed to compare LiST-estimated mortality reductions with mortality measured through demographic surveys, demonstrated that the LiST-modeled mortality reduction was within the 95% confidence interval of the measured mortality reduction.(123) However, in another example, the LiST model underestimated the measured mortality reduction,(123) which was suggested to be due to limitations of the data input into the LiST model. In another study, a comparison of LiST-modeled changes in all-cause child mortality with measured reductions in all-cause child mortality from malaria vector control studies, found the LiST modeled estimates fell within the 95% confidence intervals around the measured mortality reductions.(124) The LiST model, therefore, is considered to be one method of estimating changes in mortality, offering an alternative way of investigating a given set of national data, but it must always be compared to measured mortality changes. We built upon the 2010 RBM Progress & Impact Series report “Saving Lives with Malaria Control: Counting Down to the Millennium Development Goals”(121) to look at child survival in Mainland Tanzania and to include updated intervention coverage values for malaria control interventions and other child and maternal health interventions included in the 2010 TDHS.

The LiST model is a computer-projection model that estimates the number of deaths of children under five that can be prevented within specific cause-of-death categories due to the scale-up of maternal and child health interventions. The LiST model makes use of data on the country’s demographics (including growth rate), under-five mortality rate, breakdown of cause-specific mortality, protective effect of interventions on cause-specific mortality and intervention coverage. The national population demographic data was adjusted for the percentage of the population living in Mainland Tanzania (97.6%). The Mainland Tanzania neonatal, infant and under-five mortality rates for the baseline year of 1999 (0-4 year period prior to the survey) were obtained from the 1999 TDHS. The cause-specific breakdown of child mortality used here was developed by the Child Health Epidemiology Reference Group and the proportion of under-five deaths directly attributable to malaria was estimated to be 23.6% in the year

2000.(9, 10) The protective efficacy of vector control methods (ITN or IRS) for preventing under-five child deaths due to malaria is estimated to be 55%;(115) whereas, the protective efficacy of malaria control measures (ITN use by pregnant women or use of IPTp) during pregnancy is estimated to be 35%.(115) The intervention coverage levels for non-malaria indicators were obtained specifically for Mainland Tanzania wherever possible, primarily from the Tanzania DHS survey set (see detailed methods in Annex 2.3). The values were linearly interpolated between survey years.

One of the primary malaria prevention measures in Mainland Tanzania has been ITNs. Most malaria-attributed deaths are assumed to be in the rural areas, therefore, the rural Mainland value for the percentage of households owning at least one ITN was used to conservatively calculate the malaria-specific deaths prevented by vector control measures in all of Mainland Tanzania. Figure 48 shows the deaths averted due to the scale-up of ITNs in Mainland Tanzania from 1999 to 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 11 years of ITN scale-up, approximately 61,300 (32,100-95,100) deaths were prevented in children 1-59 months, compared to what would have happened if no vector control scale-up had occurred since 1999 coverage levels. A sharp rise in the number of lives saved occurred in 2004, corresponding to the increase in coverage of malaria control interventions.

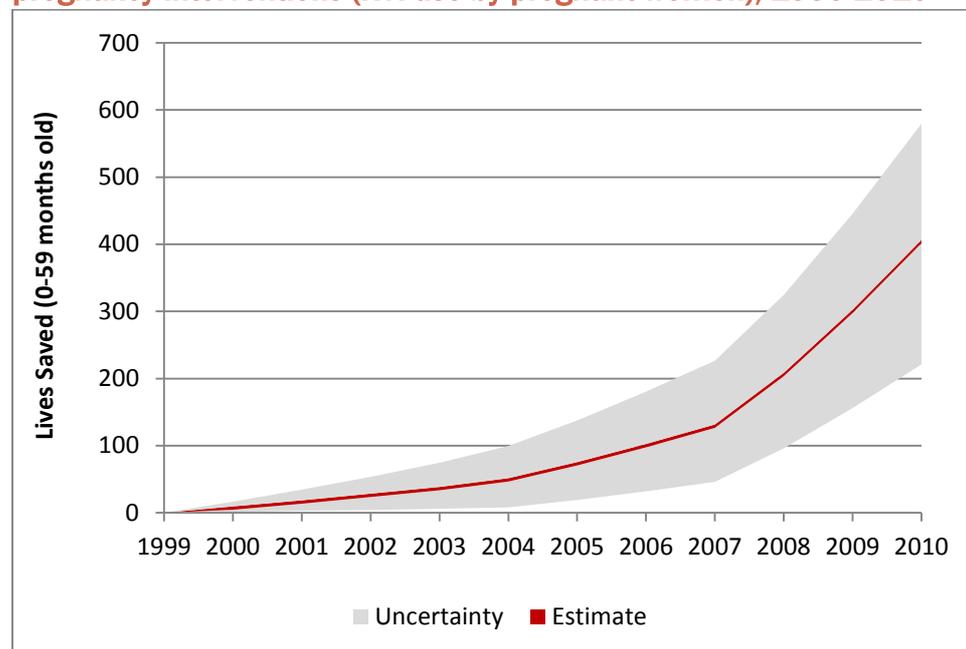
Figure 48: Lives saved by ITN scale-up, children 1-59 months, 1999-2010



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 or IPTp during pregnancy. Prevention of malaria in pregnancy is thought to reduce under-five mortality by preventing low birth weight by decreasing intrauterine growth retardation.(101, 115) In the 2010 TDHS, the percentage of pregnant women sleeping under an ITN the previous

night in rural Mainland Tanzania (58.7%) was higher than the percentage of pregnant woman in rural Mainland Tanzania who received two or more doses of IPTp during an antenatal care visit during their last pregnancy (24.6%). Therefore, in the LiST model the value for the percentage of pregnant women sleeping under an ITN was used for the malaria in pregnancy intervention coverage levels. Figure 49 shows the deaths averted due to the scale-up of ITN use by pregnant women in Mainland Tanzania from 1999 to 2010. It is estimated that approximately 1,300 (600-2,100) deaths were prevented in children 0-59 months due to the prevention of malaria in pregnancy, compared to if no malaria control intervention scale-up had occurred since 1999 coverage levels. The largest increase in deaths prevented occurs after 2007.

Figure 49: Lives saved in children aged 0-59 months by scale up of malaria in pregnancy interventions (ITN use by pregnant women), 1999-2010



The LiST analysis presented here demonstrates a 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. The LiST analysis presented here does not take into account the effects of prompt and effective treatment of malaria. The estimate of malaria deaths averted is also greatly underestimated because the LiST model does not take into account reductions in indirect malaria mortality. Finally, malaria in pregnancy interventions only affect intrauterine growth retardation and not prematurity in the model.

The LiST model estimates that the malaria prevention strategies of providing ITNs to households and prevention of malaria in pregnancy result in a decrease in overall under-five child mortality by reducing the number of malaria-specific deaths and neonatal and postneonatal deaths (the latter two from malaria in pregnancy interventions). Over the previous eleven years, approximately 63,000 (uncertainty bound 33,000-97,000) deaths were directly prevented by the

malaria preventative interventions, predominantly ITNs, which accounted for 97.9% of the deaths prevented here (see Annex 2.4 for yearly estimates of deaths prevented). The majority of deaths prevented were in the last five years following inputs of funding and commodities for malaria prevention.

The estimated number of children's (1-59 months) deaths prevented over the eleven year period of 1999 to 2010 due to the scale-up of multiple maternal and child health interventions was approximately 133,000. For a list of the interventions and coverage levels used in the model see Annex 2.3. In addition to household ownership of ITNs, several other interventions entered into the LiST model were estimated to have saved lives of children 1-59 months of age between 1999 and 2010. PMTCT and improved excreta disposal were estimated to have prevented over 5,000 deaths each, complementary feeding, DPT3 vaccine and Hib vaccine over 10,000 deaths each and vitamin A for prevention over 65,000 deaths when coverage increased relative to 1999 levels. Declining use of a water connection in the home, hygienic disposal of children's stools, and the use of oral rehydration salts for the treatment of diarrhea and fluctuating measles vaccine coverage rates were estimated to have resulted in increased deaths in children 1-59 months over this eleven-year period, compared to 1999 coverage levels.

Of the measured change in all-cause under-five mortality seen between the 1999 and 2010 surveys, according to the LiST model scale-up of ITN coverage may have contributed to approximately 15% of the reduction (10 deaths prevented per 1,000 live births). These results demonstrate a potential impact of malaria control interventions on reducing under-five mortality and support that it is plausible that malaria control interventions were responsible for a sizeable portion of the reduction in under-five mortality that has been observed in Mainland Tanzania between 1999 and 2010.

CONCLUSION

Conclusion

In this section we summarize the success of malaria control intervention scale-up and changes in malaria-related outcomes in Mainland Tanzania, and assess the evidence supporting the conclusion that malaria intervention scale-up led to changes in malaria-related outcomes and impact during the evaluation period, 1999 to 2010.

Malaria control interventions have been scaled up

Ownership of ITNs by households and ITN use among children under-five years old increased from close to zero to roughly 20% in 2004/5 to about 60% by 2010. Much of this increase in ITN ownership and use was observed following the “under-five catch-up campaign” in 2009, which distributed free ITNs to all children under-five. Socio-economic inequity in ITN ownership and use, which persisted throughout the 2000s, disappeared after the under-five catch-up campaign. In conformity with studies conducted in different settings of sub-Saharan Africa, scale-up of ITN ownership and use in Mainland Tanzania should have led to a reduction in malaria parasite prevalence, anemia, and all-cause under-five mortality.

Case-management of uncomplicated malaria changed to increasingly efficacious antimalarials, from CQ to SP in 2001, and from SP to ACTs (ALu) in 2006, with the therapeutic efficacy of ALu above 95%. In Mainland Tanzania, about 60% of children received any antimalarials the same or the next day following fever onset, and this did not change significantly during the evaluation period. The number of children receiving the recommended (more efficacious) antimalarials is gradually increasing from a very low level and can be expected to have modestly improved malaria treatment outcomes, reduced case-fatality, shortened duration of illness episodes, reduced chronic asymptomatic infection, and reduced malaria-associated anemia. ALu use was only 27% in the latter part of the decade, but changes from CQ (>50% treatment failure) to SP and then to ALu may have had a modest impact on mortality.

Since its inception in 2001, IPTp has reached barely a quarter of all pregnant women, and roughly double that number took at least one dose of SP for prevention. However, given the lack of change in the coverage of IPTp over the evaluation period, it is unlikely that IPTp contributed to the improvement in birth weight and neonatal mortality observed since baseline.

Malaria-related morbidity has declined

Severe anemia in children under-five was halved between 2004 and 2010, with larger declines in children 6-23 months, who are relatively at a higher risk of severe malaria-related syndromes and mortality. Trends in long-term malaria parasitemia representative of Mainland Tanzania were not available; however, results from all available sub-national surveys indicate declining malaria parasitemia, which may date back to the mid-1990s. The evidence suggests that malaria prevalence has continued to decline during the period of intervention

scale-up, and that the trend has continued beyond the latest national survey estimate in 2007/8.

Mortality in children under-five years of age has declined

Under-five mortality fell by 45% between 1999 and 2010. The mortality declines were larger in children residing in rural areas (49%) as compared to children living in urban areas (29%). The relative mortality decline, in children 6-23 months age was larger (49%) than children 24-59 months (34%). The largest mortality decline was observed in children 1-5 months (66%), possibly reflecting the impact of other child survival interventions. Mortality declines from 1999 to 2010 were larger in regions with medium or high malaria risk than those with low malaria risk. The timing of the change in these mortality trends broadly corresponds with the period during which malaria interventions were scaled-up.

Contextual Factors and Plausibility Argument

To examine whether the marked reduction in under-five mortality 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 the evaluation period, from 1999 to 2010.

Among the social and economic determinants of child survival, increases were seen in GDP per-capita and women's education, which could have been significant contributors to mortality decline in children under-five from 1999 to 2010. However, the dynamics of socio-economic determinants on population health is often complex and these determinants must operate through the proximate determinants to affect child survival.

Two important proximate determinants of child survival interventions increased during the evaluation period: Hib vaccinations and vitamin A supplementation. The coverage of Hib vaccinations in children under-five rapidly increased to 88% in 2010 following its introduction in 2009. While this could have contributed to a reduction in all-cause under-five mortality, it is unlikely to have substantially contributed to the mortality decline given the lag period between vaccine introduction and the latest mortality measurement was less than a year. Additionally, the 2010 mortality estimates are for the five-year period 2006 – 2010, a period before the introduction of Hib vaccination. As shown from nationally representative household surveys, the 350% relative increase in vitamin A supplementation in children 6-59 months favors lower mortality. However, other data from WHO/UNICEF, which provides annual trends and accounts for supplemental immunization activities, suggests that vitamin A supplementation was sustained above 80% since 2001, but did not increase significantly. It is therefore considered unlikely that the relative contribution of vitamin A supplementation resulted in additional reductions in under-five mortality.

Similarly, from 1999 to 2010, sustained coverage of other child survival interventions, including other immunization services, continued to contribute to

reductions in child mortality, but none sustained significant increases during the evaluation period. It is therefore likely that these interventions, while contributing to child survival, did not relatively reduce under-five mortality during the evaluation period.

An in-depth analysis needs to be undertaken to fully understand if climatic variability could have influenced malaria transmission during the evaluation period. However, an initial review of data from 23 rainfall stations suggests rainfall patterns suitable for malaria transmission persisted throughout the evaluation period, and it is unlikely that any variations in rainfall could have altered malaria transmission during this period.

In summary, the decline in under-five-mortality in Mainland Tanzania from 1999 to 2010 was observed following a 36-fold increase in ITN use among children under-five and 50% decline in severe anemia prevalence in children 6-59 months. Larger declines in under-five mortality and severe anemia were observed in rural areas, where the risk of malaria would have been higher compared to urban areas. The decline in mortality and severe anemia was also larger in children 6-23 months of age, who are at a higher risk of severe malaria syndromes and mortality, as compared to children 24-59 months of age. During the evaluation period, climatic conditions favorable for malaria transmission persisted, and no additional sustained increase in other child survival interventions were observed. It is therefore plausible to conclude that the reductions in under-five mortality in Mainland Tanzania during the period 1999 to 2010 were at least in part due to reductions in malaria-specific mortality.

The plausibility of the association between scale up of malaria control interventions and impact is further bolstered by case-study evidence showing a steep decline in parasitemia and anemia (Lindi/Mtwara and Ifakara) and in under-five mortality (Ifakara) following the scale up of ITNs.

Quantifying the deaths prevented by scale-up of malaria control interventions

Our quantitative assessment based on the LiST model of the expected impact of various health interventions – including, but not limited to malaria control – shows that ITNs are estimated to have prevented a cumulative total of 61,300 (range 32,100-95,100) under-five deaths between 1999 and 2010, with a further 1300 (range 600-2100) deaths prevented by the increase in ITN use by pregnant women. We consider this estimate to be highly conservative, because the model:

- employs rural, rather than national, coverage estimates for malaria interventions;
- does not include the indirect impact of malaria control on mortality;
- does not include the impact of prompt and effective treatment of malaria.

A recent publication using the LiST model for all of Tanzania estimated that 65,100 (range 45,000-100,400) child deaths were prevented by vector control

scale-up between 2001-2010,(125) which overlaps with the estimates obtained here.

The magnitude of modeled deaths prevented by malaria control is equivalent to approximately 18,000 deaths in 2010, when annual total mortality of under-fives amounted to roughly 112,000. In the absence of malaria control, this suggests that under-five mortality would have been roughly 15% higher. Stated otherwise, these (highly conservative) estimates predict that malaria control accounts for roughly 15% of the total reduction in under-five mortality between 1999 and 2010.

Mainland Tanzania and its partners invested significantly in malaria control in the decade 2000 - 2010. The results from this impact evaluation show that those investments paid off in important reductions in malaria morbidity and mortality in children under five years of age. Even considering that many of our estimates are conservative, tens of thousands of deaths have been prevented since the year 2000. The support of the Tanzanian Government, the excellent leadership of the NMCP and the willingness of the development partners to work together led to the substantial gains documented in this evaluation. Investments should continue or even increase to maintain and improve on current malaria control efforts.

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