An Epidemiological Profile of Malaria and its Control in Malawi

Report prepared for National Malaria Control Programme
By

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&

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Abbreviations

ACPR	Adequate Clinical and Parasitological Response
ACSI-CCCD	Africa Child Survival Initiative - Control of Communicable Childhood Diseases
ACT	Artemisinin-based Combination Therapy
ADB	African Development Bank
AERC	African Economic Research Consortium
AFRO	WHO Office for the Africa Region
AJOL	African Journals Online
AL	Artemether-Lumefantrine
ANC	Antenatal Care
ANVR	African Network for Vector Resistance
aOR	adjusted odds ratio
APRD	Arthropod Pesticide Resistance Database
AQ	Amodiaquine
AS	AQ+Artesunate
BCC	BehaviourChange Communication
BIC	Bayesian Inference Criteria
BITNet	Blantyre Insecticide Treated Net Project
BIMI	Blantyre Integrated Malaria Initiative
CBDA's	Community-Based Distributing Agents
CCAP	Churches of Central Africa, Presbyterian
CDC	Centers for Disease Prevention and Control
CDF	Colonial Development Fund
CG	Core Group
CHAM	Christian Health Association of Malawi
CIDA	Canadian International Development Agency
C-IMCI	Community IMCI
CMS	Central Medical Services
CPC	Climate Prediction Centre
CPG-DDS	Chlorproguanil—Dapsone
CQ	Chloroquine
CRDT	Constrained Refined Delaunay Triangulation
CSOs	Civil Society Organizations
DAs	District Assemblies
DALY	Disability Adjusted Life Year
DCW	Digital Chart of the World's Populated Places
DDT	Dichloro-Diphenyl-Trichlorethane
DFID	Department for International Development
Dhfr	Dihydrofolate Reductase
DHMT	District Health Management Teams
DHO	District Health Officer
Dhps	Dihydropteroate Synthase
DHS	Demographic and Health Surveys

DIC	Deviance Information Criterion
DRF	Drug Revolving Fund
DSS	Demographic Surveillance Site
DVS	Dominant Vector Species
E	Erythromycin
EAD	Environmental Affairs Department
EHP	Essential Health Package
EHRP	Emergency Human Resource Programme
EIR	Entomological Inoculation Rates
EPI	Expanded programme of Immunization
ERP	Economic Recovery Plan
ETF	Early Treatment Failure
EVI	Enhanced Vegetation Index
FANC	Focused Antenatal Care
FAO	Food and Agriculture Organization
FEWS	Famine Early Systems Network
FIND	Foundation for Innovative New Diagnostics
GAUL	Global Administrative Unit Layers
GDN	Global Development Network
GDP	Gross Domestic Product
GIS	Geographic Information Systems
GF	Gaussian Field
GLWD	Global lakes and Wetlands
GMEP	Global Malaria Eradication Programme
GMRF	Gaussian Markov Random Field
GoM	Government of Malawi
GPS	Global Positioning Systems
GRF	Gaussian Random Field
GRUMP	Global Rural Urban Mapping Project
HDI	Human Development Index
HDSS	Health and Demographic Surveillance System
HIS	Health Information Systems
HMIS	Health Management Information Systems
HSA's	Health Surveillance Assistants
HSSP	Health Sector Strategic Plan
iCCM	Integrated Community Case Management
ICEMR	International Centers of Excellence for Malaria Research
IDSR	Integrated Disease Surveillance and Response
IEC	Information, Education, and Communication
IFPRI	International Food Policy Research Institute
IGME	Inter-Agency Group for Child Mortality Estimation
IHBS	Integrated Household Budget Surveys
IMaD	Improving Malaria Diagnostics
IMCI	Integrated Management of Childhood Illness

IMF	International Monetary Fund
IMR	Infant Mortality Rate
INFORM	Information for Malaria Project
INLA	Integrated Nested Laplace Approximations
IPTp	Intermittent Preventive Treatment in pregnancy
IRS	Indoor Residual Spraying
ITN	Insecticide Treated Nets
IVCC	Innovative Vector Control Consortium
IVM	Integrated Vector Management
KAP	Knowledge, Attitude & Practices
LCF	Late Clinical Failure
LLINs	Long Lasting Insecticidal Nets
LPF	Late Parasitological Failure
LTF	Late Treatment Failures
M&E	Monitoring and Evaluation
MAC	Malaria Alert Centre
MAP	Malaria Atlas Project
MAPE	Mean Absolute Prediction Error
MARA/ARMA	Mapping Malaria Risk in Africa
mASL	Metres above sea level
MBG	Model Based Geo-Statistics
MCMC	Markov Chain Monte Carlo
MCP	Malawi Congress Party
MDGs	Millennium Development Goals
MDP&C	Ministry of Development, Planning & Cooperation
MERG	Monitoring and Evaluation Reference Group
MeSH	Medical Subject Headings
MGDS	Malawi Growth and Development Strategy
MICS	Multiple Indicator Cluster Survey
MIS	Malaria Indicator Survey
MNHP	Malawi National Health Policy
MODIS	MODerate-resolution Imaging Spectroradiometer
MoH	Ministry of Health
MoPH	Ministry of Health and Polpulation
MOWD	Ministry of Water Development
MPE	Mean Prediction Error
MPHD	Malaria Public Health Department, KEMRI, Kenya
MPR	Malaria Programme Performance Review
MPRS	Malawi Poverty Reduction Strategy
MQ	Mefloquine
MRF	Markov random field
MSH	Management Sciences for Health
NAC	Nyasaland African Congress
NASA	National Aeronautics and Space Administration

NDVI	Normalised Difference Vegetation Index
NEC	National Economic Council
NGOs	Non-Governmental Organizations
NMCP	National Malaria Control Programme
NMSP	National Malaria Strategic Plan
NOAA/NGDC	Night-time Lights Dataset
NPHL	National Public Health Laboratory
NSO	National Statistics Office
OA	Open Access
ODA	Overseas Development Assistance
OPD	Out-Patient Departments
PA*Pf*PR_{2-10}	Population Adjusted Age-corrected *Plasmodium falciparum* parasite rate
PCR	Polymerase Chain Reaction
PfPR_{2-10}	Age-corrected *Plasmodium falciparum* parasite rate
PHC	Primary Health Care
PMI	President's Malaria Initiative
POW	Programme Of Work
PSI	Population Services International
RBM	Roll Back Malaria
RDTs	Rapid Diagnostic Tests
rMIS	"rolling" MIS
RTI	Research Triangle International
SAE	Small Area Estimations
SD	Standard Deviations
SLA's	Service-Level Agreements
SMC	Seasonal Malaria Chemoprevention
SP	Sulphadoxine-Pyrimethamine
SPDE	Stochastic Partial Differential Equations
SWAp	Sector Wide Approach
TPC	Tactical Pilotage Charts
TS	Trimethoprim Sulfamethoxazole
TSI	Temperature Suitability Index
TWGs	Technical Working Groups
U5MR	Under-five Mortality Rate
UDF	United Democratic Front
UMCA	University Mission to Central Africa
UN	United Nations
UNDP	United Nations Development Programme
UNEP	United Nations Environment Programme
UNHCR	United Nations High Commissioner for Refugees
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
VHC's	Village Health Committees
VCT	Voluntary Testing and Counselling

WHA	World Health Assembly
WHO	World Health Organization
WRAIR	Walter Reed Army Institute of Research
WRBU	Walter Reed Biosystematics Unit

Executive summary

This report has been developed to assist national level partners involved in malaria control to understand the impact of recent scaled intervention coverage, define what is required to achieve universal access and to prioritize future funding needs to meet unmet intervention ambitions or to revise recommendations to accelerate impact.

The work has drawn heavily on assemblies of empirical, geo-coded parasite, vector and control coverage data and the use of model-based geo-statistics to provide information at district levels, necessary for national resource allocation and planning. The granular, district-level epidemiological data should be used in the design malaria control activities, defining resource needs and serving as a baseline for future impact analysis.

Malawi is a country broadly characterised by intense malaria transmission, but one within which there is considerable local diversity of transmission intensity. Despite very recent scaled coverage of insecticide treated nets (ITN) and the use of indoor residual house-spraying (IRS), we have not been able to demonstrate any significant changes in malaria transmission intensity between 2000 and 2010. Triangulation with other sources of data, malaria admissions to hospitals and routine health information system data, confirms that there has been little change in malaria-specific burdens from 2000 to 2010. Data collected after 2010 continue to show high rates of morbidity and parasite transmission intensity.

These data must be carefully compared with other models used by the Roll Back Malaria Partnership to estimate lives saved and any other data that might exist to challenge the observations made in this report. It is imperative that a considered appraisal of the impact of recent control efforts be undertaken before decisions can be made about future needs and expectations as part of national strategic plans and funding needs. The work presented in this report should form part of a national dialogue on the future malaria control impact - using evidence to effect change.

The data generated as part of this work has been provided to the National Malaria Control Programme so they may continue to build a national repository of epidemiological data to guide national malaria control. Furthermore these data should be shared with national research partners so they may continue to work on more detailed analysis of the impact of scaled vector control and other potential scenario's of climate variability and health service accessability.

This work, by its very nature is dynamic and new information must be assembled to measure the future epidemiological transitions. It is therefore a living, dynamic process of evidence generation, cycles of new modelling and generating new layers of information, research and enquiry necessary for effective control planning.

Future modeling work based on new data can provide a valuable comparator to 2010. The structures and policies are now in place to make a significant difference. Funding, however, will be harder to access, and demonstrating in future years that there have been changes in the epidemiology of malaria from the picture described here for 2010 will be key to the business case for sustained investment as part of any revised national malaria strategic plan.

Chapter 1

Introduction

The epidemiology of morbidity due to malaria [Snow & Marsh, 2002], the impact of vector control [Killeen et al., 2007; Smith et al., 2009; Griffin et al., 2010], cost-effectiveness of treatment and prevention [Okell et al., 2012] and timelines to malaria elimination [Cohen et al., 2010] are all dependent on parasite transmission intensity. Effective planning of malaria control depends on a reliable understanding of the temporal and spatial determinants of parasite transmission, its seasonal patterns and the dominant vectors implicated in transmission. Epidemiological profiling should form the cornerstone of any effective national malaria strategy planning cycle.

The use of survey data, maps and epidemiological intelligence was a routine feature of control planning across many African countries during the Global Malaria Eradication Programme (GMEP) era from the mid-1950s. Data included epidemiological descriptions of transmission, vectors, topography and climate. There was a recognition, over 50 years ago, that one important source of planning data was infection prevalence among children aged 2-10 years ($Pf\text{PR}_{2\text{-}10}$). This was used to define categories of endemicity risk, designed to guide and monitor progress toward malaria elimination targets [Metselaar & van Thiel, 1959; Macdonald & Göeckel, 1964; Lysenko & Semashko, 1968].

The art and skills necessary to design malaria control based on an understanding of the spatial epidemiology was lost during the 1970s when the agenda for malaria control fell under a less specialized, integrated primary care mandate focused on managing fevers. In 1996, there was a renewed plea for better malaria cartography to guide malaria control in Africa [Snow et al., 1996] and over the last decade there has been a growth in spatial data on malaria and populations not available to malariologists or programme control managers 60 years ago. The growth in data has been accompanied by the development of statistical approaches to model and map risk and intervention access in space and in time using Model Based Geo-Statistics (MBG) [Diggle & Ribeiro, 2007].

At the launch of the Roll Back Malaria (RBM) initiative, calls for universal coverage of all available interventions was probably an appropriate response to the epidemic that affected most of sub-Saharan Africa during the mid-late 1990s [WHO, 2000; Snow et al., 2012]. At a time when the international donor community is constrained by the global financial crisis, accessing overseas development assistance (ODA) and using limited national domestic funding for malaria control will require a much stronger evidence based business-case. This future business-case must be grounded in the best available epidemiological evidence to predict the likely impact of future intervention, assess the impact of current investment and, equally important, demonstrate what might happen should funding and intervention coverage decline.

In 2011, the WHO Office for the Africa Region (AFRO) developed a manual to assist countries in developing their National Malaria Strategic Plans (NMSP) including, as a prelude, the undertaking of a National Malaria Programme Performance Review (MPR) [WHO-AFRO, 2012]. It is recommended that the MPR should include a detailed review of the malaria epidemiology and stratification including the geographical distribution of malaria burden, parasite prevalence and parasite species.

The MPR for Malawi was completed in 2010 and made three specific recommendations under the epidemiology section: a) malaria prevalence survey sampling should be adjusted to show prevalences at district level; b) there is a need for detailed analysis and triangulation of the various data sources to determine the current epidemiological situation and update the malaria epidemiology map; and c) decisions on scaling up malaria control should be based on the analysis arising out of data triangulation [NMCP, 2010]. Here we develop a comprehensive approach to the assembly of a large amount of epidemiological data to address these recommendations; providing the basis for future control design and monitoring of intervention impact based on an informed epidemiological understanding.

Chapter 2 provides the country context with special reference to health administration decision making units as part of decentralized malaria planning, human settlement patterns, urbanization and the location of health services. Chapter 3 documents activities undertaken between 1900 and 2013 in relation to the control of malaria in Malawi, providing an institutional memory of what was done, where and to what effect, and an opportunity to learn from previous experience. Chapter 4 provides the epidemiological modelling of parasite prevalence in 2000 and 2010, a review of parasite species and the evidence supporting targeted seasonal malaria control in Malawi. The dominant vector species, their bionomics and resistance to insecticides is presented in Chapter 5. Finally, Chapter 6 attempts to draw together the layers of information on the epidemiology of malaria in relation to the current national strategic plan 2010-2015 [NMCP, 2011] and how future national strategies might be tailored to meet the challenges of declining ODA and increased pressure to present a credible business case for domestic funding.

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Chapter 2

Country context, administration, population & health services

2.1 Location

Malawi is a landlocked country in southeast Africa, before independence known as Nyasaland. It lies between latitudes 9° and 18°S and longitudes 32° and 36°E. Malawi occupies a land surface area of 118,000 km^2 and is 896 km in length but varies only in width by between 80 to 160 km. Malawi is bordered on the east, south and south-west by Mozambique, to the west by Zambia and to the north and northeast by Tanzania. The Great Rift Valley passes through the country from north to south. Along the eastern border of the rift valley lies Lake Malawi, Africa's third largest lake, which extends two-thirds of the country's length [Potts, 1986]. The lake is 457.2 m above sea-level and acts as an important transport route, source of food, income and a tourist attraction. The three lakes of Lake Malawi, Lake Malombe and Lake Chilwa comprise approximately 21% of Malawi's territorial surface area.

Malawi is characterized by a large plateau, between 914 m to 1219 m above sea level, to the west of Lake Malawi. Higher plateaus exist in the north, reaching between 1830 m and 2440 m above sea level, known as the Nyika Plateau. To the south of Lake Malawi are the Shire highlands (914 m above sea level) and where the Zomba and Mulanje Mountain peaks rise to 2134 and 3028 m respectively. Mulanje is the highest mountain in Central Africa. The Shire River runs from the South of the Lake, the only outlet, to join River Zambezi in Mozambique flowing towards the Indian Ocean.

The Heigoland (Anglo-German) Treaty of 1890 placed the control of the then Lake Nyasa under the jurisdiction of British governed Nyasaland [Mayall, 1973]. In 1954, the Portuguese Government, who governed Mozambique, signed an agreement with the British, placing a boundary at the middle of the lake between the two countries [Kasuka, 2013]. In 1967, Tanzania claimed an independent border line between Tanzania and Malawi, opposed by the Malawian government. The dispute has yet to be resolved and the dispute was re-ignited in 2011 when the Malawi government's gas and oil exploration initiative gained momentum [Kasuka, 2013].

Although Likoma Island (18 km^2) is surrounded by Mozambican territorial waters, it is an exclave of Malawi. Since the establishment of the headquarters of the Anglican Church by the University Mission to Central Africa (UMCA) on the island, its population size has grown to currently accommodate over 9,000 inhabitants with poor health service access and a history of resistance to the church and state [Kalinga, 2012; Mbaya, 2008].

The country is made up of a variety of woodlands, tropical rainforests, open savannah high altitude grasslands and scrub. Malawi's climate is subtropical with the three distinct seasons: rainy season extending from November to April, and the dry season from May to mid-August with temperatures at night reaching as low as 10-14^oC and the hot season from between mid-August and November. Generally, the highlands are cooler and wetter while the low lying regions are hotter and more humid.

2.2 Social and political evolution

The area now known as Malawi has been heavily influenced by large human migrations over hundreds of years. The region was once part of the Maravi Empire, a dynasty thought to have been founded in the late 15th century formed by several Bantu speaking tribes from where the name Malawi is derived. The Maravi, also known as the Chewa, attacked the original inhabitants, the Akafula, taking over their land. The kingdom included most of modern Malawi, as well as parts of present day Mozambique and Zambia. The region remained under Maravi control until the arrival of Arab traders and slavery in the mid-19th century [Rafael, 1980].

Under the Maravi Empire, the Chewa had access to the coast of modern day Mozambique that they used for trade. Portuguese explorers arrived from the present-day Mozambique coast in the 17th century. The 18th and 19th centuries witnessed dramatic increases in the slave trade, where Malawian tribes traded slaves with the Portuguese. By the 19th century the Maravi Empire's power base began to decline and the state was attacked by the Ngoni and the Yao. During this period of instability, Arab traders penetrated into the interior during the 1870s and formed trading alliances with the Yao, who were to follow the teachings of Islam. Several trading posts were established along the shore of Lake Malawi the largest being Nkhotakota. For many years there continued to be conflicts between the Yao and the Angoni, neither of whom were able to create a dominant authority [Rafael, 1980].

In 1850, the Scottish Presbyterian missionary David Livingstone led an exploration of the region and paved the way for missionaries, European adventurers and traders (www.bbc.co.uk). Livingstone arrived at Lake Nyasa in 1858 and he led the Scottish church's mission against slavery. The two dominant churches involved in early missionary life in Malawi were the Universities Mission to Central Africa and the Free Church of Scotland. In 1876, the city of Blantyre was established in the southern region as the headquarters in the continuing fight against slavery and two years later the African Lakes Company was founded to help supply missionary stations across Malawi. Livingstone's presence, until his death in 1873, was a key factor in attracting British trading companies to Malawi and subsequently its colonisation.

In 1881, a British consul was appointed and by 1891, the British formally established the Nyasaland and District Protectorate; in 1893 renamed the British Central African Protectorate. In 1907, the British Central African Protectorate was further renamed Nyasaland. Early signs of resistance to colonial rule began in 1915 when the Reverend John Chilembwe led a revolt against British rule killing white managers of a farming estate. This was a prelude to a long period of discontent that led to the formation of the Nyasaland African Congress (NAC) by Nationalists in 1944, inspired by similar movements in South Africa [Gascoigne, 2013].

Despite strong opposition from the NAC and white liberal activists, in 1953 Britain combined Nyasaland in a Federation with Northern and Southern Rhodesia (now Zambia and Zimbabwe respectively). In 1958, Dr Hastings Kamuzu Banda, returned to Nyasaland having spent time both in England and in the United States [Kalinga, 2012] to denounce the

federation and assumed leadership of the NAC which became the Malawi Congress Party (MCP). The colonial authorities banned the MCP in 1959 and arrested Banda and many of the MCP's leadership.

A state of emergency was declared between 1959 and 1960 when Banda led protests against the British. In 1961, the MCP won elections to the legislative council and later on, the British agreed to make Malawi independent in 1962. In 1963, Nyasaland was granted the self-governing status shortly before the Federation dissolved, and Banda became the prime minister although Britain still controlled Malawi's financial, security, and judicial systems. Nyasaland declared independence as Malawi on the 6th July 1964 and became a Republic two years later with a multiparty system of governance.

In 1966, the constitution was changed to a one-party state under President's Banda's rule. Opposition movements were suppressed and their leaders detained, raising concerns about human rights violations. Banda was voted President for Life of the MCP in 1970 and assumed this role from 1971 [Forster, 2001; Gascoigne, 2013]. During the 1980s, several ministers and politicians were killed or charged with treason and by 1992 several donor countries suspended aid to the country over Malawi's human rights record.

In 1992, the Catholic Church issued an open letter demanding changes to the single party state and public protests followed. When donor countries suspended bi-lateral aid, Dr Banda conceded to a national referendum in 1993, which resulted in an overwhelming support for multi-party elections. Democratic, multi-party elections were held on the 17th May 1994, won by Bakili Muluzi of the United Democratic Front (UDF).

Muluzi's government promptly closed all political prisons, re-wrote the constitution to include freedom of speech and press, and created a national free primary school system, repaired foreign relations, established mechanisms to reduce food shortages and established policies to reduce the number of people living in poverty. In 1999, Muluzi was re-elected to a second five-year term, during which his government had to contend with the famine of 2002 and allegations of corruption [Ruben, 2008]. Muluzi failed to change the constitution to allow him to serve for a third term. In May 2004, Bingu Wa Mutharika, from the UDF party, was elected President. During his term Mutharika resigned from the UDF to form the Democratic Progressive Party, overcame an impeachment motion in 2005, his vice president was charged with treason in 2006 and in 2008 several opposition figures and ex-security chiefs were arrested after Mutharika accused his predecessor, Bakili Muluzi, of plotting to depose him. Despite these difficulties Mutharika was elected for a second term in May 2009, but died while in office in 2012 to be succeeded by his vice-president, Joyce Banda.

2.3 Economy

The pre-colonial economy of Malawi was based on agriculture largely through the production of millet and sorghum. The Maravi Empire established trading links with the Portuguese and Arabs of the Mozambique coast in ivory, iron and slaves. During the colonial period when Malawi was a British protectorate, local industrialization was limited and the cash economy of Malawi depended on agriculture including coffee, tea, tobacco and cotton,

however, the geographical position of Malawi posed a serious challenge for economic development of the protectorate.

Since independence, governments have undertaken various economic policies mainly focusing on the improvement of the infrastructure, the development of the nation's education system and on developing agriculture. Unlike several of its immediate neighbours, Malawi did not follow a post-independent socialist, or pan-Africanist, economic and social philosophy, however it did increasingly marginalize Malawians of Asian origin because of their business prosperity. Malawi maintained relations with South Africa for trade and export during the apartheid years. The economy experienced a rapid growth in Gross Domestic Product (GDP) during the late 1960s, early 1970s [Droppelman et al., 2012]. During the 1970s, there was an influx of refugees from the Frelimo-Renamo conflict in Mozambique and the border was closed in 1970 causing serious economic hardships that contributed to a negative GDP growth [NEC, 1998].

In 1981, Malawi became one of the first countries in sub-Saharan Africa to implement structural adjustment programmes under the direction of the World Bank and the International Monetary Fund (IMF). These adjustment programs were aimed at diversifying the economic base, ensuring appropriate price and incomes policy, increasing the efficiency and incomes of smallholder farmers, improving the policy environment for manufacturing and trade and restructuring of fiscal budgetary allocation and expenditure [Sahn & Arulpragasam, 1994; Chirwa & Zakeyo, 2003; Chirwa 2005].

Until recently agriculture accounted for approximately 37% of GDP [AfDB & OECD, 2010; NEC, 1998], 80% of exports [GoM, 2011] and accounts for 80% of the labour force [EAD, 2001]. Tobacco production is the most important export crop and is a major source of foreign exchange for the country. Tea, coffee and sugarcane account for a further 10% of GDP. There are few natural mineral resources but a complete reliance of agriculture leaves the GDP vulnerable to climate shocks. In 2009, however, a uranium mine was opened by Paladin Energy Ltd. at Kayelekera in the northern region of the country. By 2010, production had increased by over 500% increasing the mining sector share of the GDP from 1% to 2% [MDP&C, 2011; Paladin Energy Ltd., 2011].

Malawi remains a low-income country and is today ranked as one of the poorest countries in the world. Since 2004, various policies have been implemented to enable the economy to grow including policies to sectors and areas where the poor work and live, fertilizer subsidies and improved relations with the donor community. Despite early economic growth there has been a more recent slowing down and stagnation of GDP since 2008; with a 3% estimated growth rate in 2012, compared to an average of 4.8% for Africa.

By 2010, there were foreign exchange, fuel and electricity supply shortages, all leading to major restrictions for local businesses and an escalating cost of living for the average Malawian. Inflation reached 25% in August 2012 [Cook, 2013]. In May 2012, President Joyce Banda was forced to devalue the kwacha currency by a third to satisfy International Monetary Fund requirements. The government's Second Growth and Development Strategy includes an emergency 18 month Economic Recovery Plan (ERP) that focuses on a few priorities that are "*pro-growth, represent quick wins, and are highly effective*" [GoM, 2013].

The plan stresses the need for social protection programs and identifies diversified commercial agriculture, tourism, energy, mining and infrastructure/Information Technology and Communications as sectors that can help turn around the economy and provide the initial building blocks towards structural transformation as defined in the strategy [World Bank 2013].

2.4 Poverty

In 1998, levels of poverty were very high; 65% of the population were classified as 'poor' and 29% of the population was living in 'extreme poverty' [World Bank 2013]. Recognizing the need to change the future development destiny for Malawi, in the late 1990s Malawians prepared a long-term shared vision to provide a framework for development planning and management. Malawi's Vision 2020 presents the long-term development that "*By the year 2020, Malawi, as a God-fearing nation will be secure, democratically mature, environmentally sustainable, self-reliant with equal opportunities for and active participation by all, having social services, vibrant culture and religious values and a technologically driven middle-income economy*" [NEC, 2000]. The vision has nine core themes that include "*fair and equitable distribution of income*" [NEC, 2000].

In May 2002, the government launched the Malawi Poverty Reduction Strategy (MPRS) to translate the long-term strategy of the Vision 2020 into medium-term action plans (Mwapasa, 2011). The goal of the MPRS was to achieve "*sustainable poverty reduction through empowerment of the poor*" [IMF, 2007]. The MPRS was built around four strategic pillars: sustainable pro-poor growth, human capital development, improving the quality of life of the most vulnerable and governance [GoM, 2006].

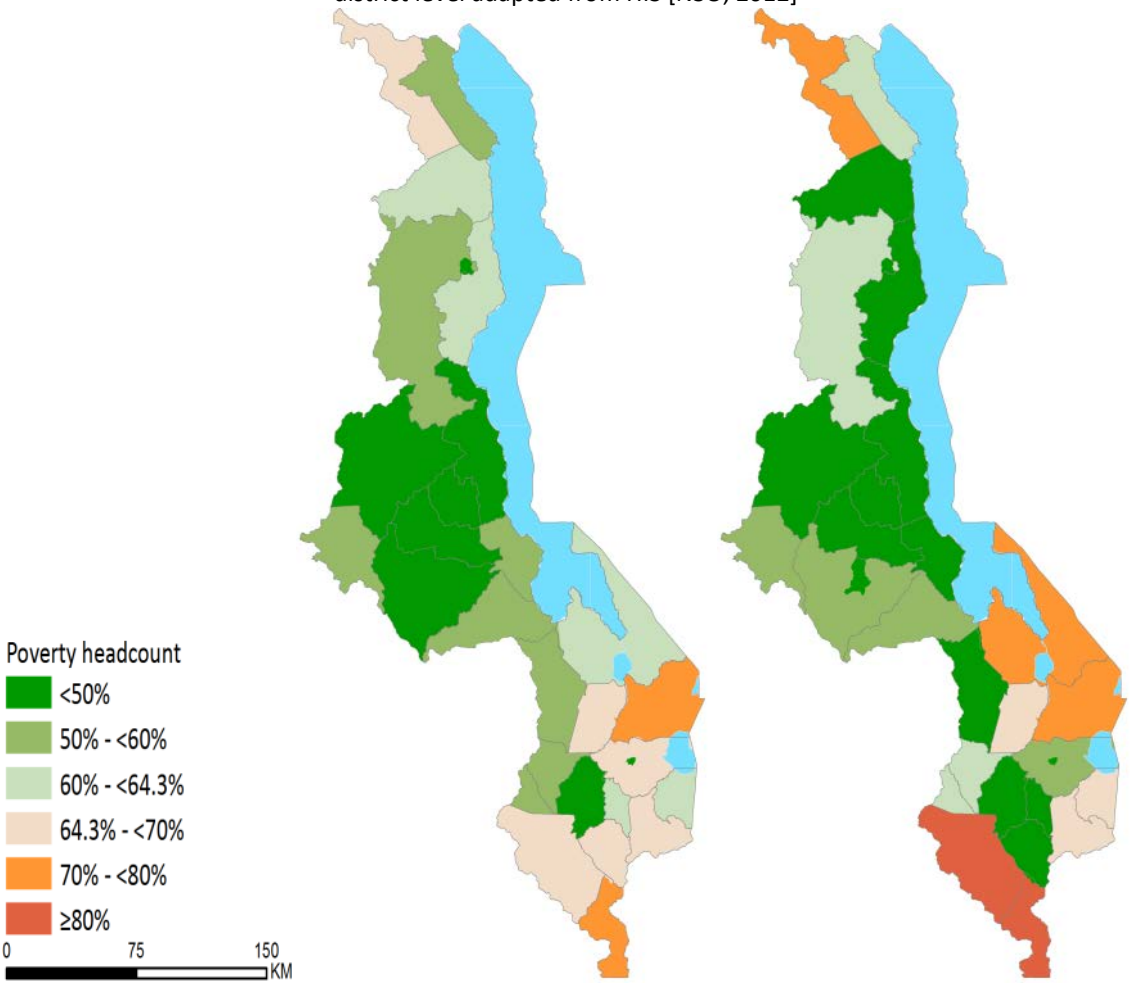
Despite long-term visions and medium-term action plans, Malawi remains one of the ten poorest countries in the world in 2012 with over 70% of the population living below a poverty line of $1.25 purchasing power parity per day [UNDP, 2012]. According to the United Nations Development Programme (UNDP), Malawi's human development index (HDI) rose only by 0.8% annually from 0.272 to 0.418 between 1980 and 2012, which gives the country a rank of 170 out of 187 countries with comparable data in 2012, placing Malawi below the regional average of 0.475 [UNDP, 2012]. Malawi therefore falls into the 'low development' classification, based on life expectancy, educational attainment, and gross national product [UNDP, 2012].

The Integrated Household Budget Surveys (IHBS) provided an empirical update on the population's socio-economic situation. The IHBS in 2010/11 showed that 25% of the population are defined as ultra-poor[1] and that this has changed very little since the previous IHBS in 2004/05 and important district-level disparities exist across the country [NSO, 2012;

[1] Poverty in Malawi is defined as having a total household consumption per year which is below the poverty line. The poverty line is a measure of the total Malawi Kwacha per person per year required to obtain a minimum level of living which is inclusive of enough food to reach a specific amount of calories; necessary energy requirement per person per day and a non-food component of basic goods and services. Persons living below the poverty line are considered poor while people living below the minimum food level consumption are referred to as ultra-poor [NSO, 2012]. In the 2010/11 IHBS, the poverty lines were defined as: those below MK 37002 – Poor while those below MK 22956 were defined as ultra-Poor

Figure 2.1]. According to a report by the UK's Department for International Development only 22.3% of the population is able to meet its basic food requirements [GoM/World Bank, 2006].

Figure 2.1 Map of poverty in Malawi - Small area estimates of poverty headcount in 2004/5 and 2010/11 at district level adapted from HIS [NSO, 2012]



2.5 Decentralization and administrative boundaries

Over time, governments across Africa have embraced decentralization. Defining the health administrative units used by a country is central to resolving health information for planning and disease burden estimation. Most currently available malaria risk maps do not resolve information necessary for planning at units of decision making used by national governments, for example those most recently developed by the Malaria Atlas Project [http://map.ox.ac.uk] and used by the Global Malaria Programme of the WHO in its 2012 World Malaria Report [WHO, 2013]. Without congruence to accepted health decision making units at national levels the cartographic information of risk has limited value [Omumbo et al., 2013].

Malawi supports a broad agenda on fiscal and administrative devolution, based on a comprehensive legal and regulatory framework for decentralization. In July 1994, the Government commissioned a comprehensive review on decentralization initiatives that led to the National Decentralization Policy approved in October 1998 [GoM, 1998]. The National

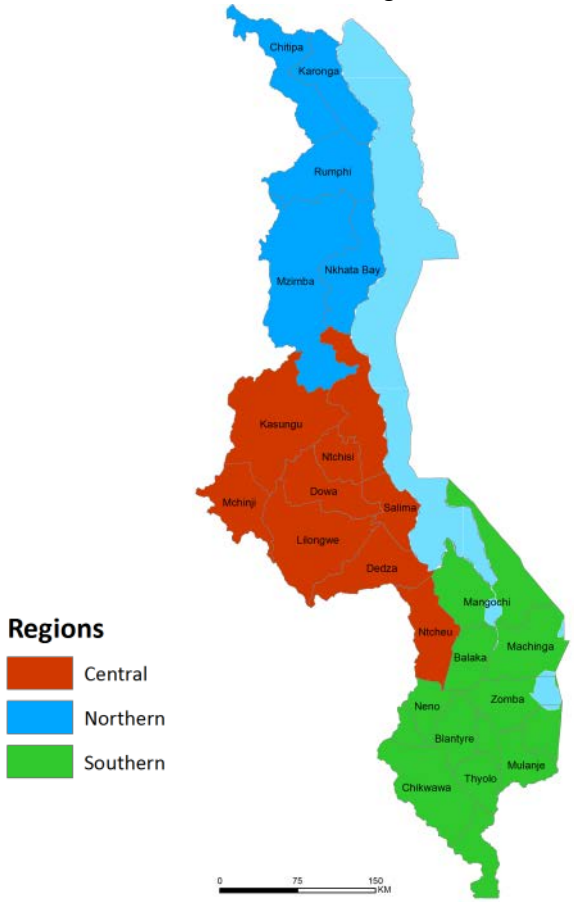
Decentralization Policy aims at integrating government agencies at the district and local level into one administrative unit through the process of institutional integration, seeks to allow for composite budgeting and provision of funds for the decentralization services; and diversifying the centre of implementation responsibilities and transferring them to the districts and promoting popular participation for the governance and development of districts [MOWD, 2002].

Malawi is divided into 3 administrative regions: Northern, Central and Southern Region (Figure 2.2). The regions are subdivided into 28 districts, which constitute the country's local government units and administered by district assemblies. At a lower levels, Malawi operates traditional authorities, sub-traditional authorities (or sub-chiefs) while the urban areas are divided into wards. Some traditional authorities straddle district borders, so these subsidiary divisions do not fit precisely into a hierarchical scheme. Political and administrative decentralization is being strengthened with common funding mechanisms and the institution of local government civil service [World Bank 2013].

In 2004, the government started implementing a health sector wide approach (SWAp) guided by a six-year joint programme of work (POW) 2004-2010 [MoH, 2010]. The POW priorities revolve around the provision of the Essential Health Package (EHP) and its implementation is through the decentralization framework and health service delivery is the responsibility of the District Assemblies (DAs).

We have used the 28 district boundaries defined in the health sector strategic plan [MoH, 2011] (Figure 2.2). However, it should be noted that Mzimba district in the Northern region has recently been sub-divided into Mzimba North and Mzimba South, but the precise gazetted and digitized boundary representing this division is not currently available [MoH, Personal Communication].

Figure 2.2: 28 health administration districts across 3 regions in Malawi



2.6 Child survival

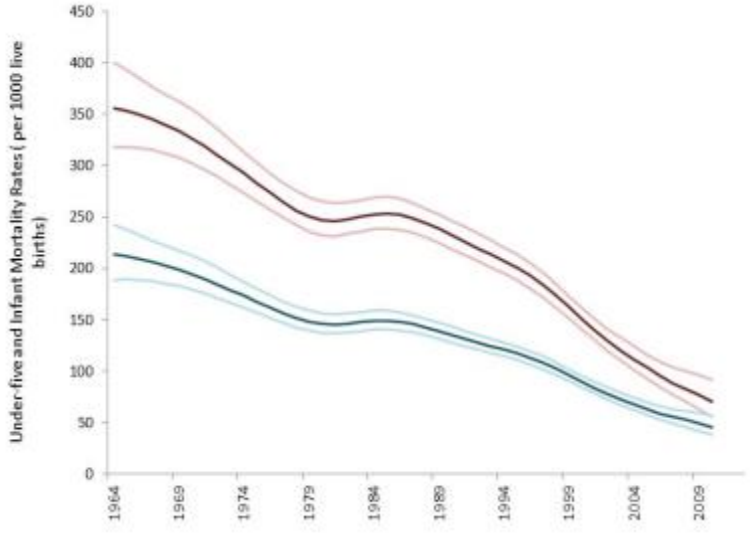
Civil registration was made compulsory in Malawi in 1904 under the colonial Births and Deaths Registration Act CAP 24.01, however it has never been enforced and registration of events remains voluntary [Ndawala & Mzumara, 1994]. Consequently, its coverage is incomplete and unsatisfactory as a source of reliable mortality data. The absence of credible civil and vital registration of childhood deaths has meant that changes in child survival have to be defined using indirect methods of estimating under-five mortality rates from birth histories reported by mothers that include information on the residence and survival of their live births [Hill & David, 1988]. These data are assembled within a life table to estimate the probabilities of dying between intervals derived from reported dates of birth and death and the numbers of children of a particular age exposed to the risk of dying during the period [Hill & David, 1988].

Data have been compiled by the Inter-Agency Group for Child Mortality Estimation (IGME), who used combinations of weighted LOESS regression techniques[2] to fit smoothed mortality trends to estimate mortality between survey periods using sample survey and census data [UNICEF-IGME, 2011]. The IGME estimates of under-five mortality (the probability of dying between birth and the fifth birthday, U5MR) and infant mortality (number deaths in the first year of life per 1000 pregnancies; IMR) for Malawi between 1960 and 2010 have been

[2] Loess is a form of non-parametric smoothing driven by the data by fitting a smooth curve through a set of data points that involves a locally weighted regression

computed from national population and housing censuses undertaken in 1966, 1977, 1987, 1998 and 2008, and Demographic and Health Surveys (DHS) undertaken in 2000, 2004, and 2010. The results are shown in Figure 2.3 [UNICEF-IGME, 2011].

Figure 2.3: Under-five mortality rates (red) and Infant mortality rates (blue) per 1000 live births for Malawi, 1964 to 2011 [UNICEF-IGME, 2011][3]

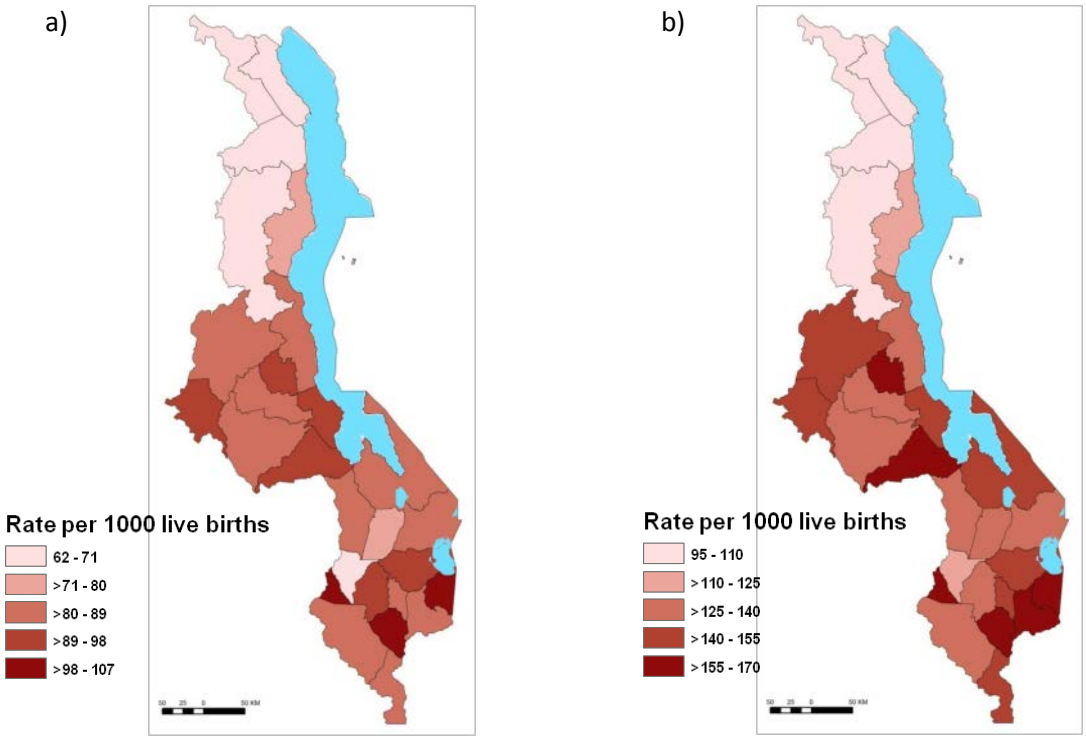


Substantial declines in both infant and under-five mortality were witnessed from 1960s through to the early 1980s. Declining rates of IMR and U5MR, however, showed evidence of stagnating during the period of severe economic difficulties, political transition and the influx of refugees from Mozambique.

The National Statistics Office (NSO) have independently computed more recent transitions in IMR and U5MR from birth histories using indirect demographic methods based on the 2008 national census and compared with previous estimates during the 1998 census, DHS in 2000, 2004 and 2010 and the Multiple Indicator Survey (MICS) 2006 [NSO, 2012]. Infant mortality rates declined from 134 to 87 infant deaths per 1,000 live births during the period 1992-2004 (the retrospective intervals from which mortality estimated during the 2000-2010 surveys). U5MRs show declines from 226 deaths/1000 in 1989 to 112 by 2007. Significant reductions in U5M were evident between all five-year periods with the most drastic decline (29%) occurring between 1996–2000 and 2000–2004. The annual DHS estimates show very close correlation with the IGME estimates [UNICEF-IGME, 2011; NSO, 2009; NSO, 2012]. Children in rural areas had considerably higher rates of IMR and U5M (91 and 147 respectively) compared to all other regions (64 and 100 IMR and U5M respectively) and show significant variations in both IMR and U5MR estimates (*circa* 2003) between districts (Figure 2.4) [NSO, 2009b].

[3] Under-five mortality rates (red) and Infant mortality rate (blue) per 1000 live births Malawi, 1964 to 2010. All rates are defined as per 1000 live births [UNICEF-IGME, 2011]. For IMR and U5MR, a country-specific local log-linear regression model is fitted to observations for one of the two indicators, within a model life table. Projections have been adjusted for projected mother-to-child HIV infection risks [You et al., 2009; Hill et al., 2012; UNICEF-IGME, 2011]. A loess line is produced with an uncertainty range (shown as boundaries to dark line in Figure 2.3).

Figure 2.4: Estimated a) IMR and b) U5MR approximately five years before the 2008 national census by district[4]



2.7 Causes of death

Special investigations of the likely causes of death were first initiated in 1937 with a detailed health, nutrition, fertility and child survival enquiry among the Atonga in West Nyasa district (Nkhata–Bay) by DP Turner [Nyasaland Protectorate, 1937]. Over 36% of 186 children aged 0-2 years examined were suffering from malaria. Of the 387 mothers interviewed, they collectively reported having 1513 live births of whom 341 (22.5%) had died before their 2nd birthday, 114 (7.5%) had died between 2 and 10 years and a further 100 (6.6%) had died after age 10 years. Turner comments that "*... I think malaria responsible for the high infantile mortality, probably concurrently with some other disease, after the children begin to walk they seem to have developed a fairly useful immunity to this disease*" [Nyasaland Protectorate, 1937].

Over 60 years later[5], the Karonga Health and Demographic Surveillance System (HDSS) was established in 2002 covering *circa* 35,000 people. Initially, the Karonga HDSS was to provide a platform to study the epidemiology of HIV, its consequences and interventions but over time has incorporated other communicable and non-communicable diseases including

[4] Lilongwe, Blantyre, Zomba, Mzuzu rural and urban areas have been averaged.

[5] A detailed DHSS was initiated at the Domasi Community Development Scheme in the 1950s to provide equivalent high intensity surveillance data on the health and mortality experiences of a community and linked to the Zomba Medical Training College [Nyasaland Protectorate, 1951]. However, details of these data have not been identified.

establishing causes of death through verbal autopsies. Data from the HDSS shows that during the period from 2002 to 2006 IMR and U5MR was 53 and 85 per 1000 births respectively [Jahn et al., 2010], lower than national averages, and has declined faster than the national average between 2005 and 2010 [Crampin et al., 2012]. The main causes of child mortality within the HDSS include Communicable diseases including: HIV/AIDS, tuberculosis, pneumonia, malaria, diarrhoea, neonatal sepsis and unspecified acute febrile diseases while other deaths were from non-communicable diseases including: prematurity/low birth weight, asphyxia/birth injury, congenital disorders, cardiovascular, respiratory infections and cancer.

2.8 Population growth and distribution

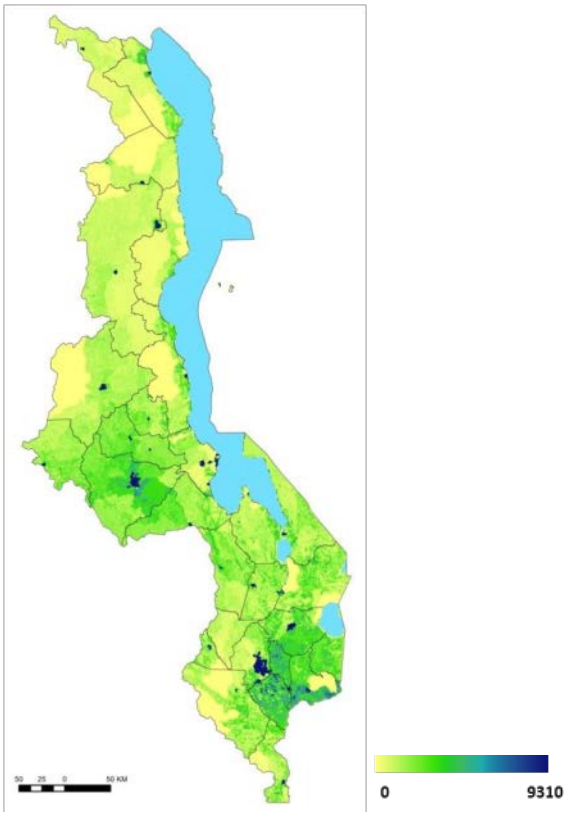
The first "census" was conducted in 1891 when Malawi was a British Protectorate but the head counts were restricted only to the European population. The second population census was in 1901 and this time included Africans. The other pre- independence censuses were conducted in the following years 1911, 1921, 1926, 1931, 1945. The most comprehensive censuses, using modern demographic methods, were undertaken since independence, starting with the 1966 census, repeated approximately every ten years thereafter. The latest census was undertaken in June 2008 [NSO, 2009].

Malawi's population is growing rapidly. In just over 40 years Malawi's population increased 3.3 fold from 4 million people in 1966 to 13.1 million in 2008. The average inter-censal annual growth rate has been 2.9% since 1966, with the highest rate of 3.7% observed between 1977 and 1987 declining to 2.8 between 1998 and 2008. The population remains young and therefore has a high growth potential. If the present growth rate continues Malawi's population will double within the next 30 years [NSO, 2009].

The crude population density for Malawi was 85 persons per km^2 in 1987 and 139 per km^2 in 2008 ranging from 35 to 3,007 inhabitants per km^2 [NSO, 2009]. About 45% of the total population lives in the Southern Region of the country with the highest population densities (185 per km^2) compared to Central Region (154 per km^2) and Northern Region (63 per km^2) regions.

For disease mapping purposes very high spatial resolution population distribution maps are required. Recently spatial modelling techniques for the reallocation of populations within census units have been developed in an attempt to overcome the difficulties caused by input census data of low spatial resolutions [Linard et al., 2010; 2012]. In brief, a dasymetric modeling technique [Mennis, 2009] has been used to redistribute population counts within 253 territorial or ward areas defined during the 2008 national census assisted by land cover data sets and satellite imagery. A different population weight was assigned to each land cover class in order to shift populations away from unlikely populated areas, for example game reserves, and concentrate populations in built-up areas. The net result was a gridded dataset of population distribution (counts) at 0.1 x 0.1 km resolution (Figure 2.5). Sub-national growth rates have been used to provide two population distribution surfaces for 2000 and 2010 (Section 4.5)

Figure 2.5: Modelled population density projected to 2010 using methods described in the text and represented as increasing density as shown in legend below. Ranging from zero to *c*. 9,310 per km^2



2.9 Urbanization

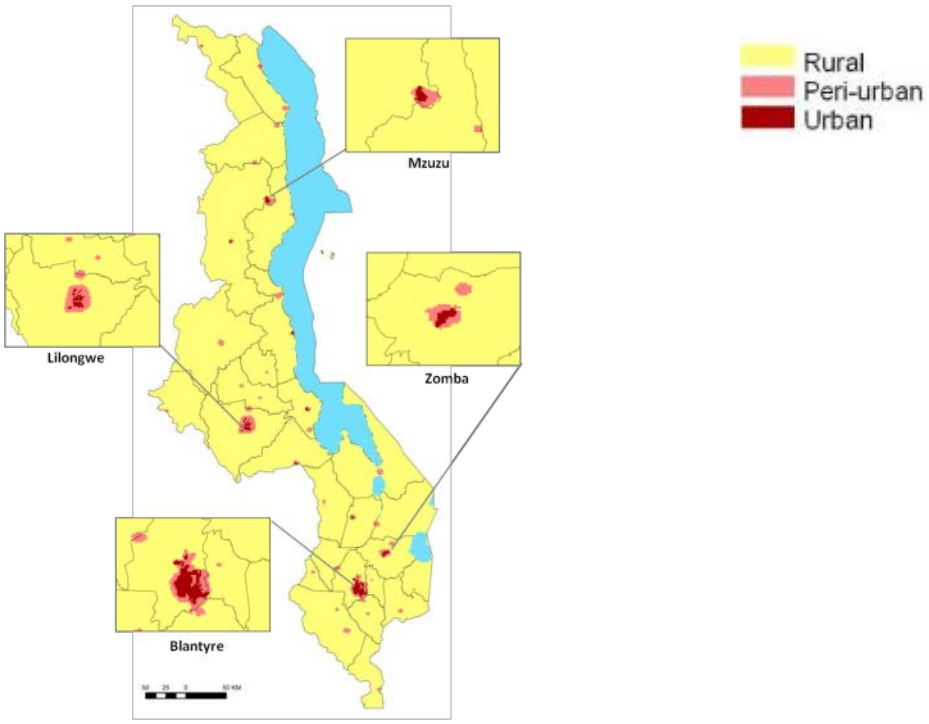
At independence Malawi inherited an extremely under-developed urban system. The first post-independence census, in 1966, showed Malawi's level of urbanization to be one of the lowest in Africa at around 5% with just over 200,000 people living in urban centres; 54% of whom were in Blantyre [Potts, 1986]. At the time only four towns (Blantyre, Lilongwe, Zomba and Mzuzu) had populations greater than 5000 people. The major urban event post-independence was the creation of Lilongwe as the new capital, replacing the colonial capital Zomba to promote greater regional equity in growth acting as a counter to the commercial capital of Blantyre. Lilongwe grew at an average rate of around 16% per year up to 1977. The growth in Blantyre (100,000 at independence) during the same period was much slower, 6.4% per year [Potts, 1986]. Malawi has seemingly undergone relatively little rural–urban transformation: from a total urban population of 10.7% in 1987 to 15.3% in 2008. Almost all of the urban population, live in four major cities (Blantyre, Lilongwe, Mzuzu and Zomba) but contribute significantly to national income [Madava, 2000]. The estimated urban population in 2008 was 2.0 million [NSO, 2009]. In 2008, Malawi remained one of the least urbanized countries in the world [Cohen, 2006; Makuwira, 2010]. The United Nations (UN) population projections estimates that by 2030, 20% of the population of Malawi will be located in urban areas much lower than the expected average for Africa at 49% [UNDP, 2012].

Inconsistent definitions of urban areas makes comparison of urbanization rates across countries complicated. Early figures included centres which would not be defined as urban in most countries (<5000 people). Defining an urban settlement only by the numbers of

residents without a spatially constrained component poses challenges in measuring the impacts of urbanization in space and time [Potts, 1986]. In Malawi today, *urban* areas refer to the four major cities of Blantyre, Lilongwe, Mzuzu and Zomba and Bomas (district administrative towns) and gazetted town planning areas.

Given the ambiguities of national definitions of urban settlements we have used an urbanization classification that combines the spatial extent of urban settlements developed by the Global Rural Urban Mapping Project (GRUMP) and population density developed by the AfriPop project [Linard et al., 2012]. GRUMP urban extent grids distinguish urban and rural areas based on a combination of the NOAA'S Night-time lights dataset (NOAA/NGDS) [Elvidge et al., 1997], settlements data and population counts. Population counts used were derived from the GRUMP spatial population database based on areal weighted census input data [Balk et al., 2004] while settlements data sources include ESRI's Digital Chart of the World's Populated Places (DCW), Tactical Pilotage Charts (TPC) from Australian Defence Imagery and Geospatial Organization and some LandSAT-derived polygons [Balk et al., 2004; CIESIN, 2013]. To define urban extents, a border was defined around each set of contiguous lighted pixels whose total population count was greater than 5,000 persons. Because not all urban settlements are 'well-lit' enough to be detected by satellite sensors, a buffer was drawn around settlement points to estimate spatial extents of the settlements. Similar to the Night-time lights-derived, urban extents, settlement extents with a total population count greater than 5,000 persons were classified as urban with the rest of the grid defined as rural. The GRUMP urban extent was further refined to produce a 'peri-urban' classification constrained by population density using the Afripop data [www.AfriPop.org]. Urban areas were defined as locations with a density of more than 1000 persons per km^2 with the rest of the GRUMP urban extent defined as peri-urban (Figure 2.6).

Figure 2.6 Urban and peri-urban settlements in Malawi (see text for definitions)



2.10 Health system

2.10.1 History of the health system

Harry Johnson was the first British doctor to the Protectorate, appointed in 1891, and served to establish the government medical service [Baker, 1976]. In the early 1900s, the country was ravaged by several epidemics including plague outbreaks in 1904 and 1906, smallpox and following the First World War the influenza pandemic. These medical crises prompted the expansion of medical facilities. By 1911 there were facilities at Zomba (European and African hospitals), Karonga (dispensary), Port Herald (Nsanje) (dispensary), Fort Johnson (Mangochi) (European and African hospitals) and Blantyre (European and African hospitals) but clinical services continued to be focussed on the health of government officials [Nyasaland Protectorate, 1937; Gelfand, 1964]. By 1911, the medical department had a principal medical officer, eleven medical officers, one matron, four nursing sisters and five sub-assistant surgeons [Nyasaland Protectorate, 1937]. Mission doctors, nurses and medical facilities complemented those of the government health services, and were more established in some areas having been founded since 1876 [Baker, 1976].

It was not until the late 1920s when there was a shift in policy, from the provision of medical services primarily to government officials to expanded care to the rest of the population [Baker, 1976]. More than 12 district hospitals and 90 rural dispensaries were established, an increase in the number of medical staff deployed, and there were increments in the amount of money spent on healthcare by the 1930s. By 1937, there were 15 African hospitals, two European hospitals, 706 hospital beds and 93 dispensaries; medical staff included a Director of Medical Services, one senior health officer, 16 medical officers, an entomologist, a pathologist, a matron, 10 nursing sisters, 16 African hospital attendants, 19 African sanitary inspectors, two European Sanitary officers and nine sub-assistant surgeons [Nyasaland Protectorate, 1937].

By 1938, the number of people with access to health care especially in the rural areas had risen. In the years following the Second World War, increasing funds from the Colonial Development fund led to a further expansion of the health services nationwide. A medical assistant training school, a mental hospital, and a leprosy settlement were built and improvements made to other facilities and dispensaries, with low level facilities being upgraded to rural health units [Gelfand, 1964]. In 1954, the medical department became the responsibility of the Federal government though many problems ensued, with concerns of inadequate medical facilities to cater for the population, discrimination against African staff, and a low number of medical specialists. The medical department became the sole responsibility of the Malawi government in 1963, after the termination of the Federation [Baker, 1976].

By 1974, 10 years after independence, medical services significantly expanded with a 50% increase in medical staff and increase in health expenditure to more than 10% of the total budget as compared to 1964 (Baker, 1976). A cholera outbreak in the early 1970s prompted the establishment of Village Health Communities (VHCs) which utilized the services of village volunteers and trained health assistants who were referred to as cholera assistants [Namilaza, 1998]. In the following years, these assistants were temporarily incorporated

into the medical department, their scope of work expanded over time to provide health care to people in communities. In 1995, their position was made permanent and they were henceforth referred to as Health Surveillance Assistants (HSAs) [Kadzandira & Chilowa, 2001].

The health policy was reviewed in the 1980s, with a focus of raising the level and quality of health for all Malawians, with an emphasis on Primary Health Care (PHC). The PHC approach had been adopted in 1978, encouraging the participation of communities in catering for their health needs, developing a basic health infrastructure to provide health care especially in rural areas which were inaccessible. This shifted care from hospitals to the community with the main focus placed on maternal and child health care. However, there was slow progress in the implementation of PHC, which could be explained by a few factors, including the shortage of qualified personnel, inadequate funding and lack of coordination from the government which had two different departments with almost similar functions [Kadzandira & Chilowa, 2001]. The country continued expanding the medical department and by 1995, 71% of the population lived within a 5 km radius of a health unit [Kadzandira & Chilowa, 2001]. Those populations living in hard to reach areas, particularly in rural areas and in households more than 8 km from a health unit, were served by HSAs through village clinics.

The formulation of a District Focus policy encouraging increased development at district level was started in 1994 [Carlson et al., 2008]. It was not until 1998 that decentralization of health care was fully implemented after establishment of Local Assemblies who would receive money allocations instead of the Ministry of Health (MoH). Health care management was then devolved from the central government to the district level, managed by District Health Management Teams (DHMTs) [Ergo et al., 2010].

In the early 2000s, Malawi became a signatory in a number of international conventions, particularly the 2000 Millennium Declaration and the Abuja Declaration, which became the basis for health care policy formulation in the country. The launch of the Malawi Poverty Reduction Strategy Paper in 2002 placed prioritization in health care provision in the already implemented EHP. The *Bakili Muluzi Health initiative* was launched in 1999 and focused on ensuring the availability of basic essential drugs as part of the EHP to the rural population within walking distance of their homes. This package addressed the provision of affordable health care to every individual in Malawi, especially the poor and vulnerable populations [Kadzandira & Chilowa, 2001]. This primary health care strategy focuses on the priority areas to achieve not only national goals set in the MPRS, Malawi Growth and Development Strategy (MGDS) but also global goals like Millennium Development Goals (MDGs).

In 2004, the Sector Wide Approach - Programme of Work (SWAp - PoW) was launched by the government and other development partners whose main focus was EHP. This programme was to guide the implementation of interventions in the health sector increasing efficiency and effectiveness. Additionally, the MoU between the government and the Christian Health Association of Malawi (CHAM) (established in 1966 as a not-for-profit organization) increased access to health care, as these Christian-owned facilities also put emphasis on EHP. This was complemented by the Service-Level Agreements (SLAs) as from 2005, which were further agreements between the government and CHAM, where facilities under CHAM would offer free health care services to people and get reimbursed by the

government. Although health care was now easily available, there was a shortage of health personnel in the country, and in response to these problems, an Emergency Human Resource Programme (EHRP) was established in the same period, leading to training and deployment of more health workers increasing the number of doctors from 43 to 241 and nurses from 3456 to 4700 between 2004 and 2009.

Malawi still experiences shortages of qualified personnel in the health sector up to date. The period after 2004 was characterized by many improvements in the health sector: increased decentralization of health care and medical facilities, improved health care provision as measured through the reduction in maternal mortality ratio and infant mortality ratio, and increased commitment of the government in health care provision with health sector expenditure increasing from 11.1% in 2005 to 12.4% in 2009/10 although still falling short of the Abuja commitment of 15% [Kadzandira & Chilowa, 2001; MoH, 2011].

In 2010, the government launched the Health Sector Strategic Plan (HSSP) 2011 – 2016 which would replace the SWAp – PoW with a more strategic emphasis on health promotion, disease prevention and increased community participation. A core group (CG) chaired by the Director of SWAp with membership from all departments of the MoH, health worker training institutions and the private sector was established to steer the formulation of the HSSP which would guide interventions in the health sector. Following the outcomes of the SWAp - PoW, the CG, with assistance from all stakeholders was to revise the EHP according to the burden of disease and address critical issues on non-EHP conditions, especially funding. The main priorities in the HSSP included: revision of the EHP (which had been reported to increase access to health care through its high cost effectiveness [Bowie & Mwase, 2011], according to the burden of disease taking into consideration changing disease patterns, available resources and new technologies; addressing staff shortages; establishing means for monitoring and evaluation to measure intervention impact and outcomes; strengthening the drug supply systems; addressing issues of health care equity in the country and revising guidelines for health delivery systems at district level to allow better alignment with government's long-term development goals. The HSSP is to be implemented in the period 2011 to 2016. The government has also started the implementation of sectorial technical working groups in all government ministries to encourage better coordination in alignment of government systems, reduce duplication of data reporting and enhance efficiency and effectiveness with a view to improve health systems [MoH 2011].

2.10.2 Current Health Care System

Institutions involved in the health sector include the Ministry of Health and Population (MoHP), CHAM Units, Non-Governmental Organizations (NGOs), community support groups and the private sector. Presently, the health care system in Malawi is composed of four levels: tertiary (central and specialist hospitals (level 4)); secondary district hospitals (level 3), primary health centres and Village Health Clincs (level 2) and community level (level 1).. At the community level, health care is offered through HSAs and Community-Based Distributing Agents (CBDA's), VHC'S and volunteers from NGOs, focusing mostly on disease prevention measures and treatment of the common childhood diseases such as malaria.

Services at this lowest level are conducted mostly through village clinics, mobile clinics and door-to-door visits, and sometimes through outreach programs [MoH, 2011].

With an increase in the number of HSAs, the population served by each HSA has decreased from 2500 to 1200 between 2000 and 2010 [Kadzandira & Chilowa, 2001; Ergo et al., 2010]. In a study conducted in Chikhwawa in southern Malawi, HSAs were seen to be an important factor in determining access to health care and aiding in reduction of problems witnessed in the formal health system like shortage of staff and long waiting times in health facilities and reduction in long distances to health facilities and cost for health care services [Masangwi et al., 2011].

Each of the 28 districts in the country is supposed to have a government district hospital, accompanied by facilities managed by CHAM; health care management at this level is done by the DHMT. Tertiary health care services are provided by central hospitals which in most instances offer specialist referral services for instance, surgical procedures and mental health services. In addition, some central hospitals like, the Queen Elizabeth in Blantyre, are also teaching hospitals and/or research centres. A major development in Malawi was the establishment, in 1986, of the first College of Medicine, with first graduates emerging in 1992 and first 'entirely home-grown' graduates emerging in 1997, who are now providing leadership in all district hospitals and in turn contributing to training of more staff at various levels. Private services compliment those provided by public sector [Chilowa & Munthali, 1999].

2.10.3 Development of health facility database and mapping

Accurate health information is the cornerstone of effective decision-making and reliable assessment of disease burden and resource needs [Detmer, 2003; WHO, 2007]. Efforts to tackle the enormous burden of ill-health in low-income countries are hampered by the lack of functioning health information structures to provide reliable health statistics [Osiobe, 1989; Boerma & Stansfield, 2007]. Central to a fully operational Health Information Systems (HIS) is a basic inventory of all functioning health facilities and the services they provide. Such an inventory requires a spatial dimension, allowing facilities to be linked to the populations they serve by level of care and other proximate determinants of health such as environment, poverty and education. This spatial linkage can be provided by geographic information systems (GIS). The use of GIS for health services planning is widespread in developed countries but there are few examples of their development and operational use in resource poor settings in Africa [Noor et al., 2009].

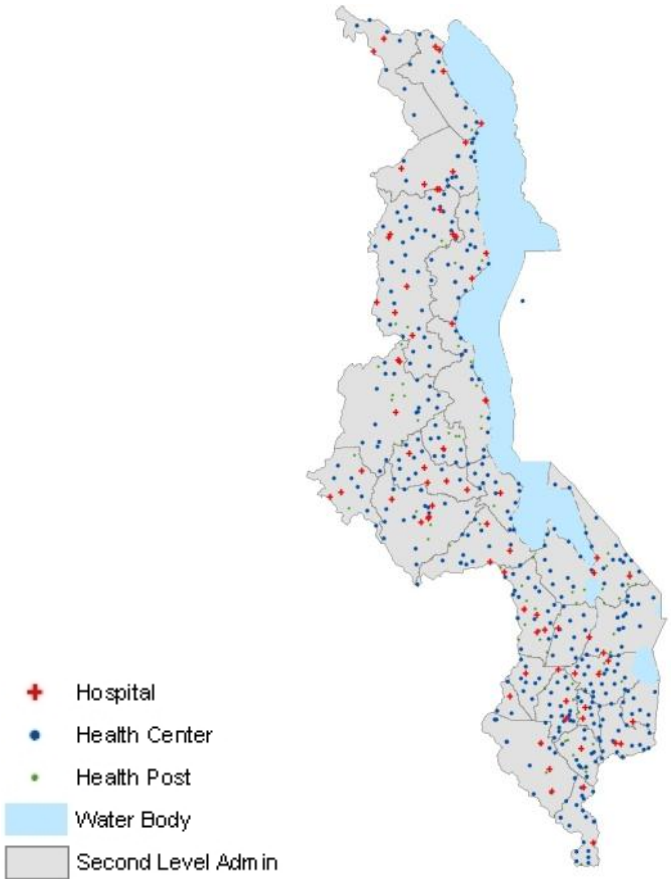
Health facility locations in Malawi, both public and private, were comprehensively surveyed in 2002 by the Japan International Cooperation Agency (JICA). The geo-coordinates for each facility, its type, ownership and funding source were included in the database [MoH & JICA, 2003]. The database contained 617 facilities and special care centres managed by government and private sectors. The composition of facilities included 74 hospitals, 108 clinics and dispensaries, 416 health centres, 15 maternity centres, a rehabilitation centre and three HIV Voluntary Testing and Counselling (VCT) centres.

Since 2002, the number of facilities has significantly increased while others have been rehabilitated and upgraded to provide full EHP. In 2010, the MoH conducted another survey of health facilities. The database had 752 facilities each with a facility type, district, geo-coordinate, and unique identifying number. However, not all the facilities had geo-coordinates (86) and were geo-located using previously assembled JICA health facility database, ENCARTA, Google Earth™, Geonames and combinations of the above in cases where the coordinates fell slightly outside the country boundary or within water body. Three private facilities were excluded as these are accessible only to those able to afford care and do not often feature in anti-malarial and net distribution supply management systems. 188 structures that were labelled refugee camps, maternity homes, rehabilitation centres, police, military or prison facilities, other specialist and teaching facilities that were unlikely to be providing routine curative services were also excluded. We retained the remaining 561 "public" facilities that were reported as managed by CHAM, government or NGOs[6]. The facilities were re-coded into three tiers of Hospitals (Rural or community hospitals, District hospitals, and central hospitals), Health Centres and Health Posts (Dispensary, Health Post, and Clinic).

Coordinates were checked with the health administrative boundary map described in Figure 2.1 to locate those facilities that were in the wrong administrative boundary and attempt re-positioning. The Global lakes and Wetlands (GLWD) database developed by the World Wildlife Fund [Lehner & Doll, 2004] was used to ensure facilities were within defined land areas. We used the spatial join tool in ArcMap 10.1 to identify facility coordinates that were located on a river/lake or in slightly outside of their correct administrative units and every anomaly was re-positioned using small shifts in combination with Google Earth™. Of the 561 public facilities, 545 (97%) were geo-located while 16 (3%) facilities remained un-positioned. The location of geo-coded facilities 77 hospitals, 387 health, and 81 health posts is shown in Figure 2.7.

[6] It has been noted that there may have been an expansion of health services since the last compete audit and it is estimated that there are currently between 602 and 604 public service providers of out-patient care. The definitive, most contemporary master-health facility list is not available but could easily be updated.

Figure 2.7: Distribution of geo-coded hospitals, health centres and health posts managed as part of the public sector (government and faith-based or NGO)



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Chapter 3

100 years of malaria control

3.1 Background

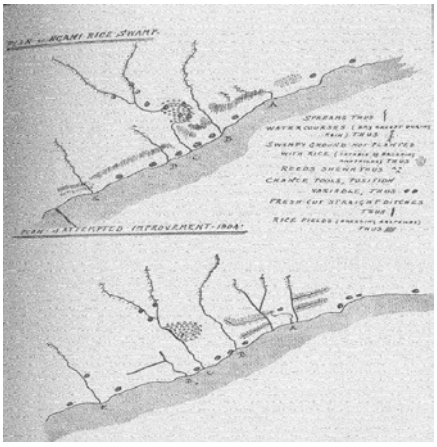
In this chapter we provide an overview of the evolution of malaria control in Malawi from the period before independence, through the era of the GMEP, to the present RBM control period. This chapter is motivated by a need to: a) capture a historical perspective of control to be applied to today's control ambitions; and b) maintain an institutional memory of the last few decades of malaria control in Malawi - who was involved, what was done, what worked and more importantly what did not work.

3.2 1900-1949: The first fifty years

In Howard's dissertation on malaria in Nyasaland, based on his experiences from 1899, he cites the impact of malaria on the European settlers in the year April 1895-March 1896 as a death rate of 97 per 1000; of 28 deaths, 20 were due to malaria fevers and of these 16 included backwater fever [Howard, 1907]. The alarming malaria death rates prompted the British Government to send Stevens and Christopher's to Blantyre in April 1899. Dr Daniels arrived from the Liverpool School of Tropical Medicine a year later and despite local opinions that the Shire highlands were malaria free, he discovered Anopheline larvae as high as 5000 feet (*circa* 1500 m). Daniels did not consider mosquito breeding site destruction as feasible means of malaria control but recommended mosquito proofing of houses and segregation of local populations were more likely to be effective. Segregation started at Fort Johnson (present day Mangochi) in 1900.

Howard made a detailed study of malaria on Likoma island, reviewing records since the Church Universities Mission established a base there in 1895 and developed detailed maps of mosquito breeding sites and villages occupied by the 23,000 inhabitants of the Island [Howard, 1907; Figure 3.1]. His interests were in mitigating against the effects of rice cultivation at Ngani on the breeding of malaria transmitting mosquitoes and optimized positioning of European settlements based on observations of Christophers and Stevens in West Africa [Christophers & Stephens, 1900].

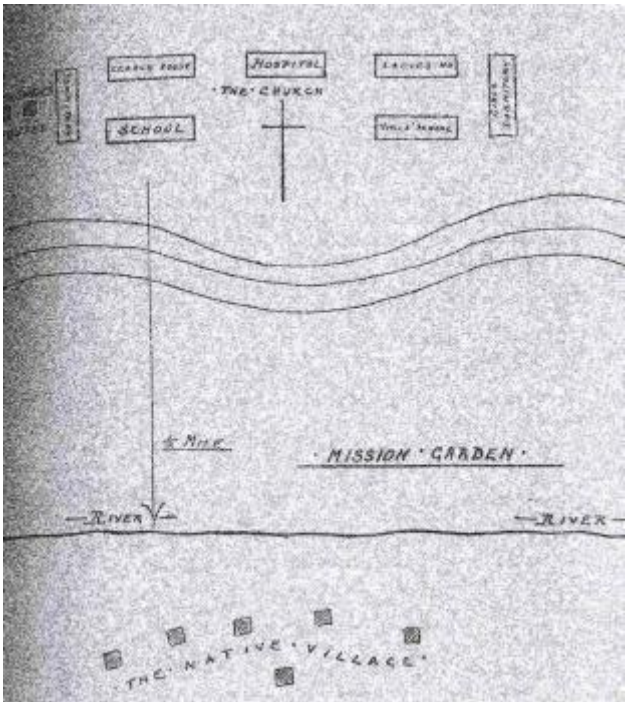
Figure 3.1: Mapping of settlements, rivers and rice cultivation for malaria risk on Likoma Island 1902



Howard undertook similar risk mapping exercises at the mission stations at Kota-Kota and Malindi in 1902, noting that the missionaries had been using mosquito nets since 1899,

screened their houses with wire gauze and took quinine prophylaxis every other day from 1903. Howard believed that "*segregation of Europeans where it can be obtained is admirable in its simplicity and efficient in its results*"; he goes on to provide an ideal plan for segregation (Figure 3.2). He did not feel that quinine prophylaxis alone would work.

Figure 3.2: Plan of ideal Mission Station (Segregation plan) [Howard, 1907]



Before the First World War, malaria control focused on protecting European residents and followed the principles of environmental management proposed by Ross [Ross, 1902]. In 1913, the annual report of the health and sanitary conditions stated that measures taken included a) mosquito reduction (periodic clearing of weeds, undergrowth and bush; filling up of hollows and depressions and draining of roads; screening of water tanks with wire gauze); b) personal prophylaxis: with quinine; use of mosquito nets and screening with wire gauze houses close to the Lake and river; and c) segregation of the general population in native locations [Nyasaland Protectorate, 1913]. The latter a result of the perceived threat posed by infected local communities on the risks to European's settled nearby and following Howard's views for Mission Stations. For environmental management reference was made to the use of prison labor, and later more special anti-malarial gangs. There was a constant reference for the need to engage other departments, including the agricultural department, in sub-soil drainage [Nyasaland Protectorate, 1914].

The lake, rivers in the Shire valley and swamps at Port Herald (Nsanje), Fort Johnson (Mangochi) and Karongo proved a constant battle for local authorities with respect to mosquito breeding. The Shire river, for example, was cited in 1920 as follows "*there is at present no prospect of an amelioration of the existing conditions regarding the prevalence of mosquitoes... to protect the inhabitants from the physical annoyance caused by mosquitoes as well as to lower the incidence of malaria some comprehensive scheme will have to be undertaken either in the future of sanitary engineering or the proper housing of the residents*'' [Nyasaland Protectorate, 1920]. However, any serious efforts to establish sanitary

engineering projects were seriously hampered by continued lack of funds [Nyasaland Protectorate, 1921].

Where funding was secured this was largely to support control in major town settlements and clearly for the protection of Europeans. Funds were allocated in Blantyre in 1921 to reduce mosquito numbers through brick and cement drainage close to the Mudi Stream, as this was in proximity to the Golf course, and drainage culverts to divert water away from Ryall's hotel and houses along Victoria Avenue [Nyasaland Protectorate, 1921]. During the same year, no funds were allocated to Fort Johnson to improve the general sanitary conditions until it was decided whether there might be a railway terminus built at the lakeshore. At Karonga, it is stated that "*the drainage channels dug last year to help drain the marsh lands near the dwellings of Europeans have fallen into disuse. They now rather tend to form pools.*" [Nyasaland Protectorate, 1921].

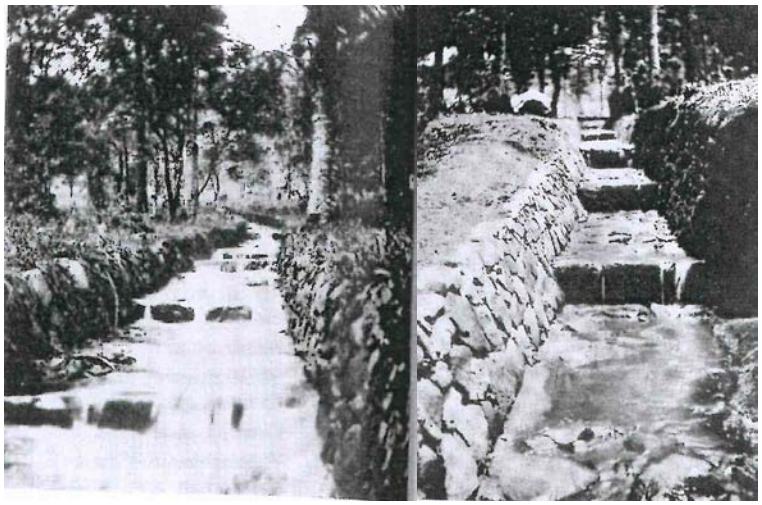
By 1925, it was widely agreed that "*preventative measures for the eradication of malaria have been heretofore of a very limited and temporary character. The sanitary gangs at work in the various townships and on government stations have done as much as possible to keep clear such places as breed and harbor mosquitoes*" [Nyasaland Protectorate, 1925]. The Director of Medical and Sanitary Services, FE Whitehead, voiced a common view held by colonial authorities at the time, and a guiding principle of public health in Britain's colonies during the early 1920s, recommending "*..strict segregation within the townships of all natives and Asiatics whose employment does not necessitate their being in the township overnight. The former should be housed in properly laid out "locations"".* He ended his recommendations with "*the constant menace to the health of Europeans from the presence of so many coloured people is obvious*" [Nyasaland Protectorate, 1925].

Little attention was given to areas without any commercial or political interest across the protectorate - "*the government stations at Liwande, Kota-Kota, Karonga and Fort Johnson, for instance, are and must remain veritable hot-beds of malaria*" [Nyasaland Protectorate, 1926].

A Sanitary Board Ordinance was introduced in 1929, leading to the establishment of sanitary boards in 1930 in Lunzu, Chiromo, Fort Manning (Mchinji), Lilongwe, Karonga and Dedza, with the district commissioner invariably acting as chairman. These local boards decided on the rates levied on plot holders relative to the block annual sums provided by government for local sanitation works. A Sanitary Inspector was appointed at Zomba in 1929, and he managed a Sanitary Gang of 75 labourers over the following years to some effect. These teams conducted regular inspections of premises to locate mosquito larvae, and from 1930, circulars were sent to all households about the importance of these inspections and the serving of "intimations" for households found with mosquito larvae. At Zomba, during 1930, 31,230 premises were inspected, 119 notices served, 2190 yards of drainage dug (Figure 3.3), 117 borrow pits were filled, vegetation cleared and sprayed with 123 gallons of oil, 475,000 square yards of grass cut, and over 1000 tons of broken stone used to drain and remove two large swamps in the town. In 1933, a third swamp was engineered to be free of standing water near the new electric power station. By the mid-1930s, Zomba, located at 3000 feet, was reported as being "*remarkably free from mosquitoes and particularly*

anophelines" a few exceptional areas existed of risk including some streams close to the model Jeanes School for African students [Nyasaland Protectorate, 1930; 1931; 1933].

Figure 3.3: Control of seasonal streams at Zomba before (left) and after canalization (right)



In 1931, significant increases in funding for sanitary works were made possible as a result of finances provided to the protectorate for general improvements in the health sector by the Colonial Development Fund (CDF). Town councils in Blantyre and Limbe received funds to improve environmental works (drainage, swamp clearance). The CDF also enabled medical officers to visit rural areas of their districts, inspect and supervise rural dispensaries and extend some sanitation works [Nyasaland Protectorate, 1933].

No specific malaria control was attempted in the rural, local communities during this time. As noted in 1934 "*the native population of this country amounts to over one and a half million, whereas the sanitary personnel to deal with this population is two European Sanitary Superintendents and 16-17 inadequately trained Native Sanitary Inspectors*" [Nyasaland Protectorate, 1934]. There was some mention of broader health initiatives from the 1930s for rural communities, for example "demonstration" model villages at Kota-Kota that were thought to educate residents on the value of sanitation across wider areas [Nyasaland Protectorate, 1932]. However, no detail on whether this was ever launched was available in the annual reports. In 1931, the chief of the Sanitary department, GM Sanderson, developed a component to the syllabus in native schools on hygiene that included information on mosquito avoidance, however these schools were largely located in townships [Nyasaland Protectorate, 1931]. From the early 1930s discussions were held around making the Jeane's School at Zomba into a training centre for Sanitary staff so they "*would be of much greater practical value to the village communities in which their future work will lie*". This was finally realized in 1935 with funds provided by the Carnegie Trust [Nyasaland Protectorate, 1934; 1935].

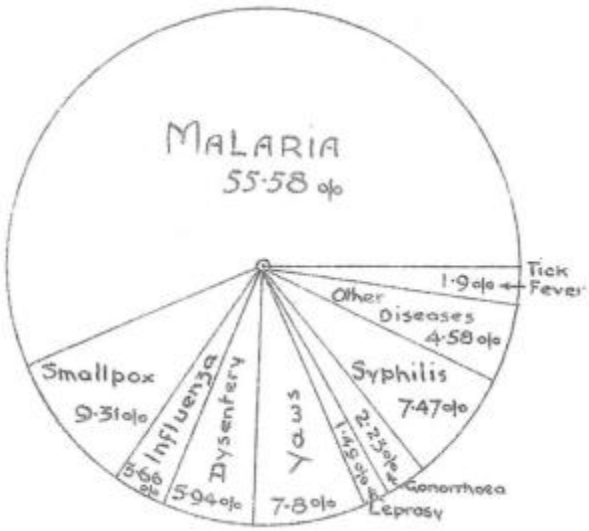
The Director of Medical Services in 1934, ADJB WIlliams, had an apparently more sympathetic view of the health of the protectorate and recognized the poor health status of the majority of its citizens, "*The general conditions under which the natives live in the rural areas of this protectorate are without doubt unsatisfactory in the extreme. They are born, live and die under the most insanitary conditions, they are, despite the benefits of education*

and the "Pax Britannia" on the whole very poor and ignorant even of the most elementary principles of hygiene. They become as soon as they are born, infected with malaria, hookworm, bilharzias and other endemic diseases, all of which are preventable" [Nyasaland Protectorate,1934].

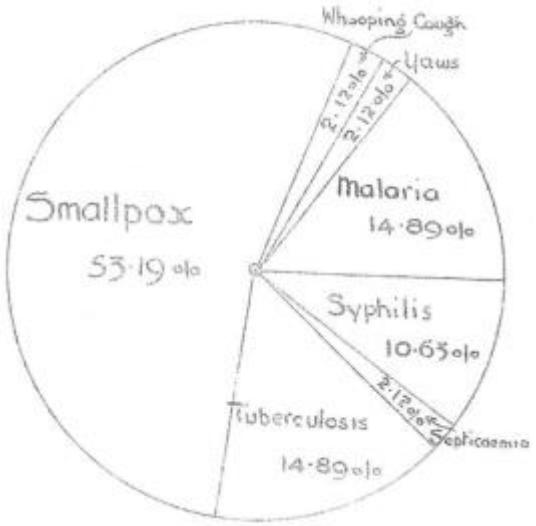
Notable during the first thirty years of the 20th century was the level of detail taken to record morbidity and mortality events in the protectorate (Figures 3.4a and 34b). Undoubtedly, these were an incomplete account of the health of African communities but did provide a relative sense of the contribution of malaria to illness and mortality for those who used government services. Over half of all illnesses and 15% of all deaths were due to malaria.

Figure 3.4: Graphic statistical presentations of disease burdens in 1930 annual medical and sanitary report [Nyasaland Protectorate, 1930]: a) morbidity reports and b) deaths among those in government facilities.

a)



b)



To highlight the continued risks posed by malaria on the European population, the 1931 census estimated that there were 1,975 Europeans resident in the protectorate; during 1931 this community experienced 19 deaths, four were due to malaria and four due to blackwater fever giving an estimated overall direct and indirect malaria mortality rate of 4 per 1000 per year. Regarding morbidity, during 1931, 144 officials were on the sick list and 36 were a result of malaria resulting in a total of 162 days lost [Nyasaland Protectorate, 1931]. These figures illustrate the effects of malaria on a population without a fully developed immune response, similar to newborn Malawian African infants and young children. The authorities, however noted that the precise burden among the African population was largely unknown and that reported cases from facilities were unreliable because "*the greater number the diagnosis was clinical only*". Notwithstanding the lack of data the 1938 annual report stated that "*we have no definitive information on the incidence of malaria in this country but it would be difficult to overestimate the importance of the infection as a cause of ill-health, inefficiency and death; for the disease is endemic throughout the protectorate*" [Nyasaland Protectorate,1938].

In 1935, the Sanitation department was merged into the Medical Department to strengthen the administration of the department and increase efficiency. During the same year an effort was launched to improve the knowledge base of infections and diseases that affected the general population. A system of "sentinel sites" was established to document the climate, living conditions and health status of communities in Chiradzulu, Cholo, Fort Johnson, Karonga, Kota-Kota, Mlange, Zomba (Chilwa Island), Dedza, Lilongwe, Kasungu, Fort Manning and Mzimba. Data was to be collected on spleen rates, protozoa infections, helminthes, haemoglobin and nutrition. Detailed reports were provided on annual surveys in end of year reports by the DMS until the outbreak of the Second World War.

Despite generating important social and biomedical evidence through regular health surveys, the authorities seemed paralyzed on what might be done with available resources to reduce the burden of malaria among the rural communities and a fear was expressed on the effects of control leading to impaired immunity, concerns raised in Tanganyika around the same time by Bagster-Wilson of the Tanga Malaria Unit [Wilson, 1936; 1939]. The 1935 annual medical report states "*very little can be done to improve existing conditions. Permanent drainage works and bonification would be necessary on a scale beyond the financial resources of the country. The more extensive use of quinine would probably result in a reduction of the infantile mortality due to malaria but while breeding grounds exist over enormous areas quininisation of the populace might possibly result in loss of immunity and the subsequent occurrence of malaria in epidemic form*" [Nyasaland Protectorate, 1935].

The differences between ambitions for urban, European settled areas versus neighbouring rural communities were again emphasized in the 1936 annual report "*The problem presented is such a vast one that the efforts of the Medical Department especially in rural areas can have but little effect in reducing the incidence. With regard to the townships a fairly satisfactory state of affairs may be said to exist, oil-spraying, drainage of pools and swamps, filling in of holes, grass-cutting etc...*". In 1936, the issues were more the allocation of financial resources than concerns over immunity.

In 1938, a reference was made to the introduction of fish into land-locked pools and streams that reduced mosquito larvae in Fort Johnston and an intriguing observation related to the establishment of bat-towers, to stop bats entering houses that "*helped in the destruction of adult mosquitoes*" [Nyasaland Protectorate, 1938].

3.3 1950-1960s: Post Second World War: the first attempts at indoor residual spraying

The first mention of using post-offices to provide quinine to the general public was made in 1933 [Nyasaland Protectorate, 1933]. This approach to increasing accessibility to anti-malarial treatment in the home continued for 20 years. The sales of anti-malaria drugs in 1950 continued but now included mepacrine and paludrine [Nyasaland Protectorate, 1950]. In 1951, the medical stores issued to the General Post Office 591,300 quinine tablets, 232,000 mepacrine tablets and 711,000 tablets of paludrine for bi-weekly prophylaxis [Nyasaland Protectorate, 1951].

An increasing number of African Sanitary Assistants were being trained at the Zomba School of Hygiene. There was a move toward creating African High Density Residential areas in Blantyre and Limbe during the early 1950s as part of urban planning projects.

Gammexane was introduced in 1950 to tackle epidemics of relapsing fever in the Central and Northern Provinces targeting the tick vector *Ornithodoros moubata*. By 1952, Vector Control Units had been established and had responsibilities for spraying houses in densely populated areas - although not much detail is provided [Nyasaland Protectorate, 1952].

From 1954, annual medical reports for public health were combined with Rhodesia under the Federation of Rhodesia and Nyasaland. In Southern Rhodesia experience with indoor residual spraying (IRS) using BHC wettable powder (Gammexane) was well established during the early 1950s, covering over 11,000 square miles in 1954/55, protecting 804,000 people at a cost of £21,379 [Federation of Rhodesia & Nyasaland, 1955]. Almost no substantive spraying activities were evident in Nyasaland and it was proposed that a demonstration project would be established with assistance and technical advice from Southern Rhodesia in 1956.

In September 1956, spray operations began using Gammexane in the densely populated districts of Zomba and Chiradzulu extending from Lake Chilwa to the Zomba plateau covering 230 square miles and over 43,000 houses [Federation of Rhodesia & Nyasaland, 1956]. This was extended to the Domasi area during the 1956/57 season. However the Zomba, Chiradzulu, Lake Chilwa triangle area was not extended beyond 1958 due to lack of staff and resources [Federation of Rhodesia & Nyasaland, 1959].

An inter-country malaria eradication project for southern African (South-East African Malaria Eradication Project), including the Federation was formed in 1959. A particular threat to Southern Rhodesia's elimination ambitions were migrant entry points from Nyasaland and Portuguese East Africa (Mozambique); monthly blood samples at the borders showed 30% infection rates [Federation of Rhodesia & Nyasaland, 1959]. From 1960, it was proposed that a single dose of pyrimethamine (60mg)-chloroquine (600mg) be given to all immigrant laborers at borders [Federation of Rhodesia & Nyasaland, 1959].

In the report for the year 1960 on IRS, it states "*the Zomba-Blantyre-Lake Chilwa area had to be abandoned because of the lack of cooperation of the people. The opposition began at the very beginning of the annual spraying campaign and chiefs and headmen announced that their people would not allow their houses to be sprayed. The people will probably reap the harvest of their folly in 1961 with a heavy child mortality and much illness in others, due to malaria*" [Federation of Rhodesia & Nyasaland, 1960].

3.4 Malaria control during the 1970s and 1980s

From 1960, to the late 1980s, there are very few details on approaches taken for malaria control. In 1973, WHO sent a mission to Malawi to conduct a detailed review of the disease burden, epidemiology, examine the efforts of urban malaria control in Blantyre and Lilongwe, evaluate the efficacy of pyrimethamine and make recommendations to the government on control options [Cheyabejara et al., 1974]. The proportion of hospital

admissions with a diagnosis of malaria between 1971 and 1972 was *circa* 11%, and malaria contributed to between 7-11% of hospital deaths. The report suggested that pyrimethamine had been used as a chemoprophylactic treatment since 1968 for children and mothers and issued at clinics. The WHO team recruited malaria cases from Domasi Rural Hospital and treated them with 1mg/kg body weight pyrimethamine. Among the 31 children who completed the seven day follow-up, 26 had cleared infections by Day 4, one cleared on Day 6 and the remaining three were still positive by Day 7 and remained infected through to Day 14 [Cheyabejara et al., 1974]. The consultants recommended that prophylaxis should be expanded nationwide and that fortnightly Chroloquine (CQ) should replace pyrimethamine.

The report highlighted the continued efforts to control malaria within the urban extents of Blantyre and Lilongwe. At Blantyre, Health Assistants supervised a foreman who managed 45 spraymen who sprayed oil along verges and possible mosquito breeding sites and followed the work of 106 "grass-cutters". The Public Works Department maintained drainage systems for storm water. Larviciding using Malariol was reported in Lilongwe [Cheyabejara et al., 1974].

As with so many previous recommendations, the WHO team suggested that "*Taking into consideration the available resources of manpower and finances, it is considered that a large scale malaria control programme is not feasible at the present time*". The team did however recommend establishing a central malaria unit, staffed by a malariologist, entomologist, parasitologists and technical staff; a primary function of this unit would be to conduct serial parasitological, entomological and resistance studies in key sentinel sites [Cheyabejara et al., 1974]. There is no evidence that these recommendations were implemented for at least another 25 years.

3.5 Malaria control 1980-1999: defining the challenge and building the programme

3.5.1 Building the programme and national strategies

In 1978, there were approximately 6,000 reported malaria admissions among children aged less than five years; within five years, by 1983, this had increased to over 16,500 malaria admissions [Khoromana et al., 1986]. By 1990, there were an estimated 50,000 malaria admissions nationwide [Wirima, 1994]. Other evidence suggested that paediatric admissions with malaria and anaemia combined accounted for 41% of all under five hospital admissions and 32% of hospital deaths during the 1990s [Ettling et al., 1994a].

Building the national malaria programme and establishing national policies from the mid-1980s was governed by a growing research platform that developed evidence of failing first-line therapies, the need for better diagnostic treatment algorithms, patterns of treatment access and the role played by malaria in pregnancy on birth outcomes and infant survival. The presence of active research teams at Mangochi[7] and Blantyre[8] provided unique opportunities to shape a decade's malaria policy in Malawi.

[7] The Centers for Disease Control (CDC), USA, became intimately involved in the malaria programme in Malawi from 1984, working through the ACSI-CCCD programme. Their technical assistance was critical to building the knowledge base for declining CQ efficacy, supporting the national malaria control committee and establishing the Mangochi Malaria Research Project, supported by the USAID [Steketee et al., 1995]. CDC's presence and

The government's commitment to malaria control efforts gained a renewed visibility within the MoH during the mid-1980s. The National Malaria Control Programme (NMCP) was created under the Division of Preventive Health services in 1984 through the formation of a National Malaria Control Committee and the first national malaria control manager, Dr Jack Wirima, was appointed in 1987. The NMCP had a legal framework within the Malawi National Health Policy (MNHP) and functions included the setting of policies, establishing strategies, coordinating, monitoring and evaluating activities, providing technical assistance to the MoH and mobilizing resources for the program.

Two national malaria strategic plans were developed after 1985. Both had a focus on effective disease management. The first five-year national malaria control plan was developed in 1984, covering the period 1984-1989, and was the first written strategic plan for malaria in Malawi. Its vision was "*to keep all Malawians free from the burden of malaria*" accompanied by a mission "*to reduce the malaria burden to a level of no public health significance in the country*" [Steketee et al., 1995]. Five basic malaria control strategies were outlined in the plan developed in 1984 and they included presumptive treatment of fevers in children and adults with CQ, continuous monitoring of antimalarial efficacy, selective antimalarial chemoprophylaxis (for pregnant women, immunosuppressed patients, children with recurring febrile convulsions or sickle cell disease), vector control (limited to major urban areas) and health education [Steketee et al., 1995; Helitzer-Allen, 1994].

Following the review of the first plan in 1989 by the MoH and its partners combined with evidence provided by key operational research initiatives, the second national malaria control plan was developed in 1990, covering the period 1990-1994 [Steketee et al., 1995]. This strategy's goal was to reduce malaria related morbidity and mortality by 10% and 20% respectively by 1994 [Steketee et al., 1995]. To achieve this, the 1990-1994 plan identified ten key elements: 1) improved understanding of malaria illness, prevention and treatment; 2) accurate diagnosis; 3) effective treatment; 4) diagnosis, treatment and reporting incorporated into health personnel training; 5) strengthening of the malaria reporting system; 6) effective prevention in high risk groups (e.g pregnant women); 7) promotion of alternative control methods (e.g insecticide treated nets); 8) effective management and administration of the MCP at all levels; 9) increased research capability; and 10) increased government and donor investment in national malaria control.

Both of the early national malaria control plans had a focus on disease management and were linked to the Africa Child Survival Initiative - Control of Communicable Childhood Diseases (ACSI-CCCD), a project funded by the United States Agency for International

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research support continued through to 1998. Although no longer at the Mangochi site, the CDC continued to provide support for research activities in Malawi through a cooperative agreement with the Malaria Alert Center in Blantyre. This support is still provided by the U.S. government today, although using PMI funds channelled through the CDC. There are currently multiple PMI/CDC/Malaria Alert Center studies ongoing in country.

[8] The Malawi-Liverpool-Wellcome Trust Clinical Research Programme carries out health research and trains clinical and laboratory scientists from Malawi and abroad. Officially opened in 1995, the Programme is strongly linked with the University of Liverpool and the Liverpool School of Tropical Medicine, and is affiliated to the College of Medicine, Malawi. Research is carried out closely with the Malawian MoH on malaria, HIV and tuberculosis.

Development (USAID) and initiated in 1984 [Steketee et al., 1995]. The decentralization of health services in Malawi to the district level in the 1990s moved the responsibility of health care from the central level (NMCP) to district management teams (DHMTs). The DHMTs were responsible for all malaria activities at the district level for each of the 28 districts in the country [Rosensweig & Williams, 2008]. There were five zonal offices in the country which were responsible for overseeing malaria activities in their respective five to seven districts. The DHMT, headed by the District Health Officer (DHO), designated a District Malaria Control Coordinator to provide support to the planning, costing, implementation, monitoring, supervising and reporting the district malaria activities.

3.5.2 Grappling with anti-malarial drug resistance and fever case-management

In April 1983, an American Peace Corps worker contracted malaria in Northern Malawi while taking CQ prophylaxis and *in vitro* assays confirmed the presence of CQ falciparum resistance [Wolfe et al., 1985].

As a prelude to the USAID funded ACSI-CCCD programme in Malawi, the efficacy of CQ was assessed at six sites across the country (Karonga, Rumphi, Dwangwa, Lilongwe, Mangochi and Machinga) between July and December 1984. Of all children who completed the recommended CQ treatment, 57% remained parasitaemic by Day 7 and the results were consistent across all six sites (range 41% to 65%) [Khoromana et al., 1986]. Although parasite resistance to CQ had been demonstrated, CQ remained the drug of choice because of efficacy in reducing clinical illness, the unavailability of alternative treatments and the general safety of CQ.

With the increase in childhood morbidity and mortality and concern that CQ resistance had intensified, the efficacy of CQ was assessed again in 1990. In 1990, at Karonga District Hospital and a subsequent follow up study in Mangochi, children less than 5 years of age with signs, symptoms and laboratory documentation of malaria were treated with either CQ 25 mg base/kg over 3 days or sulphadoxine-pyrimethamine (SP) at the WHO recommended standard dosing for age. This study found that more than 90% of children treated with CQ remained parasitemic and most resistance patterns were RII or RIII. Because treatment with CQ failed to produce ether lasting clinical improvement or adequate hematologic recovery, CQ could no longer be considered adequate therapy of clinical *Plasmodium falciparum* in Malawian children [Bloland et al., 1991; Bloland et al, 1993].

During the national household demographic and health survey of 5323 households in 225 clusters undertaken between September and November 1992, 40.5% of children aged less than five years had had a fever in the last 14 days, of whom 46% were taken to a health care provider and 28% were given an antimalarial [NSO & ORC Macro, 1992]. No details were available on the type of anti-malarial given or the timing of treatment.

A nationwide knowledge attitude and practice (KAP) malaria survey was undertaken in March-May 1992 at 30 clusters covering over 1,500 households [Ettling et al., 1994b]. Results from the survey indicated that 33% of the survey population reported fever in the previous 14 days, with infants and children reporting the highest rates at 46% and 49% respectively translating to 9.7 episodes of fever per year in children under five years [Ettling

et al., 1994b]. 20% of febrile patients self-medicated using drugs from shops, neighbours or other sources. Less than 10% of children were reported to receive an appropriate dose, limiting effective therapy and potentially promoting resistance [Slutsker et al., 1994]. The total cost of household prevention and treatment was estimated to be 7% of the household income [Ettling et al., 1994a]. In the poorest households, expenditure on malaria illnesses was reported to be US$ 19, representing 28% of mean annual household income [Ettling, 1994a]. The two major constraints for access and use of health services were identified to be low education and low household income [Macheso et al., 1994]. This was an important survey instrument, and the data were used to make programmatic decisions; develop educational messages and in establishing monitoring and evaluation platforms for malaria control activities.

A simultaneous research interest in Malawi at the time were studies aimed at selecting better discriminating symptoms for malaria among young children presenting to clinics [Redd et al., 1992; Redd et al., 1996]. These studies highlighted the very real difficulties in busy out-patient clinics to distinguish between respiratory infections and malaria in the absence of laboratory diagnosis. Studies of improved laboratory diagnosis in 1993 showed the cost and patient benefits of accurate parasitological diagnosis for febrile adult admissions to Queen Elizabeth Hospital [Jonkman et al., 1995].

The recognition of the clinical and hematologic impact of drug resistance was instrumental to informing the decision to change the national first-line antimalarial drug policy in Malawi. In 1991, a national meeting held in Mangochi was convened to review study results which were then used to change the treatment policy, and revise treatment guidelines. The new policy replaced CQ with SP as the first-line drug for treatment on malaria in young children and for chemoprophylaxis for pregnant women and discontinued Amodiaquine (AQ) as the recommended second line drug due to concerns about side effects. In 1992, a meeting was held with private sector pharmaceutical companies to encourage them to procure SP and by March 1993 the Central Medical Stores had purchased and distributed sufficient amounts of SP for use in the health system. An education workshop was organized by the NMCP in late 1992 to develop educational materials, during which treatment guidelines were finalized. Before the official national launch in March 1993, regional meetings were held between December 1992 and January 1993 to inform DHMTs of the new policy and this in-service education campaign was cascaded to all health care workers within each district [Steketee et al., 1995]. Concerted efforts were made to remove CQ from public and private sectors, resulting in a near total replacement of CQ with SP [Plowe et al., 1997]. Malawi was the first country to make the switch to SP and was also the first country to officially recommend SP for use in preventing malaria during pregnancy.

3.5.3 Malaria in pregnancy

CQ had been used for a number of years as a means to prevent malaria in pregnancy but was operationally unsuccessful as women thought it was dangerous, failed to complete doses and did not like the taste [Helitzer-Allen et al., 1993a]. Attempts to improve awareness and sugar coating were only marginally successful [Helitzer-Allen et al., 1993b; 1994]. High rates of CQ resistance also compromised the efficacy of chemoprophylaxis in pregnant women. 84 (37%) of 228 women who completed four weeks of supervised CQ

administration at four Antenatal Care (ANC) clinics along the shores of Lake Malawi in 1988 had *Plasmodium falciparum* parasitaemias, yielding an expected overall protective efficacy of only 8% [Heymann et al., 1990].

Work by scientists in Mangochi and Chikwawa districts, during the early 1990s, was instrumental in defining the burden of malaria in pregnancy and risks to the newborn child and in promoting the use of SP as a means to reduce this burden [Schultz et al., 1994a; 1994b; 1996; Slutsker et al., 1990; Steketee et al., 1996a; 1996b; 1996c; 1996d; Sullivan et al., 1999; Verhoeff et al., 1997; 1998; 1999; Kalanda et al., 2009]. The trials showed that two doses of SP in the second and third trimesters was able to significantly reduce placental malaria and, maternal anaemia and increase birth-weights and was a highly cost effective intervention. Results from these studies were presented to the NMCP in October 1992 and national guidelines were modified to recommend SP in a two-dose intermittent treatment regimen for pregnant women (IPTp). Work on IPTp from Malawi and allied studies in Kenya were instrumental in defining regional policy for malaria in pregnancy during the early 1990s.

A national household demographic and health survey was undertaken between July and November 2000 in 3092 households. Women who had had a pregnancy in the last two years were asked about the presumptive use of SP during the pregnancy; 67% of women had taken SP at least once and 29% two or more times [NSO & ORC Macro, 2001]. Among 1623 women delivering at the Queen Elizabeth Central Hospital in Blantyre between 1997 and 1999, the operational analysis of reported consumption of two doses of SP was associated with a decrease in placental malaria prevalence (from 31.9% with no SP prescription to 22.8% with two doses SP) and density, decreased prevalence of low birth-weight (from 23% in women not receiving SP to 10.3% in women given 2 doses) and higher maternal haemoglobin concentrations [Rogerson et al., 2000].

3.5.4 Bed net use

By the end of the 1990s, there was overwhelming evidence of the benefits of Insecticide Treated Nets (ITNs) in reducing all-cause child mortality from a range of different transmission sites in Africa [D'Alessandro et al., 1995; Binka et al., 1996; Nevill et al., 1996; Habluetzel et al., 1999] and allied benefits in the protection against malaria-morbidity, hospitalization and anaemia [Lengeler, 2000]. ITNs were shown to compare very well on cost-effectiveness metrics with other child survival interventions, with a cost-effectiveness range of US$ 19–85 per disability adjusted life year (DALY) averted [Goodman et al., 1999].

During the 1992 KAP survey, only 7% of households reported purchasing bed nets, conversely twice as many households (16%) reported using mosquito coils [Ziba et al., 1994]. It wasn't until the mid-1990s that nets were introduced as part of community-based programmes. In September 1995, eight villages in Chilipa area in Mangochi district, where bed net ownership was less than 3%, were selected for a pilot operational delivery of insecticide-treated curtains [Rubardt et al., 1999].

Following the community's recognition of the scale of the malaria problem, the ITN component of the Ekwendeni Malaria Control Programme began in early 1997 with the

main target groups being children under the age of five years and pregnant women. ITNs were sold at a subsidized rate for children under the age of five years and pregnant women as part of the Ekwendeni Malaria Control Programme [Dzinjalamala, 2007]. This model was later adopted by all of the Churches of Central Africa, Presbyterian (CCAP) Synod of Livingstonia (Ekwendeni, Embangweni and David Gordon Memorial) using funds from CDC available through a cooperative agreement. They developed a similar ITN programme to reach out to the community to promote the use ITN to control malaria through the primary health care delivery system [Dzinjalamala, 2007]. Two years after its inception more than 6,000 ITNs had been purchased by community members. In the same period the proportion of households using mosquito nets increased from 8% to 50% while the proportion of under-five children using treated nets rose from 0% in 1997 to 26% in 1999, to 55% by December 2004 [Dzinjalamala, 2007].

The Blantyre Integrated Malaria Initiative (BIMI) was a district-wide malaria-control effort, formed jointly in 1998 by the MoH, USAID, and the US Centers for Disease Control and Prevention (CDC, Malawi). The main goal of this initiative was to improve the demand and use of IPTp and ITNs, and improve the management of paediatric fever and anaemia across the district. Initial efforts were focused on measurement of baseline data to better guide the implementation of interventions. Later on, the program evolved into a national program aimed at providing technical assistance for the national scale-up of malaria prevention and control interventions through training and the development of policy, guidelines, and program implementation plans.

The Blantyre Insecticide Treated Net Project (BITNet) was launched in October 1998 as a social marketing project to improve ITN access and operated by Population Services International (PSI). Nets were branded as '*Chitetezo bednet*' (Protection in Chichewa; Figure 3.5). A treatment (cyfluthrin) kit was sold with each net alongside a measuring bag, and gloves for treatment of one net (*circa* US$ 4.4-6.6). An insecticide retreatment kit was also marketed (*M'bwezera Chitetezo* or Restore Protection) (*circa* US$ 0.67). The target populations were the rural and poor young children and pregnant women. By early 2000, over 90,000 nets had been sold through retail outlets, supermarkets, pharmacies and health surveillance assistants in government health centres. In February 2000, a survey among 672 households in Blantyre district with one or more children under the age of five, showed that net ownership was low (21% of households) overall, and significantly lower in rural areas (6.4%) compared to urban areas (30%). Only 3.3% of rural children had slept under a net the previous night, compared with 24% of urban children. When asked why they did not own a net, nearly all (95%) caretakers in households without nets stated they had no money to buy them [Holtz et al., 2003].

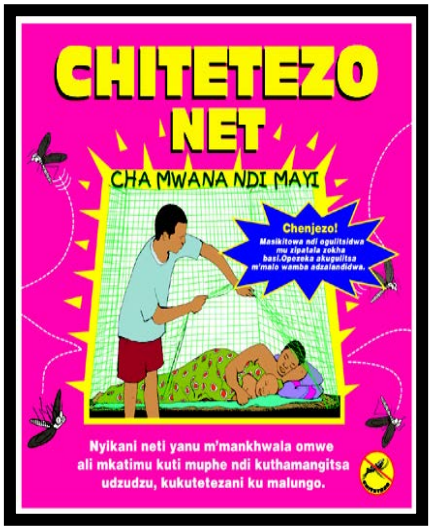


Figure 3.5: '*Chitetezo bednet*' (Protection in Chichewa) marketing materials

The findings from Blantyre district, were consistent with results from the national household demographic and health survey undertaken between July and November 2000: only 5.4% of households owned a net (16.7% urban and 3.6% rural) and only 1.4% of rural children slept under a recently treated net the night before the survey compared to 10% of urban children. Only 8% of women aged 15-49 years slept under any net [NSO & ORC Macro, 2001].

3.5.5 Grappling again with drug resistance and effective case-management

During the national DHS in 2000, approximately 35% of all recent childhood fevers had been taken to a facility following the onset of symptoms, of these 23% were given SP and very few CQ (1.3%). More febrile children were treated with drugs from a private pharmacist or shop (40%) or treated at home with previous medicines (23%) than taken directly to a public health facility (26%) [NSO & ORC Macro, 2001]. During the Blantyre household survey, in February 2000, almost 39% of recently febrile children had received medication only from home, 33% were treated at home and then taken to a facility and 25% treated only at a public health facility. Overall only 12% received an appropriate antimalarial (SP, cotrimoxizole or quinine) [Holtz et al., 2003].

While SP seemed to have effectively replaced CQ for fever treatment, universal treatment with SP among febrile children was still sub-optimal. However, from the mid-1990s concerns about the useful therapeutic life of SP began to emerge in a number of Eastern and Southern African countries.

Between February 1997 and April 1997, 641 febrile children under five years with malaria were treated with SP and followed up for 14 days at seven sites in six districts (Karonga, Rumphi, Dwangwa, Lilongwe, Mangochi and Machinga). Parasitological resistance rates (RII and RIII)[9] ranged from 7% to 19%. 80% of parasitological resistance was at the RII level. Of all children who failed parasitologically, 84 (93%) had no fever on Day 7 and their mothers did not report them as being ill; only six of 641 (0.9%) patients met the WHO criteria for clinical treatment failure. The authors concluded that "*We found that after more than 5 years of widespread use of SP in Malawi, its efficacy remains acceptable for treatment of uncomplicated malaria, and it should therefore be retained as first-line treatment*" [Nwanyanwu et al., 2000].

In July-August 1998, at Salima District Hospital, *in vivo* and *in vitro* 14 day sensitivity tests were conducted on children with malaria treated with SP, 83.1% showed RI/S resistance, 3.1% had RI (early) resistance, 12.3% exhibited RII responses and 1.5% was RIII resistant.

[9] Cases were classified as a 'parasitological success' if they had a decrease in parasite density by > 75% on day 3 and no asexual parasites on day 7 of follow-up. 'Parasitological failure' was defined as parasitaemia on or after day 7; parasitological failures were classified as RIII, RII or RI resistance. RIII failure was defined as a day 3 parasite density 25% of that on day 0 (baseline), and RII failure was defined as a positive day 3 blood smear with parasite density 25% of that on day 0 and a positive day 7 blood smear. Early RI was defined as a negative day 3 blood smear, but a positive smear anytime between day 4 and day 14, or a positive day 3 blood smear with a parasite density 25% of baseline parasitaemia, a negative day 7 smear, and a positive smear between day 8 and day 14. Sensitive (R0)/late RI was defined as a day 3 parasite density 25% of baseline parasitaemia and a negative blood smear on every follow-up examination between day 7 and day 14.

13.8% failed to clear infections by day 7 (RII/RIII). *In vitro* analysis showed that 62.1% of 29 isolates showed less than 90% inhibition at 75 nmol/l pyrimethamine of BMM, indicating resistance [Takechi et al., 2001].

Studies of SP and mefloquine (MQ) sensitivity were undertaken in Machinga district in 1998. 11.6% of children treated with SP showed evidence of Early Treatment Failure (ETF)[10], 7% had Late Treatment Failures (LTF). In the MQ group, 8.2% experienced an ETF and 2% a LTF. 10.0% and 16% of children experienced an RIII parasitological failure in the SP and MQ groups respectively. At the end of the 14-day follow-up period, 65% of children taking SP and 68% children taking MQ were classified as late RI/S [MacArthur et al., 2001].

At Dedza and Mangochi district hospitals in 2000, SP clinical and parasitological efficacy was tested on children aged 6 months to 12 years during a pharmocokinetics study in 2000. 49% of children were reported as having an Adequate Clinical and Parasitological Response (ACPR) by Day 28 with no cases of ETF. However, 9.1% and 41% children had Late Clinical Failure (LCF) and Late Parasitological Failure (LPF) therapeutic outcomes, respectively [Dzinjalamala et al., 2005].

During the early 2000s, the MoH considered the introduction of a five-day course of trimethoprim sulfamethoxazole (TS) to treat both the presumed malaria and pneumonia as part of Integrated Management of Childhood Illness program (IMCI) programmes as dual treatment of pneumonia and malaria [Hamel et al., 2005]. A study was therefore undertaken to test the *Plasmodium falciparum* efficacy of TS and the co-morbidity treatment combination of SP and erythromycin (E) in April 2001 at Chilomoni Health Centre, on the outskirts of Blantyre. Children aged six months to less than five were recruited if they presented with symptoms of pneumonia and malaria and detectable levels of parasitaemia. Among children treated with SP+E, 80% had an ACPR, 3% ETF, 9% LCF and 9% LPF [Hamel et al., 2005].

Between June and July 2000, asymptomatic infections at two primary schools of Maonga and Chimbala villages of Salima District were assayed for the prevalence of dihydropteroate synthase (*dhps*) and dihydrofolate reductase (*dhfr*) mutations, associated with decreased sensitivity to SP. A high prevalence rate (78%) of parasites with triple *dhfr* and double *dhps* mutations was found [Bwijo et al., 2003]. Samples collected at the Queen Elizabeth Hospital, Blantyre, between March 2001 and May 2003 were assayed for the *dhfr* 164-Leu mutation, which confers resistance to both pyrimethamine and chlorproguanil and was found in 4.7% of the samples [Alker et al., 2005].

[10] WHO definitions of Early treatment Failure (ETF): the development of severe malaria or danger signs on day 1, 2, or 3 in the presence of parasitemia both in intense and low to moderate transmission areas, where; Parasitemia is higher in day 2 than in day 1 irrespective of temperature; or parasitemia on day 3 with temperature ≥ 37.5^{o}C. Late Treatment Failure (LTF): Late Clinical Failure (LCF) – development of severe malaria after day 3 in the presence of parasitemia, or presence of parasitemia and temperature ≥ 37.5^{o}C on any day from day 4 to day 14 (or day 4 to day 28 in low to moderate transmission areas) without previously meeting the criteria for ETF. Late Parasitological Failure (LPF) - presence of parasitemia on day 14 and temperature ≥ 37.5^{o}C in intense transmission areas or presence of parasitemia on any day from day 7 to day 28 in low to moderate transmission areas both without previously meeting the criteria for ETF and LCF. Adequate Clinical and Parasitological Response (ACPR): Absence of parasitemia on day 14 regardless of temperature level without previously meeting any of the criteria for EFT or LFT

Following the early studies examining the efficacy of CQ, the monitoring of *Plasmodium falciparum* drug resistance continued in Malawi in Ndirande, Blantyre between 1998 and 2002. The therapeutic efficacy and parasitological resistance to standard SP treatment at Day 14 and Day 28 was measured [Plowe et al., 2004]. Results from this study showed that therapeutic efficacy remained stable, with ACPRs of 80% or higher throughout the five years of the study with trends towards diminishing clinical and parasitological efficacy over time within the study period at 28 days [Plowe et al., 2004].

Seven years after the introduction of SP, widespread evidence of molecular section for resistance was emerging and clinical failure rates were on the rise.

3.6 Malaria control 2001-2005: The early days of Roll Back Malaria (RBM)

It was not until the early 1990s, when global efforts to control malaria were re-started, that malaria gained some greater national prominence. In 1992, a global malaria control strategy aimed at preventing mortality and reducing morbidity was adopted by the ministerial conference held in Amsterdam [WHO 1992]. This strategy was adopted by the World Health Assembly (WHA) in 1993 as the global strategy for malaria control [WHO, 1993]. This culminated in the launch of the RBM Global initiative in 1998 [Nabarro & Tayler, 1998]. In 1999, the MoH, through the NMCP, embraced the RBM global strategy for the scale-up of malaria control activities in the country. Malawi was a signatory to the Abuja Declaration in 2000 to provide a minimum coverage of 60% protection to vulnerable populations by 2005 and halve the malaria burden by 2010 [WHO, 2000]. The malaria response in Malawi, during the decade from 2001 has been encapsulated in two five year national malaria strategic plans, the first of which was launched in 2001.

3.6.1 National Malaria Strategy 2001-2005

Malaria continued to be singled out as the most serious health problem facing Malawi's health sector and development goals, causing an estimated eight million illness events each year [NSO & ORC Macro, 2001]. Against this background, the first, post-RBM National Malaria Strategic Plan, covering the period 2001–2005 (NMSPI), was launched [RBM, 2013]. The purpose of the 2001–2005 malaria strategic plan was to renew efforts to reduce malaria morbidity and mortality in the context of multi-sectoral implementation of malaria control involving government, NGOs, private sector, civil societies, research institutions and communities. This was guided by six pillars: building and strengthening partnership among all stakeholders, promoting ownership of malaria activities at all levels of health care delivery, contributing to health sector reforms, strengthening the Health Information System and research, integrating malaria control activities into primary health care and other social economic development programs and increasing coverage of cost-effective interventions such as ITNs and home management of malaria [MoHP, 2001; RBM, 2013]. The overall goal of the NMSPI was to "*halve malaria mortality and morbidity by 2010 through strengthening the health system; enhancing inter-sectoral collaboration; focusing attention on the poor and community level; working with partners, private sector and NGOs; ensure the allocation of necessary resources and monitoring progress through set targets*" [MoHP, 2001].

The specific targets for NMSPI included ambitions to: a) increase the proportion of those suffering from malaria to prompt access to and able to use effective affordable treatment to 60%, including a larger engagement of community-level sectors; b) increase the proportion of children under five years and pregnant women with access to suitable and effective malaria interventions, mainly ITN, to 60%; c) increase the proportion of pregnant women, especially those in their first pregnancies, with access to IPTp to 60% [MoH, 2005].

3.6.2 Poor funding landscape for malaria

Government financing for health in many countries across sub-Saharan Africa continued to be way below the international expectations by 2005, five years after the Abuja declaration where African heads of state pledged to commit 15% of the national budgets to health. This led to a dependence on ODA. In Malawi, the health expenditure for the government (GoM) was approximately only 13% of GDP in 2004/5 [MoH, 2007a]. The majority of health sector funding was from development partners mainly: Department for International Development – United Kingdom (DFID-UK), United Nation Children's Fund (UNICEF) USAID, European Union and WHO with the greatest ODA funding secured from the Global Fund.

The Global Fund was initiated in 2002, to support effective prevention and treatment of malaria, AIDS and tuberculosis [Mtonya & Chizimbi, 2006], however Malawi only received funding for malaria from the fund after 2005, and thus was poorly funded during the NMSPI period. In addition, a large part of ODA was suspended between 1998 and 2004 due to poor governance and fiscal mismanagement by the GoM [Resnick, 2012]. The malaria ODA received by Malawi during this period was limited and was provided only through minimal per-capita needs by bi-lateral agencies such as USAID. Between 2001 and 2005, the period of the NMSPI, Malawi received only US$ 3.5 million ODA for malaria control [Snow et al., 2010; Okiro et al., 2011].

3.6.3 Insecticide treated nets (ITNs) strategies

In June 2002, the NMCP developed guidelines for ITN distribution and use to reach the NMSP1 target of 60% coverage by 2005 [MoH 2007b; MoHP 2001]. Funding and technical assistance was provided by a number of development and NGO partners notably UNICEF (procurement agent), PSI (in charge of primary distribution and social marketing), WHO, World Bank and UNDP. The emphasis was on social marketing campaigns in communities, commercial retail outlets and pharmacies. Later there was a more active engagement in subsidized net distribution through the public and CHAM facilities as part of routine ANC visits for pregnant women and health facility visits for children under five years.

During the period of the NMSPI, the dominant distribution model combined traditional, social marketing with heavily subsidized, highly-targeted distribution through the nationwide network of public health facilities. Between 2000 and 2003, the delivery of both the commercially available nets and the health facility model were expanded nationwide as part of a collaborative effort involving the Malawi Government, UNICEF, USAID and DFID. By January 2003, ITNs were being delivered through commercial outlets and public health facilities in all districts of the country. Two types of nets (blue and green) and net re-treatment insecticide were distributed through private shops and clinics. The blue conical

net was available to all through the commercial sector, while the rectangular green nets were available at health clinics for pregnant women or mothers with children less than five years of age. To further improve access to ITNs, in 2003, unbranded green rectangular nets (with a kit) were delivered via community-based groups at the subsidized price of US$ 1.2. During the period October 2002 – September 2003, a total of 942,000 nets were sold of which 8% were blue conical nets, 16% were unbranded green rectangular nets delivered via community-based channels and 76% were green rectangular nets delivered through public health facilities. The average economic cost per net delivered and the average cost per treated-net-year, over five years, was US$ 2.63 and US$ 4.41 respectively [Stevens et al., 2005].

The NMCP began organizing intensive ITN re-treatment campaigns from 2002, which would be conducted once a year during peak malaria transmission seasons. In the initial years, this project was carried out with assistance from UNICEF and PSI with DHMT's being responsible for implementation at the district level [Dzinjalamala, 2006]. While it is not possible to precisely define the source of data nor how it was computed, the NMCP estimated that ITN re-treatment increased from 7% of all nets estimated in use in 2002, to 61% in 2004 and 59% in 2005 [NMCP, 2010a; 2010b].

By 2004, ITN coverage (households owning at least one ITN) had increased to 27% with households owning at least one bed net (treated and untreated) increasing to 42%. The proportion of children under five and pregnant women who had slept under an ITN the night before the survey had increased to 15% [NSO & ORC Macro, 2005]. However, bed net ownership and use was associated with higher socio-economic status and education levels and living in urban areas [Mathanga & Bowie, 2007; Mathanga et al., 2006]. Spatial heterogeneity in ITN use is described in more detail in Section 3.4.4.

Throughout the course of the NMSPI, ITN coverage remained low, despite attempts to promote a three-tiered ITN distribution strategy to scale-up ITN coverage: full cost retail sector approaches (US$ 3.86-5.20 per net); subsidized distributions through social marketing; and heavily subsidized distributions through the public sector facilities (US$ 0.33 per net) and the community provision by DHMTs (US$ 0.66 per net) [PMI, 2007].

Despite low national ITN coverage, the social marketing, PSI-led BITNet project, launched in 1998 across Blantyre district (Section 3.4.4) had achieved higher coverage by 2002. During a case-control study of febrile malaria cases, clinic controls and community controls at Ndirande Health Centre in 2002, ITN use was over 55% in clinic and community controls, higher than the national average in the DHS in 2004, but only 35% in malaria cases, suggesting a protective efficacy odds ratio of between 40-50% [Mathanga et al., 2005]. In related studies the authors showed that there was a 52% protective efficacy against Plasmodium parasitemia among community users of ITNs [Mathanga et al., 2006]. These were the first empirical results of the morbid and infection benefits of ITNs in Malawi and the effect sizes prompted the authors to signal that "*Although ITN social marketing programmes have the potential of improving malaria control and prevention, additional efforts are required to reach those for whom even subsidized nets are still too expensive*" [Mathanga et al., 2006].

During the NMSP1, there was no evidence of pyrethroid resistance at one study undertaken at Nkhotakota district in 2003 [Chiphwanya, 2003]. The NMSPI did not actively promote IRS and consequently before 2005 there were very few active IRS projects in Malawi (Section 3.7.3.3).

3.6.4 Malaria in Pregnancy

Malaria in pregnancy is a three pronged approach: IPTp, ITNs and case management including treatment of anaemia. During this period, efforts to improve malaria prevention and control in pregnant women using IPTp and ITN were fully integrated into the Focused Antenatal Care (FANC) services. IPTp was offered free of charge and ITNs were heavily subsidized [NMCP, 2010a]. Despite high ANC attendance nationwide (more than 90% of pregnant women attended an ANC clinic at least once and 57% attended four times or more) the uptake of the recommended doses of IPTp was reported to be low during the national DHS survey in 2004, with 77% of women having received at least one dose of SP, with 47% receiving the recommended two doses during their last pregnancy [NSO & ORC Macro, 2005; Mathanga et al., 2012].

Gravidity, the late presentation of pregnant women to ANC clinics, shortages of SP, poor training and lack of understanding of policy guidelines by health workers, lack of water and cups to take SP under direct observation were identified as reasons behind low coverage of the recommended IPTp doses during studies during this period in Blantyre and Mangochi Districts [Holtz et al., 2004; Ashwood-Smith et al., 2002; Launiala & Kulmala, 2006; RBM, 2013].

The only operational impact data available during this period comes from longitudinal data collected between 1997 and 2006 in Blantyre for pregnancy outcomes among 8131 pregnant women. Peripheral and placental parasitaemia prevalence declined from 23.5% to 5.0% and from 25.2% to 6.8% respectively between 1997 and 2006 but there were smaller declines in the prevalence of low birth weight and anaemia. Throughout this period the coverage of IPTp and ITN increased and the increasing numbers of SP doses was associated with declines in placental parasitaemia, maternal anaemia and low birth weight from 1997–2001, but not from 2002–2006. Bed net use protected from peripheral and placental parasitaemia and low birth weight but not anaemia [Feng et al., 2010].

3.6.5 Increasing access to malaria treatment and initiating the second drug policy change

During the national household survey 2000, 4,245 care-givers of children with a fever in the last 14 days, reported seeking drugs over the counter (35%), followed by visiting a health facility (28%) and home medicine (27%). Traditional medicines were preferred by 4.3%, while another 6.4% did not seek care [NSO & ORC Macro, 2001]. Analysis of the 2000 national household survey showed significant spatial variation in the choice of a provider and the determinants of choice of provider (place of residence, access to media, caregiver's age and inaccessibility of care) [Kazembe et al., 2007].

To increase access to interventions, the Malawi government adopted the IMCI strategy in 1998. IMCI is an approach to reduce childhood mortality, morbidity and disability in developing countries and to contribute to improved growth and development of children

under-five years of age. It encompasses improving case management skills of health providers (components 1), the health system (component 2) and family and community practices (component 3). By the end of 2005, it was being implemented in 18 districts and 13 districts were implementing all the three components. Despite the challenges in implementing the community aspect of IMCI, a follow up survey of Community IMCI (C-IMCI) conducted in 2004 and compared to the 2000 baseline, revealed that children with fever treated with SP at home increased marginally from 18% to 22%; but knowledge of danger signs for malaria and other childhood diseases improved from 20% to 40% [UNICEF, 2004).

3.7 Malaria Control 2005-2010: Roll Back Malaria (RBM) going to scale

3.7.1 National Malaria Strategy 2005-2010

In October 2004, the NMCP recommended that a new five year national malaria implementation plan for 2005—2010 be prepared that would include a change plan for the national malaria treatment policy, with a clear timeline for effecting a drug policy change. The NMCP was supported by various Technical Working Groups (TWGs) on various aspects of malaria control: case-management, vector control and monitoring and evaluation.

The second National Malaria Strategic Plan (NMSPII) was launched on 22nd November 2005 at the SADC malaria commemoration week. The NMSPII's vision was to "*keep all people in Malawi free from the burden of malaria*" with a mission to "*reduce the malaria burden to a level of no public health significance in Malawi*". The strategic plan focused on scaling up of interventions so as to significantly reduce the malaria morbidity and mortality in the country. Three strategic areas identified for the scale-up included case management, IPTp and use of ITN.

The targets by 2010 included: a) increase access to appropriate treatment by all populations at risk of malaria to at least 80%; b) increase access to appropriate treatment by all pregnant women to at least 80%; c) increase access to malaria prevention for pregnant women, ITNs and two IPTp doses with SP, to at least 80%; and d) increase the proportion of U5's sleeping under ITN's to at least 80% [MoH, 2005]. The introduction of IRS into four districts was also mentioned in the NMSPII but there was no mention of Integrated Vector Management (IVM) or the use of larvicides or specific-urban malaria control. The NMSPII also recognized the need to address human resource shortages in the country, strengthen communications activities through information, education, and communication (IEC) efforts in advocating for malaria control, operational research and strengthen monitoring and evaluation to be able to track progress and measure results [MoH, 2005].

3.7.2 Funding and staff changes 2005-2010

The year 2005 was a landmark year as this was a point that witnessed substantial increases in both PMI and Global Fund support for malaria control activities. In 2005, the Global Fund signed a Round 2 malaria grant with Malawi worth US$ 18 million for a period of two years. The aim of the grant was to increase the availability of ITNs, increase access to IPTp, ensure that people at risk of malaria have access to prompt and effective access to treatment, help

build capacity of the national health system, increase IEC of malaria prevention and control and build the district systems capacity to detect and respond to increase to seasonal malaria transmission [Mtonya & Chizimbi, 2006]. However, it wasn't until 2006 that Malawi received its first disbursement of funding. At the same time, the management of ODA had changed to include a SWAp developed in 2004 by the MoH, other government ministries, NGOs and Civil Society Organizations (CSOs) to guide the implementation of interventions within the health sector. This was done through the formulation of a Joint Program of Work to pool most of the funding from the GoM and other donor organizations like the Global fund and improved donor coordination, enabled integrated monitoring and evaluation and increased accountability and transparency in utilization and distribution of funds. However, by 2007 funding allocation for Malawi still had not began to meet per-capita at risk needs. By 2007, Malawi had received cumulative amount of 51.2 million USD working out to 1.26 per person at risk p.a. [Snow et al., 2010]

The Round 7 malaria grant was signed in 2009 and consolidated with Round 2 to provide US$ 36 million over a period of three years. The focus for this grant was to scale up the universal coverage of malaria control and prevention interventions including case management with artemisinin-based combination therapy (ACTs), the procurement of long-lasting insecticide nets (LLINs) for mass distribution and rapid diagnostic tests (RDTs).

In Malawi, PMI aimed to work to support existing strategies, working with international and national partners to complement their funding and efforts. Funding from the US-PMI began in 2006, with start-up funds of US$ 2 million for malaria activities in Malawi. Between 2007 and 2010, PMI had contributed approximately a total of US$ 80 million. These funds supported four main malaria control and prevention measures: procurement and distribution of LLINs, the support of IRS activities, training health workers in IPTp with SP, health worker training on diagnostic testing and treatment and the procurement and distribution of ACTs.

In 2005, the NMCP consisted of four technical officers: a program manager (Storn Kabuluzu), deputy program manager, ITN specialist and medical entomologist and three zonal malaria coordinators. In addition, there were 28 district malaria coordinators who reported to the District Health Officer. The malaria coordinator was usually, a clinical officer or a clinical nurse in each district in charge of malaria case management and sometimes an employee of the Environmental Health Office in charge of ITN distribution [Rosensweig et al., 2008]. The NMCP was understaffed and under-resourced at the headquarters level and a proposition was passed by the Presidents Malaria Initiative (PMI) to fund deployment of new officers and procure equipment in the year 2006 for the NMCP office [PMI, 2007].

In 2008, a comprehensive review of NMCP was supported by PMI to establish its strengths and weaknesses and lay out a framework of support. This review found that the MCP was understaffed, the existing staff had limited access to management training and lacked a sufficient operational budget. The staffing levels had not changed from the 2005 levels, and the then programme manager held multiple positions within the ministry. The recommendations of the review were to establish three or four of the following positions; Monitoring and Evaluation (M&E) Specialist, Case Management Specialist, IEC Specialist,

Administrative Officer, Data Management Specialist, Pharmacologist, and Global Fund Grant Manager [PMI, 2008]. To-date, only the M&E Specialist has been recruited.

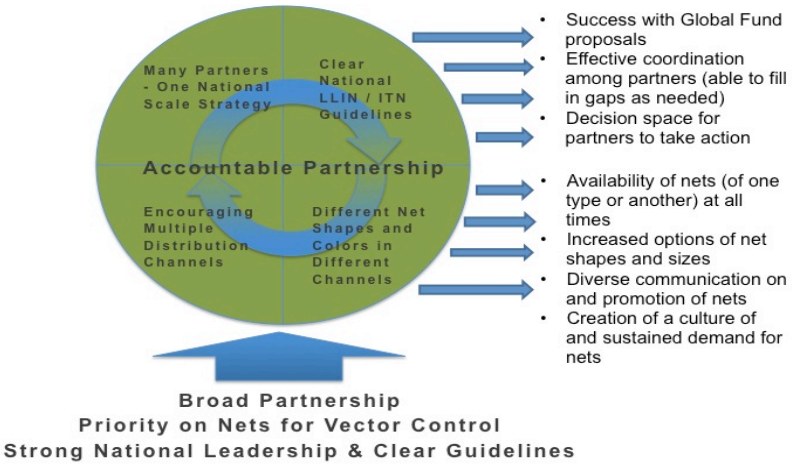
3.7.3 Vector control

3.7.3.1. ITN

In March 2006, at two districts, Mwanza and Phalombe, the integration of free LLIN into routine Expanded Programme of Immunization (EPI) clinic attendance was piloted. Nets were donated by Exxon Mobil, the Canadian, American and Finnish Red Cross Societies, the American International Women's Club of Geneva, and private Swiss donors through the International Federation of the Red Cross and Red Crescent Societies. Nets were distributed to 28 health clinics by PSI and community health workers transported nets to an additional 129 outreach clinics. All children attending routine services who had completed vaccination were given a free LLIN. 15 months after the start of the project in June 2007 a follow-up coverage survey was undertaken to examine changes in household net usage. The percentage of households with at least one ITN did not change and in 60–90% of households without an ITN, respondents said that they did not have enough money to buy one. ITN ownership in households with a pregnant woman or a child aged 12–23 months increased substantially from baseline to follow-up in the intervention districts but not in the control district (Chiradzulu). Among households with a child aged 12–23 months, the proportion that owned at least one ITN increased from 39% to 83% in Mwanza and from 65% to 86% in Phalombe [Mathanga et al., 2009].

Based on this pilot, in 2007, the Malawi ITN policy was changed [MoH, 2011] with a focus on LLINs and a shift to more approaches to scaling coverage including: a) routine distribution through ANC clinics for pregnant women and EPI clinics for children; b) periodic mass campaigns; and c) social marketing in communities and commercial outlets. The strategy still recognized the need for a broad partnership for success (Figure 3.6). Recognizing the constraints to improved coverage posed by an inability to pay, it was stated that pregnant women should receive a free LLIN during their first ANC visit or at childbirth and children would receive a free LLIN at their first EPI visit or during any health facility visit if not given at birth. Free mass distribution campaigns targeting rural areas were originally planned to every two to three years as catch-up campaigns to routine distributions [Skarbinski et al., 2011]. In 2006/7 Malawi negotiated for free nets to the poorest population distributed through mass campaigns.

Figure 3.6: Enabling partner environment for scaled ITN coverage [RBM, Lessons in brief 2011a]



The first mass campaign was launched in 2008, targeting children and pregnant women who had not been reached through routine delivery systems. The target population was resident in hard to reach areas and were identified by community health workers/Health surveillance assistance and village leaders who created a register of potential beneficiaries not able to get nets from clinics. In total, 1.1 million nets were distributed during this campaign [Skarbinski et al., 2011].

Routine EPI facility distributions went to scale from 2008, the same year as the free mass campaign. A household survey was undertaken in eight districts (Lilongwe, Blantyre, Mwanza, Chiradzulu, Phalombe, Rumphi, Nkhotakota, and Karonga) in April 2009. 59% of all households owned an ITN, 57% obtained from a routine clinic visit, 2% from the mass campaigns and 2% purchased from commercial sector. Of households with at least one child below five years of age or a recently pregnant woman, household ownership of ITN was 67%. The poorest households were significantly less likely to own an ITN compared to the least poor households despite free distribution through health facilities [Skarbinski et al., 2011]. Distance to health facilities was greater among households that did not possess ITNs and did not use an ITN the previous evening [Larson et al., 2012]. In multivariable models adjusting for district, socioeconomic status and indoor residual spraying use, ITN use by children under the age of five years was associated with a significant reduction in asexual parasitemia (adjusted odds ratio (aOR) 0.79) and anaemia (aOR 0.79) [Skarbinski et al., 2011].

Accurate sub-district or district level distribution data since 2005 is not available, summaries of national distribution estimates are provided in Table 3.1. The majority of nets were provided through routine ANC and EPI services for each year with the exception of the mass campaign in 2008.

Table 3.1: National ITN Distribution in Malawi, 2005–2009 [NSO; Charles Yuma, PSI, unublished data; MCP, MPR 2010]

Year	ITN Distribution	Mid-year Population	Per capita distribution	%age per capita distribution
2002	372,991	11,174,648	0.033	3.34
2003	1,069 845	11,548,841	0.093	9.26
2004	1,364,773	11,937,934	0.114	11.43
2005	815,620	12,341,170	0.066	6.60
2006	1,508,735	12,757,883	0.118	11.83
2007	673,348	13,187,632	0.051	5.11
2008	2,520,044	13,102,076	0.192	19.23
2009	957,000	13,520,101	0.071	7.08
2010	1,258,001	13,947,592	0.090	9.02
2011	1,337,776	14,388,550	0.093	9.30
2012	6,370,073*	14,844,822	0.429	42.91

* Includes 5.6 million LLIN distributed by NMCP as part of mass campaign

3.7.3.2 Modelling and mapping ITN Coverage 2000-2012

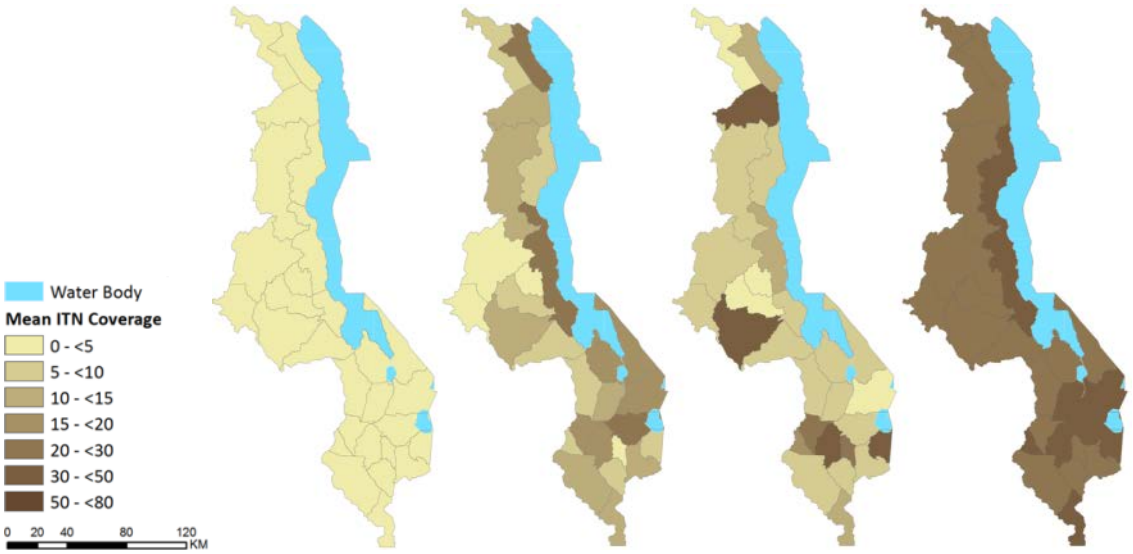
Five national household surveys have been undertaken in Malawi since 2000 and one sub-national survey (Annex A.1). Typically, national household surveys are designed to be precise at national and regional levels and rarely at lower levels such as districts. Therefore, simply aggregating survey data to provide district level estimates of an outcome of interest will lead to values of low precision. District level estimates, however, are more important to planners in order to accelerate policy interventions, optimise inputs and improve coverage of health interventions. Small Area Estimation (SAE) methods handle the problem of making reliable estimates of a variable at these areal units under conditions where the information available for the variable, on its own, is not sufficient to make valid estimates [Rao, 2003; BIAS, 2007].

We have used hierarchical spatial and temporal SAE techniques with a fully Bayesian geo-additive regression approach [Banerjee et al., 2004; Best et al., 2005; Fahrmeir & Lang, 2001; Kamman & Wand, 2003; Wand, 2003] to estimate the ITN coverage in all age groups by district for the years 2000, 2004, 2006, 2010 and 2011. Importantly, we have elected to predict quantities among all age groups as this now represents the important indicator for universal coverage and necessary when computing likely impacts on malaria transmission [Smith et al., 2009; Griffin et al., 2010]. Details of model procedures and accuracy metrics are presented in Annex 3. The data-driven, modelled predictions of the proportions of all age groups sleeping under an ITN for the survey years are shown in Figure 3.7. Sensitivity of district level predictions are shown in Annex Figure A.1.1 as standard deviations of predicted means.

In 2000, no district had more than 2% of its population protected by an ITN. By 2004, 15 districts had achieved ITN coverage amongst its entire population in excess of 10% and four districts exceeded 20% (Nkhotakota, Salima, Karonga and Zomba). Overall coverage remained relatively constant by 2006 while patterns of coverage changed; six districts had

predicted all-age ITN coverage of 20% or greater (Lilongwe, Rumphi, Blantyre, Chiradzulu, Phalombe and Neno). By 2010, there was a perceptible change in the landscape of ITN coverage nationwide, every district had achieved over 20% coverage of its entire population, ten districts had achieved coverage in excess of 30% but none had reached 40% coverage. By 2010, disparities remained in the household ownership of more than one ITN between urban (38%) and rural (25%) communities and the least poor (52%) compared to the most poor (15%) [NMCP, 2010b]. 58% of children aged less than five years and 54% of pregnant women slept under an ever treated net the night before the survey in 2010 [NMCP, 2010b].

Figure 3.7: Mean ITN coverage predictions in Malawi for the years: a) 2000; b) 2004; c) 2006; and d) 2010



The MPR undertaken in 2010 recommended that "*The government should adopt a policy for universal coverage with LLINs for all populations at risk of malaria in the new malaria strategic plan and develop an integrated vector management strategy that includes IRS and larval source control*" [NMCP, 2010a].

3.7.3.3 IRS

The only IRS activities in Malawi before 2007 involved small-scale IRS projects using pyrethroid insecticides in two rural areas of Ntchisi district in 2006. These projects were supported by the African Development Bank as part of a research study on the feasibility of IRS in Malawi. In addition, there were three independent IRS activities: one mounted by CHAM's Nkhoma Mission Hospital and two significant private sector initiatives that have included IRS in their malaria control operations.

Nkhoma Mission: As part of the Mission's outreach to villages, the Nkhoma Mission Hospital partnering with the Presbyterian Church USA (PCUSA), the MoH, UNICEF and World Vision, established an IRS programme with a responsibility of spraying its catchment area which is within Lilongwe District. This programme has been in operation since 2009, and during the 2012/13 spraying season covered approximately 28,000 households with over 108,000 people [Nkhoma Hospital Annual Report, 2012].

Paladin Africa: Paladin Africa, an Australia-based global uranium mining company, operates the Kayelekera uranium mine (Figure 3.8) and has taken malaria control seriously since 1999 for its 1200 workers. Interventions have included education on prompt parasitological diagnosis and treatment and provision of ITNs. In addition, Paladin Africa and International SOS began a programme of vector control covering the site of the mine and six neighbouring villages (Kayelekera, Juma, Wiliro, Thulwe, Amos and Chiteka) using quarterly IRS (pyrethroids), larval control (twice weekly), environmental modifications, insecticide management, and entomological monitoring.

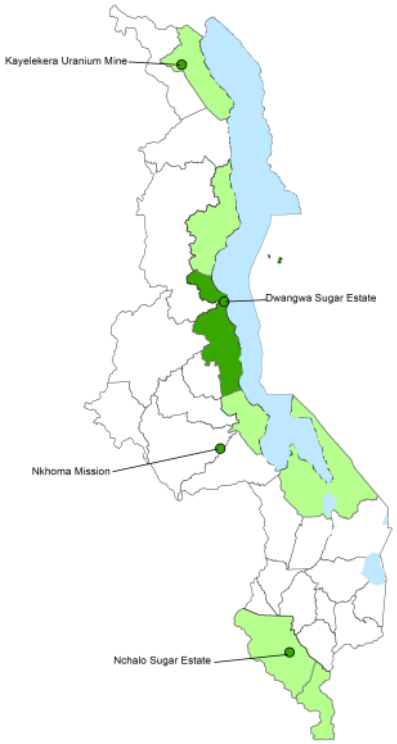
Illovo Malawi: At the Nchalo and Dwangwa Estates, the Illovo sugar company (Figure 3.8) has implemented a number of malaria control measures, including IRS, since the late 1990s. All households in the company's area of operations have been sprayed twice a year using a combination of insecticides (organophosphates and pyrethroids) on a rotating basis. Given the company's experience with IRS, Illovo Malawi played an important role in assisting with the pilot of IRS activities in Nkhotakota District: training for spray operators and instructors and providing insecticide storage facilities, calibrating equipment during spray operations and fuel for transport. In 2007, IRS staff from Illovo Malawi provided technical assistance in developing the national IRS implementation guidelines. Illovo Malawi also maintains environmental management schemes and have built 12 clinics and health centres on the two estates, where LLINs are distributed and treatment with ACTs is provided to those patients with RDT-confirmed malaria. The sugar estates have also served as a malaria research site for the NMCP and the University of Malawi College of Medicine, and data collected from the estates have informed the development of malaria control policies in Malawi.

The MoH launched its first IRS pilot in one district (Nkhotakota) in 2007 (Figure 3.8). The project was supported by Research Triangle International (RTI) with funding from PMI using 10% lambdacyhalothrin slow-release capsule suspension (ICON). The first round of IRS occurred in the northern parts of the district in December 2007 (28,227 structures) and the second round of IRS occurred in October–November of 2008 (42,044 structures) in an expanded area. Between 2007 and 2009, approximately 127,000 houses were protected, covering over 0.5 million residents [PMI, 2011]. In April 2009, six months after the second spray round, the impact on malaria parasitaemia and anaemia prevalence was assessed among 899 children less than five years of age where comparisons were made using binomial regression between children living in a household sprayed with IRS (direct IRS) with those in a household not sprayed with IRS, but in an IRS area (indirect IRS) and those living in a household not sprayed with IRS and not in an IRS area (no IRS). Adjusting for bed net use, house construction, and socioeconomic status, direct IRS and indirect IRS were significantly associated with a 33% and 46% reduction in parasitemia and a 21% and 30% reduction in anaemia prevalence, respectively [Skarbinski et al., 2012].

Encouraged by the pilot project, IRS was expanded to additional districts. Between July 2010 and 2011, IRS was carried out by the NMCP and other developmental partners, notably PMI in seven targeted districts. PMI supported IRS in two districts; Nkhotakota and Salima, while the Malawi MoH fully funded IRS activities in the five other districts namely, Karonga, Nkhata bay, Mangochi, Chikwakwa and Nsanje [NMCP, 2012]. Pyrethroids were used once at the start of the rainy season. In the first spray round, IRS activities began in November

2010 in Nkhotakota and Salima districts. However, these activities were prematurely discontinued after 21 days due to insecticide stock out. In the remaining five districts IRS was started in January 2011 and lasted for 48 days. In Salima and Nkhotakota districts a total population of 364,349 in 97,329 structures were protected by IRS. In the remaining districts supported by the MoH (Karonga, Nkhatabay, Mangochi, Chikwawa, and Nsanje), 85.2% of the 536,620 targeted households were sprayed with a target to protect 1,967,154 residents [NMCP, 2012; PMI, 2012]. Coverage with IRS by 2010 had increased to an estimated 430,000 households covering *circa* 2.7 million people [NMCP, 2010b]. Among 75 households surveyed in Nkhotakota district during the 2010 Malaria Indicator Survey (MIS), 83% had been sprayed in the past 12 months, however across the rest of the country only 6% of households had been sprayed in the preceding 12 months [NMCP, 2010b].

Figure 3.8: Location of IRS sites: Dark green early adopting areas, light green second phase



In late 2011, a second spray round was carried out, covering all the seven districts involved in the first IRS campaign: Nkhotakota district (PMI funded) and Karonga, Nkhatabay, Mangochi, Chikwawa, Salima and Nsanje (MoH funded) between November and December. In Nkhotakota, 87.7% of the 88,490 target structures were sprayed protecting 321,919 residents. In the other six districts, 84.9% of estimated targeted structures were sprayed protecting over 2 million residents. Follow up visits were carried out during the last week of the IRS campaigns to increase coverage, revisiting households which had already been sprayed and spraying additional households which could be reached and hadn't been sprayed [NMCP, 2012; PMI 2012; Chemonics International, 2012]. A summary of IRS coverage by district is shown in Table 3.2.

IRS has faced a number of challenges including technical and logistical issues and the refusal of residents to be included in any IRS activities. During the 2010-2011 IRS campaigns, the country wide fuel shortage affected many activities as mobility was constrained while there

were additional shortages of supplies and breakdown of some equipment [NMCP, 2012; Chemonics International, 2012]. Reports have documented pyrethroid and carbamate resistance in the *An. funestus* malaria vector in Nkhotakota and Salima districts leading to a switch from pyrethroids to an organophosphate (pirimiphos-methyl) and in Likoma Island which might reduce the effectiveness of IRS [Hunt et al., 2010; Skarbinski et al., 2012]. More details are provided in Section 5.5.

Table 3.2: IRS activities carried out on all the districts between 2010 and 2011

	2010 - 2011 Spray Round			Nov - Dec 2011 Spray Round		
District	**Targeted Structures**	**Sprayed Structures**	**Coverage (%)**	**Targeted Structures**	**Sprayed Structures**	**Coverage (%)**
Karonga	72,462	64,491	89.0	75,314	65,561	87.1
Nkhata Bay	45,683	41,297	90.4	54,198	48,724	89.9
Mangochi	241,520	169,064	70.0	245,640	201,425	82.0
Chikwakwa	99,955	86,661	86.7	120,709	101,758	84.3
Nsanje	77,000	68,530	89.7	93,963	77,989	83.0
Nkhotakota*	72,000	52,163	72.4	88,490	77,647	87.7
Salima	62,000	46,166	74.5	88,643	80,488	90.8
Total	**670,620**	**527,372**	**78.6**	**766,957**	**65,3592**	**85.2**

***** Due to pyrethroid resistance PMI supported direct spraying in Nkhotakota with organophospahtes in 2011

3.7.4 IPTp from 2007

In 2010, 83% of mothers had received at least one dose of SP, 60% of pregnant women had received two or more doses of IPTp during an ANC visit in their last pregnancy leading to a live birth within the previous two years [NMCP, 2010b]. In a bid to increase coverage of IPTp, Malawi is promoting capacity building strategies to ensure that services are being provided according to policy guidelines. SP stock-outs are being tracked through health facility monitoring to ensure adequate supply for IPTp. In addition, HSAs visit pregnant women during pregnancy and after delivery; encourage ANC visits and ensure appropriate effective interventions are being provided at all times [Nsona et al., 2012; RBM, 2013].

3.7.5 Monitoring and evaluation (M&E) framework

Since 2002, the MoH has maintained an integrated routine Health Management Information System (HMIS) across the country. However, this routine information system has not been able to provide all the required information necessary to plan malaria control and it was agreed that HMIS data would be complemented by periodic surveys, Integrated Disease and Response (IDSR) in all districts and research [MoH, 2003].

The National Malaria Monitoring and Evaluation (M&E) Plan 2007 – 2011 was launched in 2007 by the NMCP covering a broad range of issues which include: drug quality surveillance, strengthening of sentinel site surveillance for monitoring of impact indicators, vector assessments for IRS and ITN program monitoring, household and facility surveys (including the collection of biomarkers), and post-market surveillance, pharmacovigilance, and drug resistance testing following the introduction of artemether-lumefantrine (AL) [MoH, 2011].

The NMCP has six districts where drug efficacy/ therapeutic efficacy testing is done every two years. These districts include Karonga, Lilongwe, Machinga, Mangochi, Nkhotakota, and Rumphi. Other partners such as the Malaria Alert Centre (MAC)[11] established sentinel sites for entomological indices monitoring in clude Nsanje, Chikwawa, Machinga, Salima, Mchinji, Nkhotakota, Nkhatabay and Karonga [PMI, 2006]. Since 2005, MAC has also conducted repeated surveys at several sites to measure malaria parasitemia and prevalence of anemia in children 6-30 months old in six districts four from Southern Region (Chiradzulu, Mwanza, Phalombe, and Blantyre), and one each from Central Region (Lilongwe) and Northern Region (Rumphi). This was extended to include two additional districts in 2007, 2008 and 2009 Nkhotakhota in the Central Region and Karonga in Northern Region. These surveys were conducted in April of each year at the end of the wet high transmission season [Don Mathanga, Personal Communication]. This project ended in 2009.

In addition, with funding from USG in Year 1 to 3, PMI established a framework for data collection in 10 sites comprising of 8 districts with data currently being collected at four health facilities [PMI, 2010]. PMI initiated sentinel surveillance sites at four hospitals in 2010 to track changes in morbidity indicators including the testing all fever presentation for parasitemia using microscopy (Mwanza district Hospital, Mitundi Hospital, Rumphi District Hospital and Nkhotakota hospital). This project ended in 2013 [PMI, 2011]. A new monitoring and evaluation tool has been initiated and tested by the Malawi-Liverpool-Wellcome Trust Clinical Research Programme in Malawi as part of a randomized control trial to monitor the malaria burden in Chikhwawa district in southern Malawi were a continuous ("rolling") MIS (rMIS) has been conducted since May 2010 covering 50 villages, with every village sampled at least once in a 6 month periods. Data on both malaria impact (prevalence of anemia and parasitemia) and coverage indicators (ITN and IRS coverage and access to treatment) are collected in children 6 to 59 months [Roca-Feltrer et al., 2012]. The International Centres of Excellence for Malaria Research (ICEMR) has also established sites where malaria morbidity and entomology data is collected. These sites are in Blantyre city, Chikwawa and Thyolo district with surveys conducted biannually in the dry and rainy seasons [Terrie Taylor, Personal Communication].

3.7.6 Malaria case management challenges during the AL era

3.7.6.1 The second antimalarial treatment policy change

In October 2004, the National Malaria Advisory Committee recommended that a new five-year national malaria implementation plan for 2005—2010 be prepared that would specifically include a plan to change the national malaria treatment policy, with a clear timeline for effecting a drug policy change. The change plan recognized the need to base policy change on evidence for efficacy, safety, affordability, convenience and availability of the chosen alternatives. Clear objectives were defined for the plan, and tasks and targets were assigned to various stakeholders under the leadership of the NMCP secretariat. This process began in January 2005, which included drug efficacy studies of candidate

[11] The Malaria Alert Centre (MAC) was also established in 2002 by the College of Medicine with funding from the Gates Malaria Partnership. Since its inception, the centre has supported the NMCP through operational research and monitoring evaluation of the program.

combination treatments in order to obtain locally acquired evidence under the stewardship of the M&E/research TWG.

Drug efficacy studies were carried out at three (Rumphi, Nkhotakota and Machinga) of the six established sentinel sites for monitoring antimalarial drug between March to August 2005 and tested four drug combinations, one being a non-artemisinin combination (AQ+ SP), AQ+Artesunate (AS), chlorproguanil—dapsone (CPG-DDS)+AS[12] and AL for efficacy against SP. In summary, the efficacy of all four combination drugs was equivalent both at 14 days and at 28 days, by either per-protocol, intention-to-treat, or survival analysis (ACPRS >93%). SP had a much lower ACPR (32%) by day 28.

Difficulties were faced in relation to concerns over the costs of replacement options and guarantees of regular supply, adherence to six-dose regimens and competing interpretations of efficacy, notably the claim that after seven years of sustained use 20% failure rates and the presence of resistance mutations were acceptable to some [Plowe et al., 2004] and not others [White, 2004; Ringwald, 2004]. In addition, policy options were confused by how to interpret observations of the decline in the prevalence of the *pfct* point mutation, responsible for CQ resistance, in Blantyre [Kublin et al., 2003] and Salima district [Mita et al., 2003] and reported improved clinical efficacy in Blantyre [Laufer et al., 2006]. This led to conflicting suggestions and significant international concerns that CQ might still have a therapeutic role to play [Vogel, 2006; Muula, 2007; Ursing et al., 2007].

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The NMCP finally submitted its recommendations to the policy formulating body in the MoH in early 2006. The ministry sought further consultation with regional technical partners, notably WHO and donors and reviewed more efficacy evidence from Zambia and Zanzibar before releasing a final decision in May 2006 stating that AL was to replace SP as first-line treatment, AQ+AS to be used for second-line treatment, quinine was to be reserved for the treatment of severe malaria and in special cases of uncomplicated malaria during the first trimester of pregnancy and SP was retained for IPTp [Malenga et al., 2009]. Under the revised treatment policy, all febrile children under the age of five years would be presumptively treated with ACTs, however patients above five years would be required to undergo a diagnostic test before treatment [NMCP, 2007]. The process of changing policy was not as easy as it was for the change from CQ to SP. While Malawi was one of the first countries in Africa to abandon CQ it was one of the last to abandon SP.

3.7.6.2 Implementation of AL policy and coverage

AL supply was plagued by several supply chain issues. Even before the shift to AL, in 2004, there were reports of drug shortages of malaria treatments in the Central Medical Services (CMS) which led to rationing of drugs to ensure each facility received some stock. In addition, CHAM facilities who had previously signed a MoU with the MoH under the EHP were forced to purchase drugs from the private sector. This prompted the GoM to contract a Chicago-based firm, Glocoms, to manage CMS in addressing management and inventory

[12] An earlier open-label trial, unpublished at the time of the drug policy review was undertaken at the Queen Elizabeth Central Hospital, Blantyre between June 2002 and October 2004 as part of a multicentre trial with The Gambia comparing CPG-DDS and CPG-DDS+AS [Wooton et al., 2008]. Efficacy was evaluated in the Day 3 per-protocol (PP) population using mean time to reduce baseline parasitemia by 90% (PC90). CPG–DDS plus artesunate demonstrated advantages over CPG–DDS alone for Day 3 PC90

issues and prepare the CMS to become a semi-autonomous entity where drugs would be purchased by districts using a Drug Revolving Fund (DRF) managed by district health assemblies [Masuku, 2006]. In November 2006, an AL quantification exercise was undertaken by the US-funded agency Management Sciences for Health (MSH) [Rutta et al., 2006]. This consultation estimated that between US$ 9-10 million was required per annum to fund the AL requirements nationwide and additional funds required to strengthen pharmaceutical management. PMI agreed to fund the first 12-months of AL procurement while the NMCP prepared to work on Round 7 Global Fund proposals. Importantly, unlike what was routine in the DRF system, where money is re-collected from the sale of drugs and used to replenish stock, AL was to be provided free-of-charge to patients and therefore a different drug class/system within the DRF. In January 2007, a Drug Change Plan Task Force was established by the MoH. Three sub-groups were established to deal with; 1) IEC/BCC strategies for implementing the change; 2) case management policy and guideline changes; training materials and plans; and 3) the pharmaceutical management and logistics.

Following the launch of the new treatment malaria policy supporting ACT's as the first-line anti-malarial for uncomplicated malaria, all health workers had to undergo training on the use of this new drug with additional refresher courses for malaria diagnosis and malaria in pregnancy. In a review conducted between August and September 2008 in 50 governmental and CHAM facilities, 76% of health workers were found to have been trained in case management with ACTs [MSH, 2008]. The training costs were met through funds from -PMI and the Global Fund [PMI, 2008]. Job aids and instructions on the dispensing register and stock taking of the new drug were provided to health facilities alongside IEC materials which included posters and leaflets which would assist in increasing awareness of the new policy, both to untrained health workers and patients. However, these materials only reached 20% of the facilities [MSH, 2008]. Posters, leaflets and pamphlets, social activities like skits and plays, community involvement through focus groups and women groups were initiated as part of broader community awareness strategies with funds from -PMI partnering with PSI [PMI, 2008]. Small grants were also awarded to community based organizations to mobilize communities in using available malaria interventions. It was not until January 2008 that the new ACT policy was effectively implemented.

During a survey of 92 doctors and pharmacists across the country, undertaken between April and September 2010, only 74% had ever received information on ACTs and only 32% had received training on management of malaria using ACT. 72% respondents reported that they had heard that ACTs might cause side effects but only 25% had received training on how to report adverse events [Kalilani-Phiri et al., 2011]. Among staff at 15 pharmacies in Blantyre district, only 27% knew the correct dose regimen of AL and none of them knew the condition of taking AL with a fatty meal for improved absorption [Minyaliwa et al., 2012]. Additionally, PMI also funded studies in the outpatient and inpatient settings in 2011 and 2012 respectively to look at case management practices.

3.7.6.3 Improving access, treatment and adherence to AL

During the national demographic and health survey in 2004, only 13% of childhood fevers were treated in a public health facility compared to 20% of fevers treated with drugs purchased from the retail or private sectors [NSO & ORC Macro, 2005].

In 2008, the IMCI unit rolled out the integrated community case management (iCCM) to 4000 hard to reach villages protecting an estimated 10% of the population with funding from WHO, UNICEF, CIDA, USAID and the Bill and Melinda Gates Foundation [Nsona et al., 2012; RBM, 2013]. The iCCM would utilize the services of HSAs, that have a target population of *circa* 1000 to improve accessibility of health care services especially in rural areas [Nsona et al., 2012; Makaula et al., 2012]. By 2009, 432 HSA's had been trained in iCCM [PMI, 2009]. By September of 2011, 3,296 HSAs had received training in IMCI, and 2,709 VHCs were functional [Nsona et al., 2012]. By 2010, more than 3,000 HSA's had been trained on iCCM, including malaria case management, and deployed across the country, with over 500 of them being trained on drug logistics and tracking to be able to use the health management information system [PMI, 2010]. 12,000 HSAs had been trained on IMCI in Malawi by 2011 [UNICEF, 2013].

Despite these initiatives to improve treatment access, the 2010 national Malaria Indicator Survey, revealed that among 849 childhood fevers in the last 14 days, only 31% took at antimalarial and 27% within 48 hours [NMCP, 2010b]. Significantly more urban children were promptly treated with an antimalarial (40%) than rural children (26%) and overall only 20% of febrile children took AL within 48 hours [NMCP, 2010b]. These disappointing results have been investigated further in more detailed behavioural and descriptive studies.

In 2008, a social science investigation was undertaken in Mwanza district to understand the perceptions and barriers to treatment of fever among 151 caregivers and 46 health workers [Chibwana et al., 2009]. The majority of caregivers were able to recognize fever and link it to malaria. Despite high knowledge of malaria, prompt treatment and health-seeking behaviour were poor, with the majority of children first being managed at home with treatment regimens other than effective antimalarials. Traditional beliefs about causes of fever, unavailability of anti-malarial drugs within the community, barriers to accessing the formal health care system, and trust in traditional medicine were all associated with delays in seeking appropriate treatment for fever. In all focus group discussions, lack of access to anti-malarial drugs was mentioned as one of the problems that prevented caregivers from giving drugs promptly. Financial constraints to buying anti-malarial drugs, inadequate knowledge on the correct dosage, fear of giving expired drugs from shops and distance to health facilities were some of the main reasons given for failing to provide an effective anti-malarial treatment within the home [Chibwana et al., 2009].

In Chikhwawa district, two cross-sectional, household surveys in 13 villages conducted in June 2009 and February 2010 showed that distance was a significant factor in accessing malaria treatment, with those living in hard-to-reach villages being less likely to attend a formal health facility compared to those living near the hospital. When the use of CHWs was analyzed, consulting a CHW reduced subsequent attendance at health facilities. In addition, household costs for attending a facility were greater for those in poorer, hard to reach villages (US$ 5.24 per episode) compared to those living in wealthier households closer to the district hospital (US$ 3.45) [Ewing et al., 2011]. Similar results were obtained from independent cross-sectional fever surveys in Chikhwawa district in the Southern Region using hierarchical modelling techniques that identified distance and costs as the main barriers to effective malaria treatment [Masangwi et al., 2010].

Among patients who attended public health facilities and received AL, there remained issues related to adherence. At three clinics in Phalombe district in October 2009, both pill counts and in-home interviews on medication consumption 72 hours after 386 adult and child patients received AL were measured and logistic regression used to identify factors associated with complete adherence. Only 65% were completely adherent and patients were significantly more likely to be completely adherent if they received their first dose of AL as directly observed therapy at the clinic, received instructions using the medication package as a visual aid and preferred AL over other antimalarials [Mace et al., 2011].

3.7.6.4 Improving diagnosis

During the period 2005–2010, Malawi's national policy recommended presumptive treatment for malaria in children below the age of five years but encouraged diagnostic testing for person's greater than five years before malaria treatment. However, only 25% of health facilities had the capacity to conduct diagnostic testing by 2010 as compared to the 60% target set for the same time period in the NMSPII [RBM, 2013].

In March 2009, a laboratory assessment in nine hospitals and five health centres in Southern and Central Malawi was conducted by a team from the Improving Malaria Diagnostics (IMaD) project using funding from PMI. Though the laboratory technicians in these facilities were highly accurate in reading blood films, they were overwhelmed by heavy workloads due to high incidences of fever [IMaD, 2009). IMaD then proposed to support the development of a national policy on malaria diagnosis in conjunction with the MCP and key development partners. These guidelines would identify, train and retain laboratory technicians; develop a program of in-service training for existing laboratory staff (first at hospital level); work with NMCP and partners to identify essential laboratory supplies and clinical equipment at health centre and hospital levels; determine which facilities should prioritize microscopy and which RDTs; and establish a QA/QC system to improve the quality of malaria microscopy in general. In September 2010, the MoH with support from IMaD launched a quality assurance program for both clinical and diagnostic testing for malaria case management involving the introduction of the Outreach Training and Supportive Supervision program (OTSS) in 16 districts covering 60 health facilities. District level laboratory and clinical supervisors would be engaged in quality assurance activities improving diagnostic levels for malaria in Malawi. Approximately 200 people were trained in the same year. In addition, the National Public Health Laboratory (NPHL) in Malawi was supposed to conduct refresher training and assess competency for all laboratory supervisors for malaria microscopy [IMaD, 2009].

In 2011, the introduction of RDTs for malaria diagnosis warranted additional training sessions for all health workers. Between 2012 and 2013 the US-PMI provided materials and trained more than 1000 health workers on malaria diagnosis with RDTs nationwide [PMI, 2013].

3.8 Consolidation of progress and the future: the third NMSP 2011-2015

3.8.1 NMSP III 2011-2015

Before the development of the NMSP III (2011 - 2015) a MPR was undertaken to assess the current strategies and activities with a view of strengthening the malaria control program performance and redefining the strategic direction and focus. Among the MPR recommendations were the following: a) adoption of a policy for universal coverage with LLINs for all populations at risk of malaria accompanied by an integrated vector management strategy including IRS and larval source control; b) update to the treatment policy to include parasitological confirmation for all suspected malaria cases; c) strengthening the quality assurance and quality control system for laboratory diagnosis and rapidly expand the use of RDT as primary tool for malaria diagnosis at all levels; d) intensify BCC messages; e) Strengthen the capacity of the district malaria coordinators; f) review the logistics system for distribution of malaria commodities to eliminate stock-outs of malaria commodities; and g) strengthen data collection, analysis and reporting at all levels [NMCP, 2010a].

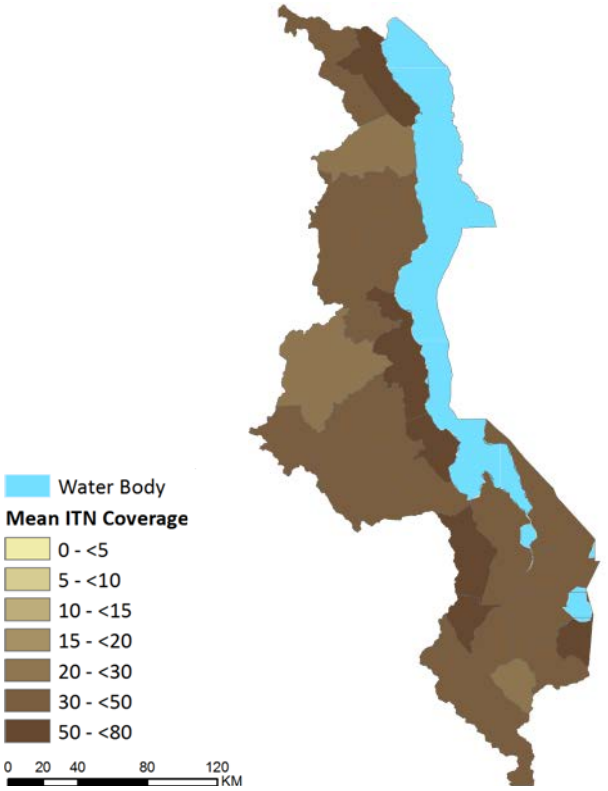
The NMSPIII recognized the recommendations of the MPR and was launched in 2011 under the banner of "*Toward Universal Access*". The NMSIII has an optimistic vision to make sure that "*all people in Malawi are free from the burden of malaria*", with a supporting mission to "*reduce the malaria burden to a level of no public health significance*". It was estimated that the NMSPIII would require approximately US$ 331 million to achieve its ambitions by 2015. The primary goal of this new plan is to reducing by half the 2010 levels of malaria morbidity and mortality in Malawi by the year 2015; where every citizen of Malawi will be reached with all malaria interventions including care and effective cure. The four strategic objectives and their 2015 targets were specified as follows: 1) achieve universal coverage of all interventions in order to have 80% utilization rate of the interventions; 2) strengthen advocacy, communication and social mobilization capacities for malaria control; 3) strengthen surveillance, monitoring and evaluation systems including operational research for tracking progress in the implementation of malaria control activities; and 4) strengthen capacity in programme management in order to achieve malaria programme objectives at all levels of health service delivery. Notable under Strategic objective 3 is the "*Promoting use of information for planning and decision making*", in part one the main objectives of the present epidemiological profile review.

3.8.2 ITN - aiming for universal coverage

Perhaps one of the most significant achievements of the NMSPIII to-date has been the mass free distribution of ITNs in 2012. The NMCP and its partners conducted the Universal Access Campaign with financial and technical support from various stakeholders including the MoH, The Global Fund, PMI, Against Malaria Foundation, Millennium Villages Project, WHO, Southern Africa Regional RBM Network and the Alliance for Malaria Prevention. The campaign was conducted between May and June 2012, during which 5.6 million nets were distributed. The aim of this campaign was to attain universal access to LLINs national wide, which was defined as one net per 1.8 persons, first piloted between December 2010 and June 2011 in the districts of Nkhotakota, Salima, Mwanza, Neno, Likoma and Phalombe

where experiences were used to inform nation-wide implementation. The spatial and temporal SAE techniques describe above (Section 3.7.3.2; Annex A.1) based on the household data from the 2012 MIS were used to estimate the ITN coverage in all age groups by district in Malawi in 2012 (Figure 3.9). The estimates show that few districts had greater than 50% of their inhabitants protected after the mass campaign, however this does not take into consideration the fact that the 2012 MIS overlapped with the 2012 mass campaign which is one reason that may explain the low coverage estimates.

Figure 3.9: Mean ITN coverage predictions for Malawi for the year 2012



3.8.3 IRS & IVM

In 2011, given the high insecticide resistance to pyrethroids, PMI was forced to change from using a pyrethroid to an organophosphate. Furthermore, PMI scaled back its direct support for IRS spraying to one district (Nkhotakota District) in 2011 12 because of costs associated with organophosphate use. For the 2012 and 2013 spray seasons, PMI did not provide direct support for spray activities, but continued to fund substantial technical assistance to the GOM IRS program.The IRS program directly run by the MoH faced technical problems that resulted in missed targets during the 2010 spray campaign. Funding problems resulted in the program being suspended in 2011 and 2012, although there are plans to spray only three districts in 2013.

Malawi does not have an IVM strategy that includes other vector control interventions such as larviciding and environmental control that could be appropriate for urban areas. Plans are underway to put together an IVM strategy which will support the use of evidence based methods to counter the growing threat of insecticide resistance. As part of this strategy, the NMCP will engage research organizations and other implementing partners to undertake

some of the following activities to understand: a) the impact of pyrethroid resistance; b) resistance management strategies (rotational or mosaic approaches); c) alternative vector control innovations; d) pilot use of dichloro-diphenyl-trichlorethane (DDT) and other long-lasting insecticide formulations for IRS; e) the diversity of vectors; and f) the role of other vector management strategies such as larviciding (also called larval source management) and environmental management. Recently, a Cuban delegation visited Malawi at the invitation of the former President of Malawi to explore how larviciding could be used in the country for malaria control.

3.8.4 Diagnosis and treatment

Currently, the national malaria treatment policy stipulates the use of AL as the first line treatment for malaria illness. Under this new treatment policy, all patients regardless of age are supposed to receive treatment based on laboratory diagnosis. The new malaria RDT policy outlines the framework and strategies for scaling up diagnostic testing using RDTs in Malawi [MoH, 2011]. In line with the national malaria strategic plan 2011-2015, malaria RDTs will be scaled up over a five year period, in two phases: in 2011-2012, malaria RDTs were deployed in all public health facilities, with and without microscopy. From 2013, malaria RDTs are to be implemented at community level, especially in hard to reach villages which are run by community health workers. *SD Bioline Ag Pf* and *Paracheck Ag Pf* are the recommended RDTs and have been selected based on the findings of a RDT study carried out in 2009 by the MoH in collaboration with College of Medicine, University of Malawi [Chinkhumba et al., 2010].

Prompt access to treatment in Malawi remains a challenge because of the poor health system, inaccessibility of the health services, inadequate drug stocks and lack of money to pay for services. To address this, the Malawi government has introduced village clinics in hard to reach communities to ensure access to effective treatment.

3.8.5 Cross-border collaboration

RBM's Southern African Regional Network, facilitated a ministerial agreement around a cross-border initiative involving neighboring provinces in Malawi, Mozambique and Zambia [RBM, 2012]. This was initially referred to as the Trans-Luangwa Initiative (TLMI) but renamed MAZAMO-mi. It included five districts in Malawi (Mchinji, Lilongwe, Dedza, Mwanza and Mzimba), five districts in Mozambique (Chifunde, Macanga, Angonia, Maravia and Moatize) and three districts in Zambia (Chipata, Chadiza and Katete). MAZAMO-mi is an agricultural and tourist region and a trade route between Malawi, Mozambique and Zambia of economic importance for all three countries. The agreed Vision was to create "*Malaria/parasite free MAZAMO-mi communities with social and economic prosperity- by 2025*" with a specific goal to achieve "*Near zero transmission in MAZAMO-mi by 2020*" [RBM, 2012]. Although no further discussion has taken place since the first meeting, the NMCP intends to highlight cross border issues in the coming year through a) encouraging operational research to understand the migration trends of people across the three countries in order to come up with proper cross border initiatives; and b) establish a real time surveillance system across this border where data is shared and appropriate actions taken.

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Chapter 4

Mapping malaria transmission intensity

4.1 Context

The clinical epidemiology [Snow & Marsh, 2002], the impact of vector control [Killeen et al., 2007; Smith et al., 2009; Griffin et al., 2010], cost-effectiveness of treatment and prevention interventions [Okell et al., 2012] and timelines to malaria elimination [Cohen et al., 2010] are all dependent on pre-control, parasite transmission intensity. There was a recognition over 50 years ago, across Africa, that one important source of planning data was infection prevalence among children aged 2-10 years (*Pf*PR_{2-10}), used to define categories of endemic risk designed to guide and monitor progress toward malaria elimination targets [Metselaar & van Thiel, 1959; Macdonald & Göeckel, 1964; Lysenko & Semashko, 1968]. Many African countries began to develop epidemiological profiles and risk maps in preparation for elimination during the 1950s, but the art and demand for risk maps died with the end of the GMEP in Africa.

4.2 Previous map use in Malawi

There is no evidence of any national malaria risk maps for Malawi before independence, however, narrative descriptions were provided by the colonial medical authorities of ubiquitous risks across the territory. In 1936, it was stated "*malaria is hyperendemic over the whole territory but varies from season to season*" [Nyasaland Protectorate, 1936].

In 1938, a more climate and vector based approach was used to define the epidemiology of transmission in the protectorate "*Nyasaland has only one rainy season, which starts in December and continues until March the following year. During this period rains are heavy and streams run full and are therefore not dangerous, but mosquito breeding is favoured by the creation of pools in low-lying areas, swamps, seepages and artificially made holes. With the close of the rains, stream beds steadily become the most prolific breeding places, for pools are formed in the beds as the flow of water grows less. Nyasaland has a cool season which corresponds to the summer months in the northern hemisphere, but it is doubtful whether; except in the highland areas of the country, the cold is severe enough to interfere either with anopheles breeding or the activities of the species that transmit malaria*" [Nyasaland Protectorate, 1938].

In 1942, malaria was defined as per the 1938 description but with an additional commentary "*No part of the country is free from malaria. In the low lying areas infection apparently occurs throughout the year and the population develops in time, considerable immunity. In the foothills and highland areas, the incidence is highest after the rains*" [Nyasaland Protectorate, 1942].

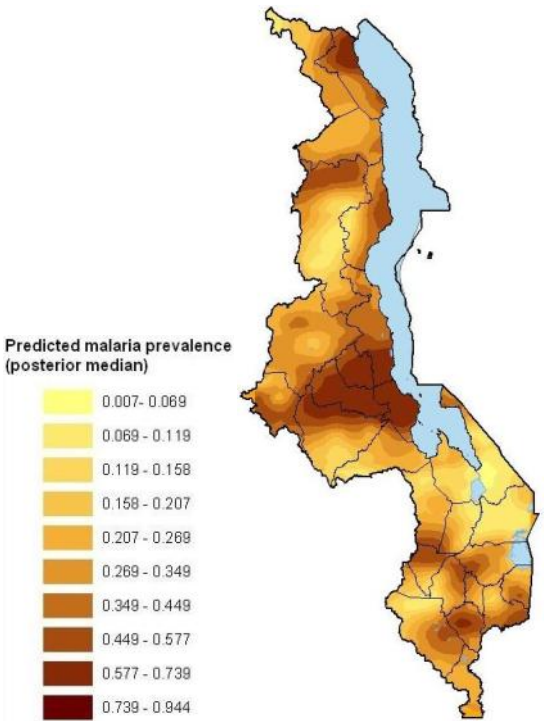
A WHO mission visited Malawi between October and December 1973 to assess the malaria situation and undertake epidemiological investigations across the country, focussing primarily on agricultural and rural development areas [Cheyabejara et al., 1974]. Several parasitologcial, entomological and clinic record reviews were undertaken to provide recommendations to the Ministry of Health on optimal stratified interventions. The team concluded "*malaria is endemic throughout the country with the probable exception of a few isolated areas in the higher-mountain regions. The endemicity varies from meso- to hyper-*

endemic and transmission is perennial in areas where suitable breeding places persist in the dry season" [Cheyabejara et al., 1974]

At the launch of RBM, as part of developing the first national malaria strategic plan no map was provided [NMCP, 2001]. Detail was provided on the organization and structure of the health system, the extent of the malaria burden on the health system and only one reference to the epidemiology of transmission "*In 1973, the World Health Organisation (WHO) mission determined malaria to be meso- to hyper endemic in Malawi, except in isolated higher altitudes mountainous regions*" [NMCP, 2001; referring to Cheyabejara et al., 1974]. No references to the epidemiological patterns of transmission, dominant vector species or disease burden were made in the second national malaria strategic plan 2005-2010 [NMCP, 2005].

It was not until 2006 that empirical data on malaria infection prevalence was used with model based geo-statistical methods to provide predictive quantities of risk across Malawi [Kazembe et al, 2006]. This work used data on malaria prevalence from 73 survey locations where children aged 1-10 years that had been sampled between 1970 and 2001. Mean annual maximum temperature, rainfall, potential evapotranspiration and elevation were all used as covariates to help predict infection prevalence at un-sampled locations using information and correlates with sampled locations. Bayesian statistical inference was used to provide predicted estimations using prior distributions around each of the parameters. The final product is shown in Figure 4.1. This was a revolutionary step forward in describing the diversity of malaria transmission in Malawi, but was not used in any NMCP product until the MPR in 2010 [NMCP, 2010].

Figure 4.1: Posterior predicted malaria prevalence among children aged 1-10 years based on a MBG approach to interpolating risk from 73 empirical survey data points [Kazembe et al., 2006].



In the MPR, the Kazembe map was presented and comment made that "*Malaria is hyper-endemic and transmission occurs throughout the year in most places in Malawi, except in the mountainous areas in the north and south. Transmission is greatest during rainy season from November to April and along the low-lying areas. However the whole population of Malawi is at risk of malaria*". Then in relation to the work by Kazembe and colleagues "*indicates that higher risk areas are in the central and northern region districts as well as along the lakeshore districts on the east central side of Malawi..... Other notable areas with relatively higher risk are in the south-western region (parts of Ntcheu, Zomba, Mwanza and Balaka districts). Low rates of between 0.7–16 percent are around the southern region over the highland ranges of Zomba, Blantyre, and Mwanza and parts of Chikwawa. Other areas with low rates are on the north-western regions, such as districts of Mzimba, Rumphi and Chitipa which are predominantly at high altitude (l,260–2,400 m above seas level)*" [NMCP, 2010].

The Kazmebe map shown in Figure 4.1 was also presented in the NMSPIII (2011-2015) against a more detailed description of the malaria epidemiology than had been presented in either of its two predecessors, including for the first time a confirmation of dominant vectors and variation in risk across the country [NMCP, 2011a]. The NMSPIII states that "*Malaria is hyper-endemic in Malawi, and transmission occurs throughout the year in most places, except in the mountainous areas in the North and South. Transmission is greatest during the rainy season and in the low-lying areas. Due to great variations in rainfall and population movement, a substantial portion of the population is at risk of malaria epidemic and pregnant women and children aged 3 months to 5 years are at the greatest risk due to compromised immunity. Ninety-eight percent of malaria infections are caused by Plasmodium falciparum, with Anopheles funestus, A. gambiae, and A. arabiensis, the primary mosquito vectors in Malawi. Malaria transmission occurs throughout the year in most places in the country; however, there is variation in intensity of transmission from low, medium and high based on season and topography. Transmission is highest during the rainy season and along the low-lying areas. Transmission is higher in areas with high temperatures and during Malawi's rainy season(October through April), particularly along the lakeshore and lowland areas of the lower Shire Valley*" [NMCP, 2011a].

Throughout the history of malaria descriptions in Malawi, its seasonal nature has often been commented on but rarely presented in a mapped form. During the early 2000s the Mapping Malaria Risk in Africa (MARA/ARMA) collaboration developed several maps of seasonal profiles of malaria in Malawi, however, these have never been used by the NMCP in describing risk across the country. We revisit these and more updated maps of malaria seasonality in Section 4.9.

Other mapped products available to the NMCP between 2000 and 2012, but not used, included a climate suitability map developed by the MARA collaboration, based on the likelihood of stable transmission using a rules-based approach [Craig et al., 1999][13] and a MBG model of risk using 396 data points and a Markov Chain Monte Carlo (MCMC) Bayesian

[13] The models were based on fuzzy logic and use long-term rainfall and temperature data [Hutchinson et al., 1995] to model the effects on transmission from dominant vectors to human hosts of climatic conditions. The fuzzy logic model of suitability used monthly temperature ranges and consecutive months of rainfall to assign fuzzy values between 0 (unsuitable) and 1 (suitable).

model to produce an interpolated map of childhood malaria prevalence for the year 2010[14] as part of the Malaria Atlas Project (MAP) [http://map.ox.ac.uk]. Neither product was resolved to district-level decision making units and lacked a national ownership that limited their application with national strategic planning processes.

By 2010, there was a growing sense that information on the epidemiology of transmission might be an important prelude to the design of control in Malawi. The MPR made three specific recommendations: a) malaria prevalence survey sampling should be adjusted to show prevalence levels at district level; b) there is a need for detailed analysis and triangulation of the various data sources to determine the current epidemiological situation and update the malaria epidemiology map; and c) decisions on scaling-up malaria control should be based on the analysis arising out of data triangulation [NMCP, 2010].

Between 2011 and 2012, two rapid approaches to using empirical parasite prevalence data from 2009-2010 [RBM, 2013] and subsequently from 2000-2010 [Bennett et al., 2013] have produced updated MBG mapped products of infection prevalence in Malawi. These have been important extensions of initial work by Kazembe and colleagues, the work included national partners and information has been resolved to district-levels. However, these initial models have not used all available parasite prevalence information, including the national Malaria Indicator Survey of 2012, and remain anchored in either simple interpolation methods [RBM, 2013] or more complex MCMC methods [Bennett et al., 2013]. Here we present a more detailed assembly of data, use simpler adaptations of MBG to make predictions in time and space, and taking the MPR recommendations forward [NMCP, 2010], resolve all information to district-level decision making units to triangulate information between different sources in examining the current malaria status.

4.3 Malaria parasite prevalence data assembly, modelling and risk mapping

The following sections provide a detailed description of how empirical parasite prevalence data were assembled, geo-positioned and pre-processed. This description should serve as a meta-data for the final database of contemporary parasite prevalence data in Malawi; and therefore a reference source to the final curated database. We describe how these data were modeled to provide district level estimates of malaria risk. These data are then used to provide population-adjusted estimates of risk by district. We also describe, where possible, the distribution of parasite species in Malawi (Section 4.8). Finally, given the importance of seasonality in historical descriptions of the malaria epidemiology, we revisit maps of these features for planning specialized control in these target areas (Section 4.9).

4.3.1 Parasite prevalence data search strategy

Electronic data searches: Online electronic databases were used as one means for identifying peer-reviewed, published data on malaria infection prevalence. Due to its wide coverage of the biomedical literature, PubMed [http://www.ncbi.nlm.nih.gov/sites/entrez] was used as the basis for all the initial online searches of published sources. In addition, we

[14] Predicted malaria prevalence 2010 was based on assembled data from 396 clusters 1985 to 2010 using MCMC Bayesian methods with the inclusion of 14 covariates [Gething et al., 2011a], the large set of covariates will have over-fitted predictions [Murtaugh, 2009].

used the Armed Forces Pest Management Board – Literature Retrieval System [http://www.afpmb.org/publications.htm]; The World Health Organization Library Database [http://www.who.int/library]; the Institute de Recherché pour le Development on-line digital library service [http://www.ird.fr]; and African Journals Online (AJOL) [http://www.ajol.info]. In all digital electronic database searches for published work the free text keywords "*malaria*" and "*Malawi*" were used. We avoided using specialised Medical Subject Headings (MeSH) terms in digital archive searches to ensure as wide as possible search inclusion. The last complete digital library search was undertaken in September 2013.

Titles and abstracts from digital searches were used to identify possible parasite cross-sectional survey data undertaken since January 1980 in a variety of forms: either as community surveys, school surveys, other parasite screening methods or intervention trials. We also investigated studies of the prevalence of conditions associated with malaria when presented as part of investigations of anaemia, haemoglobinopathies, blood transfusion or nutritional status to identify coincidental reporting of malaria prevalence. In addition, it was common practice during early antimalarial drug sensitivity protocols to screen community members or school attendees to recruit infected individuals into post-treatment follow-up surveys, often data from the survey sites present the numbers screened and positive. Surveys of febrile populations or those attending clinics were excluded.

Publications with titles or abstracts suggestive of possible parasite data were either downloaded from journal archives where these have been made Open Access (OA) or sourced from HINARI [http://www.who.int/hinari]. If publications were not available OA from HINARI we visited UK library archives at the London School of Hygiene and Tropical Medicine, the Liverpool School of Tropical Medicine and the Bodleian library at the University of Oxford. References not found following these searches were requested using world catalogue searches through the Oxford libraries at a per-page cost. All publications from which data were extracted were cross-referenced using the bibliographies for additional sources that may have been missed or that may correspond to unpublished or 'grey' literature (i.e. not controlled by commercial publishers). In addition, tropical medicine and malaria meeting abstract books were identified from as many sources as possible produced as part of national and international conferences and congresses. These were used to signal possible data that were followed up through correspondence with abstract authors.

Unpublished archived survey reports: We undertook manual searches of archives at the WHO libraries in Geneva and Brazzaville at separate archive locations as Project, Country and Parasitology Department files. As part of the RBM monitoring and evaluation initiative national, household surveys were resurrected as a means to monitor country-level progress [RBM-MERG; Corsi et al., 2012]. These surveys were initially embedded in the DHS as a malaria module and were largely focussed on intervention coverage measures until 2005 when it was agreed to include malaria infection prevalence into survey protocols or as standalone surveys when undertaken as MIS's. In Malawi, national MIS surveys have been undertaken in March 2010 [NMCP, 2011b] and March-April 2012 [NMCP & ICF, 2012]. In addition, national household sample micronutrient surveys included investigations of

malaria infection in September 2001 [MoH/UNICEF/CDC, 2001] and July-August 2009 (UNICEF/Irish Aid/CDC, 2009].

We contacted malaria scientists based in Malawi, many of whom generously provided unpublished, raw data from study sites, districts and regions for investigations of malaria they were involved with (all acknowledged at the beginning of this report). Most notable were survey data from the Malaria Alert Centre's sentinel districts (Lilongwe, Nkhotakota, Karonga, Rumphi, Blantyre, Phalombe and Chiradzulu) [Mathanga et al., 2010], repeat surveys of malaria in Chikwawa district since 2010 [Roca-Feltrer et al., 2012] and fifty school surveys undertaken in May 2011 in Zomba district [Save Children and 3ei, unpublished data].

4.3.2 Data abstraction

The minimum required data fields for each record were: description of the study area (name, administrative divisions), the start and end dates of the survey (month and year) and information about blood examination (number of individuals tested, number positive for *Plasmodium* infections by species), the methods used to detect infection (microscopy, Rapid Diagnostic Tests (RDTs), Polymerase Chain Reaction (PCR) or combinations) and the lowest and highest age in the surveyed population. Given its ubiquity as a means for malaria diagnosis, the preferred parasite detection method was microscopy. No differentiation was made between light and fluorescent microscopy[15].

Data derived from randomized controlled intervention trials, were only selected when described for baseline/ pre-intervention and subsequent follow-up cross-sectional surveys among control populations. When cohorts of individuals were surveyed repeatedly in time we endeavoured to include only the first survey and subsequent surveys if these were separated by at least five months from the initial survey to avoid a dependence between observations based on treatment of preceding infected individuals. If it was not possible to disaggregate repeat surveys these were finally excluded from the analysis. Where age was not specified in the report for each survey but stated that the entire village or primary school children were examined, we assumed age ranges to be 0-99 years or 5-14 years respectively. Occasionally, reports presented the total numbers of people examined across a number of villages and only the percentage positive per village; here we assumed the denominator per village to be equivalent to the total examined divided by the total number of villages. Some survey results were reported as an aggregate in space (e.g. a single *Pf*PR for a group of villages) or time (e.g. a mean *Pf*PR estimated from four different surveys conducted over time). In such cases, we either sought additional reports of the same surveys with higher spatial or temporal resolution. Where this was not possible and where clusters of villages exceeded 5 km^2 we excluded the record from the analysis (see below).

[15] The quality of slide reading [O'Meara et al., 2006; Gitonga et al., 2012], variations in sensitivity/specificity between RDTs [WHO-FIND, 2012] or the ability of field teams to reliably read RDTs [Rennie et al. 2007; Harvey et al., 2008] and selection of primers for PCR [Okell et al., 2009] all influence descriptions of prevalence and will have intrinsic variance between surveys included in the database. RDTs have been shown to yield higher false positive rates than microscopy [Endeshaw et al., 2008; Keating et al., 2009] but seem to stratify both the lowest (<1% parasite rate) and highest (>50% parasite rate) more accurately compared to microscopy [Gitonga et al., 2012].

Where additional information to provide unique time, village specific data was necessary we contacted authors to provide any missing information.

4.3.3 Data geo-coding

Data geo-coding, defining a decimal longitude and latitude for each survey location, was a particularly demanding task. According to their spatial representation, data were classified as individual villages, communities or schools or a collection of communities within a definable area, corresponding to an area within 5 km grid or approximately 0.05 decimal degrees at the equator. Where possible we aimed to retain disaggregated village "point" level data rather than data across a "wide-area". Where data were reported across communities that exceeded at 5 km grid we regarded these as too low a spatial resolution, with significant possible variation within the polygon of information to be included within the modeling phase. In practice, this was a difficult criterion to audit as most survey reports did not provide enough detail on the size of the area surveyed. More recent use of Global Positioning Systems (GPS) during survey work does enable a re-aggregation of household survey data with greater precision and useful in maintaining 5 km grid criteria while combining clusters of small sample sizes in space. To position each survey location where GPS coordinates were not available in space we used a variety of digital resources, amongst which the most useful were Microsoft Encarta Encyclopedia (Microsoft, 2004) and Google Earth (Google, 2009). Other sources of digital place name archives routinely used included GEOnet Names Server of the National Geospatial-Intelligence Agency, USA [http://www.earth-info.nga.mil/gns/html/cntry_files.html]; Falling Rain Genomics' Global Gazetteer [http://www.fallingrain.com]; and Alexandria Digital Library prepared by University of California, USA [http://www.alexandria.ucsb.edu]. In addition we used digital place name gazetteers developed by the Malawian census bureau.

Although standard nomenclatures and unique naming strategies are attempted in digital gazetteers [Hill, 2000], these are difficult to achieve at national levels where spellings change between authors, overtime and where the same names are replicated across different places in the country. As such, during the data extraction, each data point was recorded with as much geographic information from the source as possible and this was used during the geo-positioning, for example checking the geo-coding placed the survey location in the administrative units described in the report or corresponded to other details in the report on distance to rivers or towns when displayed on Google Earth. While in theory GPS coordinates should represent an unambiguous spatial location, these required careful re-checking to ensure that the survey location matched the GPS coordinates. As routine we therefore rechecked all GPS data from all sources using place names and/or Google Earth to ensure coordinates were located on communities.

All coordinates were subject to a final check using second level administrative boundary Global Administrative Units Layers (GAUL) spatial database developed and revised in 2008 by Food and Agriculture Organization (FAO) of the United Nations [FAO, 2008]. The GLWD database developed by the World Wildlife Fund [Lehner & Doll, 2004] was used to ensure inland points were within defined land area. Here we aimed to identify survey coordinates that fell slightly on the lakes or in incorrect administrative units, every anomaly was re-checked and re-positioned using small shifts in combination with Google Earth.

4.3.4 Database fidelity checks, exclusions and pre-processing

Data checks: The entire database was first checked with a series of simple range-check constraint queries to identify potential errors that could have occurred during data entry. These queries assessed all data fields relevant to modelling for missing or inconsistent information. The final objective was to check for any duplicates introduced during the iterative data assembly process. Pairs of survey sites found within 1 km or within five months at the same location were identified. These may have been entered erroneously into the data assembly where multiple reviewed reports described similar data. These were listed, checked and duplicates removed.

Data exclusions: The search strategy identified 1038 time-survey locations where malaria infection prevalence had been recorded between June 1986 and April 2012. We were able to geo-locate every survey location. The final data series was then subjected to various exclusion rules as defined below.

> *Ensuring sample precision*: Sample size is inversely related to prevalence where, at low sample sizes, biases in prevalence estimates are introduced, dependent on the true prevalence of the population and translates into large standard errors [Gregory & Blackburn, 1991]. There is a critical threshold of between 10 and 20 individuals sampled below which the standard error increases exponentially in most surveys of parasitic infections and the curve starts to flatten at a sample size of about 50 and reaches an asymptote at about 100 [Jovani & Tella, 2006]. The sample size of individual survey samples is also important in the derivation of correlations with covariates of endemicity, in testing plausible associations between say rainfall and prevalence during covariate selection small, imprecise samples can lead to over-fitting. We aimed to combine communities in close proximity where any village had less than 15 people sampled and where communities were within 5 km of each other, sampled at exactly the same time by the same investigators. Using these criteria we were unable to merge data from 53 time-space locations and these were excluded from the final analysis. 30 of the small sample size survey data points were from the 2012 MIS.
>
> *Likoma*: Given the difficulties of matching environmental covariates to the small islands including Likoma we excluded 34 survey data points from Likoma from surveys undertaken in November 2011 [Simwaka et al., 2011] and will present the mean risks on the islands separately.

The final database contained 921 temporally data points at 895 unique survey locations.

4.3.5 Age standardization

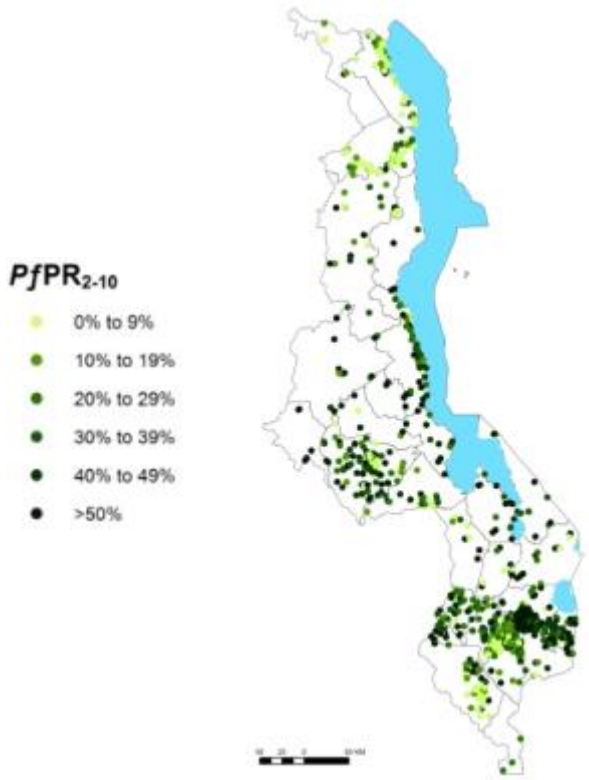
There was a large diversity among studies in the age ranges of sampled populations. To make any meaningful comparisons in time and space, a single standardized age range is required. Correction to a standard age for *P. falciparum* is possible based on the observation and theory of infectious diseases where partial immunity is acquired following repeated exposure from birth. We have retained the classical age range of 2-10 years as this best

describes the exposure to infection among semi-immune hosts at any given location and conforms to classifications established in the 1950s [Metselaar & Van Thiel, 1959]. We have adapted catalytic conversion Muench models, first used in malaria by Pull & Grab (1974), into static equations in R-script that uses the lower and upper range of the sample and the overall prevalence to transform into a predicted estimate in children aged 2-10 years, *Pf*PR_{2-10} [Smith et al., 2007].

4.3.6 Parasite prevalence data summaries

The overall spatial distribution of *Pf*PR_{2-10} data is shown in Figure 4.2. Of the 921 unique time-space survey locations identified through the data search strategy described above, all but 10 (99%) were provided as unpublished raw data, linked to a report, thesis, peer-reviewed publication or conference abstract, but not available at the spatial resolutions necessary for modelling purposes within the report. Survey data were located for time-space survey data points using GPS (657, 71%), combinations of GPS and third-level administration unit shape files to combine data of small sample size with a 5 km radius (183, 20%), Encarta (19, 2%), Google Earth (3, 0.3%), other digital place names sources, e.g. schools and village databases (47, 5%), and coordinates provided by individual scientists for which sources were not certain (12, 1%). Of the time-space survey data, infection was recorded in 667 (72%) using microscopy alone and 254 (28%) used RDTs (SD Bioline, First ResponseR Malaria Ag. and ICT Malaria Pf), no survey data were collected using PCR or combinations of diagnostic methods.

Figure 4.2 Data distribution of age-corrected *Pf*PR_{2-10} estimates from 921 surveys at 886 unique locations from surveys undertaken between 1986 and 2012



4.4 Model Based Geostatistical (MBG) modelling of age-corrected parasite prevalence

4.4.1 Model form

MBG methods interpolate from observed measures of interest of known locations in space and time to provide predictions of quantities and the empirical estimates of their uncertainty at locations and times where data do not exist [Diggle & Ribeiro, 2007]. MBG methods fit the data where the spatial and temporal covariance is used to generate samples of the predicted posterior distribution from which point estimates and the uncertainty around these estimates are computed simultaneously using Bayesian inference [Chilés & Delfiner, 1999; Diggle et al., 2002].

Data were used within a Bayesian hierarchical space-time model, implemented through an adapted Stochastic Partial Differential Equations (SPDE) approach using Integrated Nested Laplace Approximations (INLA)[16] for inference [Rue et al., 2009; Cameletti et al., 2012; R-INLA Project, 2013] to produce predictions of *Pf*$PR_{2\text{-}10}$. In the SPDE approach, the overall hierarchical space-time binomial model of the parasite prevalence was represented as the realization of a spatial-temporal process of the observed *Pf*$PR_{2\text{-}10}$ at the community location and survey year, selected covariates at sampled locations, the coefficient vector and the measurement error defined by the Gaussian white noise process[17]. Continuous predictions of *Pf*$PR_{2\text{-}10}$ at 1×1 km spatial resolutions for the years 2000 and 2010 were made using the first and second data time-series. Full details of the model and prediction accuracies are provided in Annex A1.

4.4.2 Selection of covariates

In statistical modelling, a set of independent covariates of the main outcome measure is often used to improve the model fit and increase the precision of predicted estimates. The inclusion of these covariates increase model complexity and, if not carefully selected, risk over-fitting (using up too many degrees of freedom), which occurs when more terms or covariates than is necessary are used in the model fitting process [Babyak, 2004; Murtaugh, 2009]. Over-fitting can lead to poor quality predictions because coefficients fitted to these covariates add random variations to subsequent predictions and make replication of findings difficult [Babyak, 2004]. Where too many covariates are used, the model tends to produce highly fluctuating regression coefficients increasing the chances of large covariate coefficients and an overly optimistic fit, especially with small sample sizes of empirical. This problem can be particularly pronounced when data assembled are from observational

[16] Markov Chain Monte Carlo (MCMC) algorithms, although widely used in Bayesian inference in disease mapping, suffer from convergence and dense covariance matrices that increase computational time and cost significantly [Rue et al., 2009]. INLA are alternative algorithms with faster computational speeds and can be undertaken in open source, easily adaptable R packages [R-INLA Project, 2013].

[17] The realization of state process or the unobserved level of *Pf*$PR_{2\text{-}10}$ is defined by a spatial-temporal Gaussian field that changes temporally as a second-order autoregressive function. The space-time covariance matrix informs the spatial range and temporal lag of the prediction model for each tile such that observations have decreasing effect on the predictions at a given location the more distal in space and time they are to that location. Outside of the spatial and temporal range the autocorrelation of the contribution data becomes almost null.

studies based on different study designs, sampling considerations and sample sizes which are then combined to describe a random process [Craig et al., 2007].

The choice of covariates should be underpinned by the principle of parsimony (few strong and easily interpretable covariates) and plausibility (a clearly understood mechanism by which the covariate influences the outcome). In disease mapping, there must a pre-determined aetiological explanation of the relationship of the disease and the covariate under consideration. The important determinants of uncontrolled malaria transmission are climate (rainfall and temperature) and ecological (potential breeding sites and urbanisation) [Molineaux, 1988; Snow & Gilles, 2002]. These factors affect the development and survival of the *P. falciparum* parasite and the malaria-transmitting *Anopheles* vector thereby reducing the risks of infection. A detailed description of the covariate data selected for testing in the Malawi model are provided in Annex A2.

Statistical selection process of covariates: To begin the covariate selection process the values of the assembled covariates were extracted to each *Pf*PR_{2-10} survey location using ArcGIS 10 *Spatial Analyst* (ESRI Inc. NY, USA) tool. A correlation test was then undertaken to examine variable that were highly correlated (>0.85). Where two covariates had correlation >0.85, the aim was to select the one with the highest Bayesian Inference Criteria (BIC) for inclusion in the bootstrap and total set analysis using the results of a bivariate regression analysis. Using total-set analysis, the *bestglm* algorithm selected the covariates resulting best-fit model and displayed these together with their coefficients, 95% CI and P-values.

The relationship of *Pf*PR_{2-10} with temperature, Temperature Suitability index (TSI), enhanced vegetation index (EVI), precipitation and urbanisation (combined urban and peri-urban classes) were all tested and analysis showed that only urbanisation contributed significantly to the variation in *Pf*PR_{2-10} and comprised the best fit model (coefficient -0.18 (95%CI: -0.022,0.87; p<0.001). In the analysis performed by Bennett et al. (2013), urbanization and TSI proved to be good model fits, however testing of covariates in this MCMC model included many very small sample sized cluster points. The ubiquity of data in time and space means that fewer parsimonious, plausible covariates are required to improve model precision and the actual sampled data prove more useful in predicting across un-sampled space and time locations.

4.5 Model predictions and populations at risk

We used the data from the age-corrected infection prevalence surveys (sample size, adjusted numbers positive) at known locations (longitude and latitude), times (month and year) and urbanisation within the Bayesian hierarchical space-time model, implemented through SPDE INLA for inference using a super-computing facility established in Kilifi, Kenya for proteomic analysis. The model took approximately 14 days to run and was repeated to provide precision metrics. The continuous predictions of mean *Pf*PR_{2-10} at each 1 x 1 km grid for 2000 and 2010 is shown in Figure 4.3a.

The continuous *Pf*PR_{2-10} maps were then classified into adapted traditional endemicity classes and generated by computing the posterior probability of belonging to a range of *Pf*PR_{2-10} from the posterior marginal distribution of the predictions at each 1 x 1 km grid. The

adaptations were made entirely within the meso-endemic range to capture the more granular changes in spatial risk with time across the dominant class for Malawi. The final eight classes were as follows:

- **Malaria Free**: Areas where malaria transmission cannot be supported because of the effects of low ambient temperature on sporogyny in mosquito vector[18]
- **Hypoendemic**: areas supporting predicted *Pf*PR_{2-10} <10%
- **Mesoendemic 1**: areas supporting predicted *Pf*PR_{2-10} 10%-19%
- **Mesoendemic 2**: areas supporting predicted *Pf*PR_{2-10} 20%-29%
- **Mesoendemic 3**: areas supporting predicted *Pf*PR_{2-10} 30%-39%
- **Mesoendemic 4**: areas supporting predicted *Pf*PR_{2-10} 40%-49%
- **Hyperendemic**: areas supporting predicted *Pf*PR_{2-10} >50%-74%
- **Holoendemic**: areas supporting predicted *Pf*PR_{2-10} ≥75%

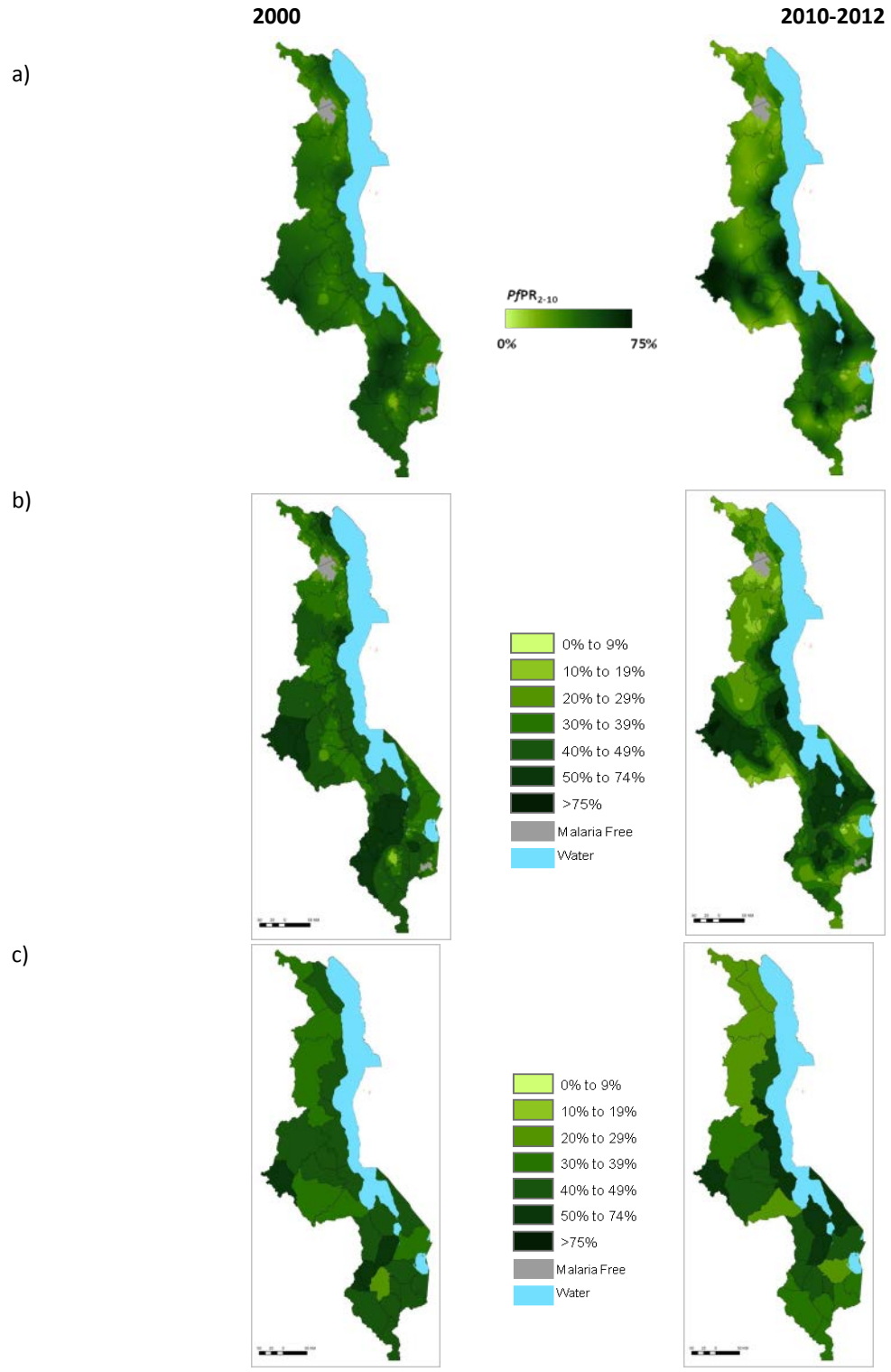
The final re-classified endemicity risks are shown for 2000 and 2010 in Figure 4.3b.

This newly edited population grid was then used to extract populations at risk by health district at each 1 × 1 km *Pf*PR_{2-10} grid location classified by predicted malaria risk class using the *Zonal Statistics* function in ArcGIS 10.1. The population totals (%) within each risk class for 2000 (Table 4.1) and 2010 (Table 4.2) for each of the 28 districts.

Given the over-distribution of both population density (Figure 2.5) and malaria risk (Figures 4.3a and 4.3b) within each district, we computed a Population Adjusted *Pf*PR_{2-10} (PA*Pf*PR_{2-10}) for each district by first multiplying the *Pf*PR_{2-10} at each 1×1 km grid location with the corresponding population at the same spatial resolution to compute the number of people who are likely to be positive for *P. falciparum*. This surface was then used to extract the number of people positive for *P. falciparum* in each district and divided by its total population in 2000 to compute PA*Pf*PR_{2-10} for 2000 and the same for 2010 predictions. The district values of the mean PA*Pf*PR_{2-10} in 2000 and 2010 are shown in Tables 4.1 and 4.2 respectively, and Figures 4.3c. The overall percentage of Malawi's population in each of the eight endemicity classes is shown in Figure 4.4.

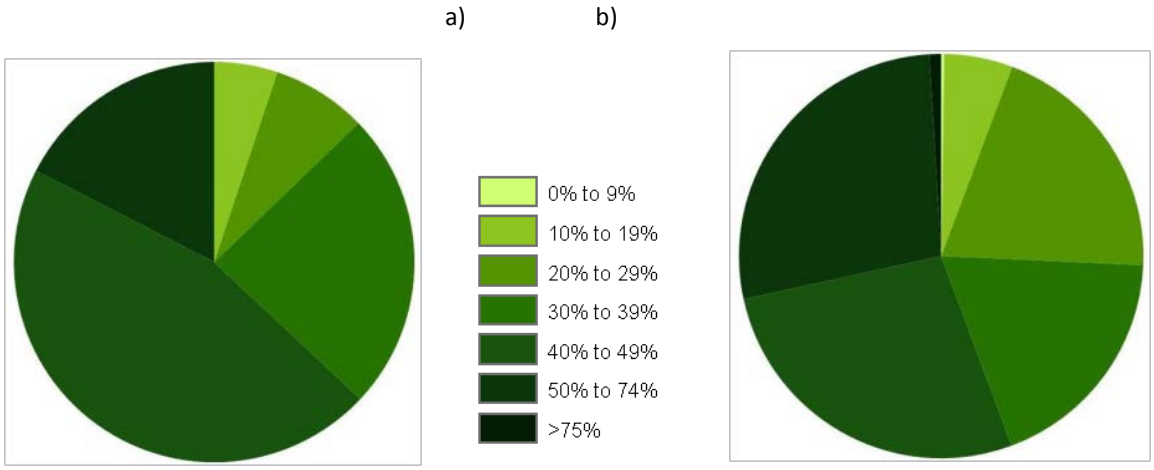
[18] To provide a plausible mask to eliminate the possibility of transmission, we used the temperature suitability index (TSI) [Gething et al., 2011b; Figure 4.3b]. Areas unable to support transmission were classified as having TSI values of zero. These areas are notably those parts of Malawi with mountain and plateaux peaks in Rumphi, Chitipa and Mulanje districts.

Figures 4.3: a) Continuous 1x1 predicted mean *Pf*PR$_{2-10}$ for 2000 and 2010; b) re-classified endemicity classes using the posterior distribution for 2000 and 2010; c) Population-weighted mean *Pf*PR$_{2-10}$ per district for the two years.



Very few (0.05%) Malawians live in areas regarded as free from malaria. In 2000, there were no people living under conditions that supported hypoendemic transmission (*Pf*PR_{2-10} < 10%). However in 2000, 82% of the population lived in areas traditionally described as mesoendemic (*Pf*PR_{2-10} 10-49%), 17% lived in areas that were regarded as hyper-endemic (*Pf*PR_{2-10} 50-74%) and no one was living in an area that could be predicted to be holoendemic (*Pf*PR_{2-10} >= 75%). By 2010, 1% of the population were at risk of holoendemic transmission, the population living in areas that supported hyperendemicity had increased to 27%, the population in areas of traditional mesoendemic transmission had consequently declined to 71% and only a small fraction of the population in 2010 enjoyed hypoendemic transmission (0.2%).

Figure 4.4: Percentage of Malawi's population at various classes of *P. falciparum* risk in a) 2000 & b) 2010



Finer level changes within the broad meso-endemic class are shown in Figures 4.3a and 4.3b. Overall, we show a predicted rise, or at least a situation consistent with no change, in malaria transmission intensity over the decade 2000 to 2010. Mean population-weighted PfPR2-10 (PA*Pf*PR_{2-10}) for the country as a whole was 37.7% in 2000, rising to 42.7% in 2010.

There are however several districts which had a predicted decline in risk during the 2000-2010 interval that deserve mention (Figures 4.3c; Tables 4.1 & 4.2): Dedza and Kazungu (Central Region); Chitipa, Karonga, Mzimba and Rumphi (Northern Region); and Chikwawa, Mwanza, Neno, Nsanje and Zomba (Southern Region). Why these districts have declined more than others deserves further investigation.

4.6 Model uncertainty and validation statistics

A series of model uncertainty and validation statistics were generated to assess model performance. For each prediction year, the standard deviations of *Pf*PR_{2-10} were first computed for each 1 × 1 km grid location. The probability of belonging to an endemicity class was also computed from the posterior marginal distributions at similar spatial resolutions. Conventional model accuracy was estimated by computing the linear correlation, the mean prediction error (MPE) and mean absolute prediction error (MAPE) of the observations and predictions of a 10% hold-out dataset. The hold-out set was selected using a spatially and temporally declustered algorithm [Isaacs & Svritsava, 1989] which

defined Thiessen polygons around each survey location. Each data point had a probability of selection proportional to the area of its Thiessen polygon so that data located in densely surveyed regions had a lower probability of selection than those in sparsely surveyed regions setting a high threshold for model performance. Sampling and testing hold out sets was done for each regional and time-segmented tile. The Bayesian SPDE using INLA was then implemented in full using the remaining 90% of data and predictions were made to the 10% hold-out within each regional tile.

The MPE, MAPE and the correlation coefficient of the observed and predicted *Pf*PR_{2-10} for the full space time *Pf*PR_{2-10} model for Malawi were -1.49 %, 8.80% and 0.84 respectively indicating a good model accuracy. For both 2000 and 2000 mean predictions of $PfPR_{2-10}$ all pixels were within less than one standard deviation of the posterior mean $PfPR_{2-10}$ indicating good precision around estimates of risk (Annex A1.1.3).

Table 4.1: Population (%) in **2000** exposed to various classes of malaria and population-adjusted *Pf*PR_{2-10} by district

Region/District	Total Pop 2000	Malaria Free	*Pf*PR_{2-10} <10%	*Pf*PR_{2-10} 10-19%	*Pf*PR_{2-10} 20-29%	*Pf*PR_{2-10} 30-39%	*Pf*PR_{2-10} 40-49%	*Pf*PR_{2-10} 50- 74%	*Pf*PR_{2-10} 75%+	Population weighted mean *Pf*PR_{2-10}
Central										
Dedza	541,480	1,081 (0.2%)	0 (0%)	0 (0%)	17,663 (3.3%)	240,279 (44.4%)	282,254 (52.1%)	0 (0%)	0 (0%)	39.85
Dowa	492,247	0 (0%)	0 (0%)	0 (0%)	10,686 (2.2%)	169,720 (34.5%)	289,083 (58.7%)	22,759 (4.6%)	0 (0%)	42.26
Kasungu	546,111	0 (0%)	0 (0%)	0 (0%)	0 (0%)	93,588 (17.1%)	353,927 (64.8%)	98,594 (18.1%)	0 (0%)	44.51
Lilongwe	1,617,720	0 (0%)	0 (0%)	0 (0%)	510,524 (31.6%)	253,611 (15.7%)	560,276 (34.6%)	293,309 (18.1%)	0 (0%)	39.75
Mchinji	393,234	0 (0%)	0 (0%)	0 (0%)	0 (0%)	92 (0%)	18,906 (4.8%)	374,214 (95.2%)	0 (0%)	54.82
Nkhotakota	262,746	0 (0%)	0 (0%)	0 (0%)	0 (0%)	40,052 (15.2%)	222,694 (84.8%)	0 (0%)	0 (0%)	43.10
Ntcheu	401,364	265 (0.1%)	0 (0%)	0 (0%)	1,910 (0.5%)	76,274 (19%)	154,624 (38.5%)	168,292 (41.9%)	0 (0%)	48.64
Ntchisi	213,978	0 (0%)	0 (0%)	0 (0%)	814 (0.4%)	74,451 (34.8%)	138,714 (64.8%)	0 (0%)	0 (0%)	40.87
Salima	284,183	0 (0%)	0 (0%)	0 (0%)	0 (0%)	46,070 (16.2%)	238,113 (83.8%)	0 (0%)	0 (0%)	43.09
Northern										
Chitipa	153,445	302 (0.2%)	0 (0%)	0 (0%)	17,930 (11.7%)	122,109 (79.6%)	12,952 (8.4%)	77 (0%)	0 (0%)	34.41
Karonga	231,698	0 (0%)	0 (0%)	129 (0.1%)	4,866 (2.1%)	11,526 (5%)	134,430 (58%)	80,746 (34.8%)	0 (0%)	46.32
Likoma*	9,000	NA	NA	NA	NA	NA	NA	NA	NA	NA
Mzimba	741,465	100 (0%)	0 (0%)	0 (0%)	104,619 (14.1%)	291,488 (39.3%)	345,209 (46.6%)	0 (0%)	0 (0%)	37.85
Nkhata Bay	147,787	131 (0.1%)	0 (0%)	0 (0%)	3,150 (2.1%)	34,504 (23.3%)	57,975 (39.2%)	52,027 (35.2%)	0 (0%)	44.87
Rumphi	143,890	329 (0.2%)	0 (0%)	1,217 (0.8%)	22,255 (15.5%)	105,390 (73.2%)	14,699 (10.2%)	0 (0%)	0 (0%)	34.72
Southern										
Balaka	280,184	0 (0%)	0 (0%)	0 (0%)	0 (0%)	566 (0.2%)	5,606 (2%)	274,012 (97.8%)	0 (0%)	57.85
Blantyre	832,721	0 (0%)	0 (0%)	569,674 (68.4%)	91,546 (11%)	40,196 (4.8%)	47,599 (5.7%)	83,706 (10.1%)	0 (0%)	24.73
Chikwawa	376,650	0 (0%)	0 (0%)	0 (0%)	0 (0%)	15,603 (4.1%)	278,563 (74%)	82,485 (21.9%)	0 (0%)	48.96
Chiradzulu	248,858	0 (0%)	0 (0%)	0 (0%)	23,231 (9.3%)	38,966 (15.7%)	186,471 (74.9%)	190 (0.1%)	0 (0%)	40.96
Machinga	418,845	0 (0%)	0 (0%)	0 (0%)	1,407 (0.3%)	330,645 (78.9%)	79,691 (19%)	6,964 (1.7%)	0 (0%)	38.49
Mangochi	692,437	0 (0%)	0 (0%)	0 (0%)	5,015 (0.7%)	204,939 (29.6%)	427,830 (61.8%)	54,481 (7.9%)	0 (0%)	43.18
Mulanje	451,955	119 (0%)	0 (0%)	0 (0%)	15,365 (3.4%)	108,931 (24.1%)	321,176 (71.1%)	6,090 (1.3%)	0 (0%)	41.91
Mwanza	79,255	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	10,401 (13.1%)	68,854 (86.9%)	0 (0%)	53.38
Neno	92,590	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2,729 (2.9%)	89,861 (97.1%)	0 (0%)	58.05
Nsanje	205,835	0 (0%)	0 (0%)	0 (0%)	0 (0%)	15,224 (7.4%)	190,417 (92.5%)	0 (0%)	0 (0%)	45.78
Phalombe	267,353	1,661 (0.6%)	0 (0%)	0 (0%)	3,375 (1.3%)	86,950 (32.5%)	175,117 (65.5%)	0 (0%)	0 (0%)	41.33
Thyolo	503,552	0 (0%)	0 (0%)	1,621 (0.3%)	12,943 (2.6%)	142,673 (28.3%)	346,298 (68.8%)	0 (0%)	0 (0%)	40.73
Zomba	575,837	1,428 (0.2%)	0 (0%)	0 (0%)	11,792 (2%)	162,582 (28.2%)	203,672 (35.4%)	196,335 (34.1%)	0 (0%)	44.94

Table 4.2: Population (%) in **2010** exposed to various classes of malaria and population-adjusted *Pf*PR$_{2-10}$ by district

Region/District	Total Pop 2010	Malaria Free	*Pf*PR$_{2-10}$ <10%	*Pf*PR$_{2-10}$ 10-19%	*Pf*PR$_{2-10}$ 20-29%	*Pf*PR$_{2-10}$ 30-39%	*Pf*PR$_{2-10}$ 40-49%	*Pf*PR$_{2-10}$ 50- 74%	*Pf*PR$_{2-10}$ 75%+	Population weighted mean *Pf*PR$_{2-10}$
Central										
Dedza	711,911	1,368	24,527	141,988	290,785	125,216	102,572	25,187	0	27.98
		(0.2%)	(3.4%)	(19.9%)	(40.8%)	(17.6%)	(14.4%)	(3.5%)	(0%)	
Dowa	647,813	0	0	0	11,007	231,347	178,829	226,629	0	46.12
		(0%)	(0%)	(0%)	(1.7%)	(35.7%)	(27.6%)	(35%)	(0%)	
Kasungu	716,371	0	0	38,361	397,723	131,748	33,202	115,335	0	32.82
		(0%)	(0%)	(5.4%)	(55.5%)	(18.4%)	(4.6%)	(16.1%)	(0%)	
Lilongwe	2,168,240	0	0	29,315	193,640	252,741	919,407	773,137	0	47.87
		(0%)	(0%)	(1.4%)	(8.9%)	(11.7%)	(42.4%)	(35.7%)	(0%)	
Mchinji	510,763	0	0	0	0	2,056	17,292	413,154	78,234	69.29
		(0%)	(0%)	(0%)	(0%)	(0.4%)	(3.4%)	(80.9%)	(15.3%)	
Nkhotakota	345,594	0	0	0	0	13,932	47,423	236,230	48,009	61.73
		(0%)	(0%)	(0%)	(0%)	(4%)	(13.7%)	(68.4%)	(13.9%)	
Ntcheu	522,143	311	0	850	32,244	99,577	166,750	222,411	0	46.72
		(0.1%)	(0%)	(0.2%)	(6.2%)	(19.1%)	(31.9%)	(42.6%)	(0%)	
Ntchisi	282,238	0	0	0	0	74,532	110,349	95,094	2,263	48.37
		(0%)	(0%)	(0%)	(0%)	(26.4%)	(39.1%)	(33.7%)	(0.8%)	
Salima	379,410	0	0	0	709	2,514	21,547	354,640	0	60.13
		(0%)	(0%)	(0%)	(0.2%)	(0.7%)	(5.7%)	(93.5%)	(0%)	
Northern										
Chitipa	201,151	380	8,445	48,181	97,132	46,918	0	0	0	23.84
		(0.2%)	(4.2%)	(24%)	(48.3%)	(23.3%)	(0%)	(0%)	(0%)	
Karonga	304,616	0	0	40,744	147,261	107,966	8,644	0	0	28.24
		(0%)	(0%)	(13.4%)	(48.3%)	(35.4%)	(2.8%)	(0%)	(0%)	
Likoma*	9,000	0	0	9,000	0	0	0	0	0	10.96*
		(0%)	(0%)	(100%)	(0%)	(0%)	(0%)	(0%)	(0%)	
Mzimba	984,789	126	0	232,934	624,932	105,467	20,779	490	0	24.71
		(0%)	(0%)	(23.7%)	(63.5%)	(10.7%)	(2.1%)	(0%)	(0%)	
Nkhata Bay	194,761	180	0	6,075	36,596	43,033	65,487	43,391	0	41.23
		(0.1%)	(0%)	(3.1%)	(18.8%)	(22.1%)	(33.6%)	(22.3%)	(0%)	
Rumphi	190,021	341	1,448	60,041	122,274	5,917	0	0	0	21.51
		(0.2%)	(0.8%)	(31.6%)	(64.3%)	(3.1%)	(0%)	(0%)	(0%)	
Southern										
Balaka	368,301	0	0	0	0	0	76,267	292,034	0	56.88
		(0%)	(0%)	(0%)	(0%)	(0%)	(20.7%)	(79.3%)	(0%)	
Blantyre	1,175,940	0	0	0	0	50,967	926,303	195,650	3,022	45.08
		(0%)	(0%)	(0%)	(0%)	(4.3%)	(78.8%)	(16.6%)	(0.3%)	
Chikwawa	501,569	0	0	11,632	86,844	189,668	161,490	51,851	84	38.56
		(0%)	(0%)	(2.3%)	(17.3%)	(37.8%)	(32.2%)	(10.3%)	(0%)	
Chiradzulu	321,096	0	0	0	352	11,439	161,632	147,673	0	48.74
		(0%)	(0%)	(0%)	(0.1%)	(3.6%)	(50.3%)	(46%)	(0%)	
Machinga	546,285	0	0	214	36,989	105,583	172,169	230,886	272	46.38
		(0%)	(0%)	(0%)	(6.8%)	(19.3%)	(31.5%)	(42.3%)	(0%)	
Mangochi	909,203	0	0	0	26,208	134,759	184,109	556,098	7,813	52.62
		(0%)	(0%)	(0%)	(2.9%)	(14.8%)	(20.2%)	(61.2%)	(0.9%)	
Mulanje	588,780	468	0	5,532	169,616	229,101	176,820	6,898	0	35.13
		(0.1%)	(0%)	(0.9%)	(28.8%)	(38.9%)	(30%)	(1.2%)	(0%)	
Mwanza	103,308	0	0	0	12,079	47,191	44,038	0	0	38.75
		(0%)	(0%)	(0%)	(11.7%)	(45.7%)	(42.6%)	(0%)	(0%)	
Neno	124,608	0	0	0	0	27,422	90,481	6,705	0	43.52
		(0%)	(0%)	(0%)	(0%)	(22%)	(72.6%)	(5.4%)	(0%)	
Nsanje	267,030	0	0	18,083	75,199	146,912	26,594	0	0	32.40
		(0%)	(0%)	(6.8%)	(28.2%)	(55%)	(10%)	(0%)	(0%)	
Phalombe	343,810	1,983	0	0	52,926	213,733	74,853	0	0	35.78
		(0.6%)	(0%)	(0%)	(15.4%)	(62.2%)	(21.8%)	(0%)	(0%)	
Thyolo	660,682	0	0	2,084	248,405	199,575	130,713	79,886	0	35.84
		(0%)	(0%)	(0.3%)	(37.6%)	(30.2%)	(19.8%)	(12.1%)	(0%)	
Zomba	762,749	1,962	1,844	175,714	301,021	161,507	120,000	666	0	27.85
		(0.3%)	(0.2%)	(23%)	(39.5%)	(21.2%)	(15.7%)	(0.1%)	(0%)	

In November 2011, 1853 children aged 1-11 years were sampled for malaria infection living in 35 communities on the Islands [Simwaka et al, 2011; unpublished]; 203 (11%) were found positive by microscopy and we have therefore assumed that the circa 9,000 people on Likoma island in 2010 would have been exposed to mesoendemic class 1

4.7 Triangulating changing parasite prevalence with changing clinical incidence

The HMIS provides passive surveillance data on outpatient and inpatient malaria cases reported from government and mission health facilities in Malawi. There have been attempts to re-construct HMIS out-patient data from across Malawi routinely reported in the HMIS annual bulletin. These, however, will have been imperfect representations of the national and sub-national trends given the problems associated with HMIS in many African countries. In spite of these short coming according to the HMIS, the number of reported cases of malaria in all age groups increased from 3.7 million in 2005 to 6.8 million in 2010 [PMI, 2012].

At least 6.8 million new cases of Malaria were reported at out-patient departments (OPD) in the Financial Year 2009/10, 49% were among children under the age of five years [MoH, 2010]. The results indicate that on average at least 484 persons per 1,000 population were notified as malaria cases presenting to government facilities, 9% higher than the preceding year and a substantive increase since 2005/06 [MoH, 2010]. Analysis by the HMIS data shows significant differences between districts and between years 2002-20011 (Figure 4.5). It is important to interpret these data with caution and in this repscte we highlight several caveats: one it is possible that reporting rates may have improved over times reflecting more case in later years hence these trends may reflect an improvement in data capture: two the observed patterns could also reflect geographical variation in reporting rates and lastly RDTs were introduced in Malawi in 2011.

A detailed review of malaria morbidity burdens has been undertaken at four hospital settings where inpatient paediatric registers have been reviewed for the period 2000 to 2012 [Okiro et al., 2013]. Malaria and non-malaria diagnoses were extracted by month from registers from district hospitals at Mwanza, Rumphi, Zomba and Salima (Figure 4.6). The complete assembly covered 259,635 admissions among children aged 0-4 years, of which 98,773 (38%) were classified on admission as malaria admissions [Okiro et al., 2013].

The catchment areas for each hospital were defined and this was used to to extract the populations-at-risk using population density distributions described in Section 2.8. The computed monthly malaria admission, population-at-risk adjusted rates were subjected to time-series analysis[19]. There was no evidence at any site of a sustained decline in malaria admission rates between 2000 and 2010. Malaria admission rates increased at Salima and Zomba from January 2000 to December 2010 and remained unchanged at Mwanza and variable at Rumphi [Okiro et al., 2013] (Figure 4.7). These data have continued to be collected at the four hospitals and while there remains no evidence of change at Rumphi and Mwanza hospitals there are lower incidences recorded in 2011 and 2012 at Salima and Zomba (Figure 4.11)

[19] Moving average smoothing methods were used to identify long-term trend signals within each temporal 11 year series while filtering out short-term annual fluctuations and random variation using an ARMAX autoregressive model with established explanatory variables including rainfall in the current and or preceding months and changes in service use (captured by non-malaria admission rates) resulting in a predicted or smoothed malaria admission rate per month for each hospital site over the period 2000 to 2010 [Okiro et al., 2013].

Figure 4.5 District level trends in new malaria cases per 1000 population by district between 2002 and 2011 [Adapted from HMIS data]: in the reporting Neno and Mwanza districts are combined.

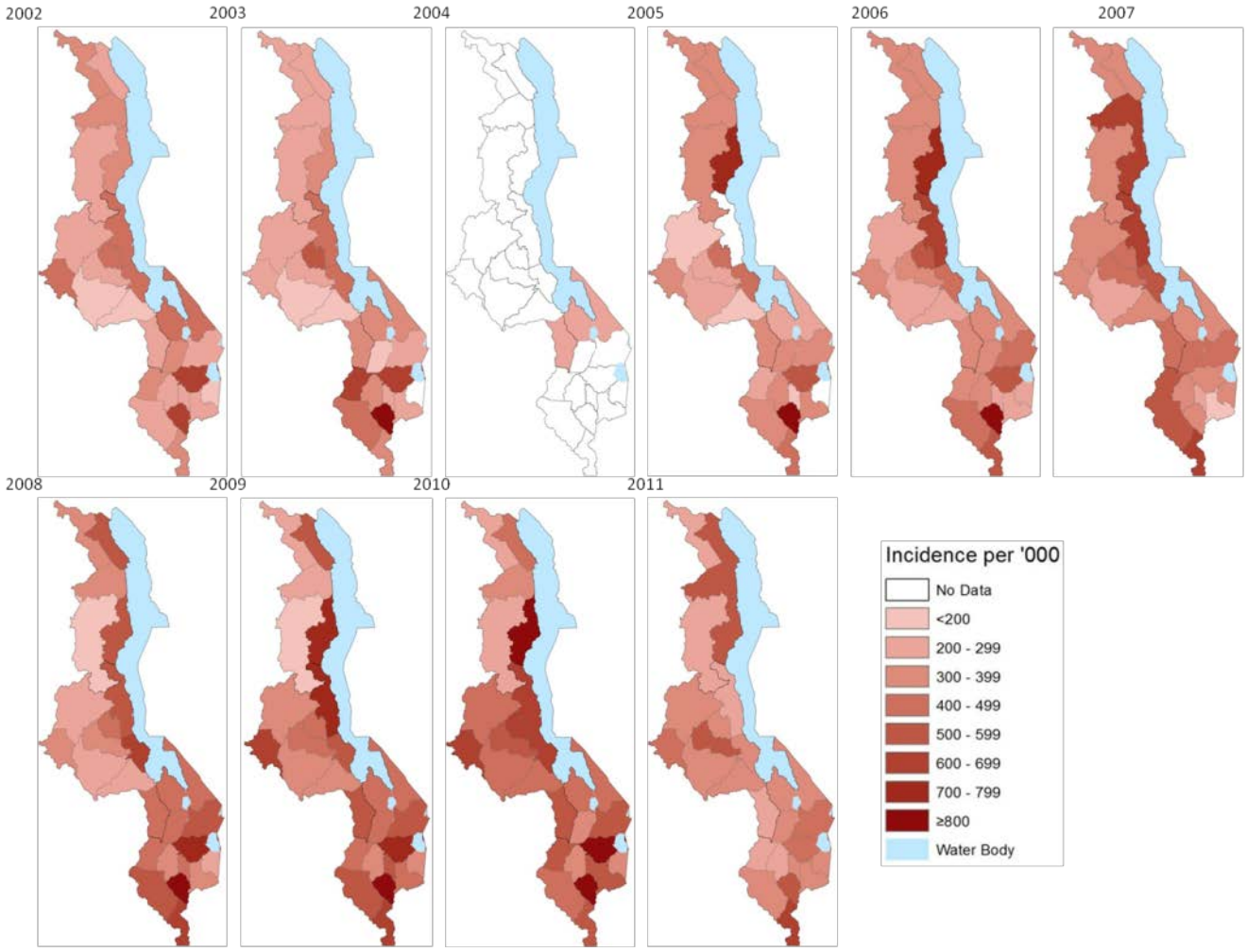
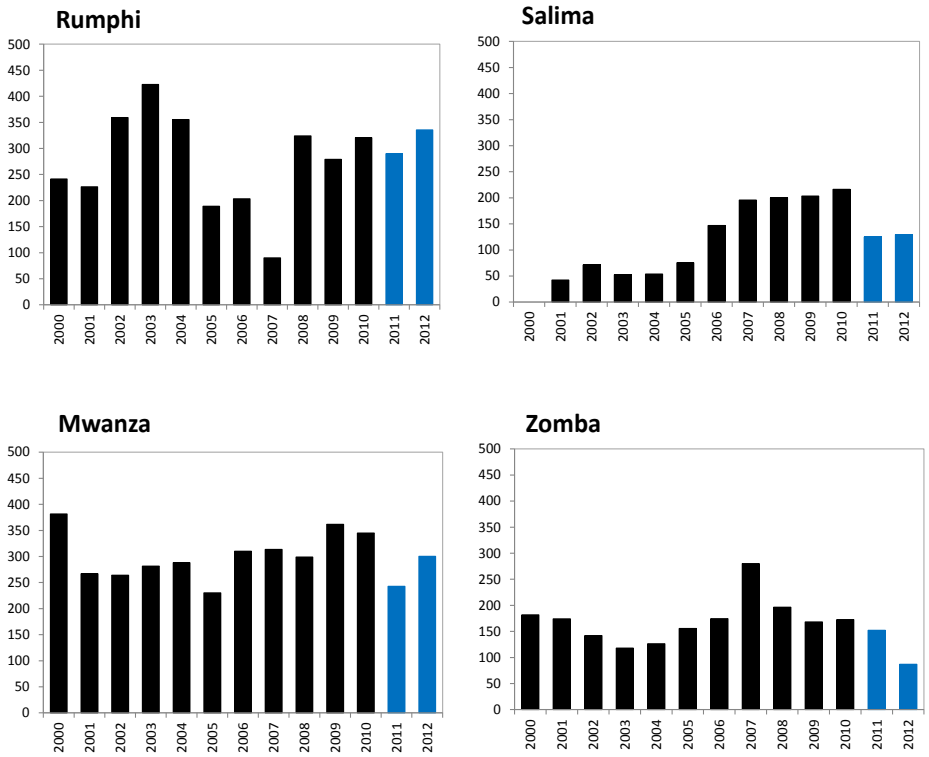


Figure 4.6: Location of Rumphi, Salima, Zomba and Mwanza (2000-2010) long-term hospital data in Malawi showing hospital catchment areas in grey.

Figure 4.7: Annual paediatric admission rates per 1000 (Y-axis) from Rumphi, Salima, Mwanza, and Zomba district hospitals 2000-2010 [Okiro et al.,2013] and 2011-2012 new data.



Additional observations have been made at the Queen Elizabeth Central Hospital in Blantyre (Figure 4.6), where investigators examined malaria hospital admissions and slide positivity between 2001 and 2010 [Roca-Felter et al., 2012]. Slide positivity among childhood out-patient attendees remained constant during the interval and admission to the intensive care ward with cerebral malaria dropped slightly from 2001 to 2005 and then rose in 2010 to its highest levels recorded in last 10 years [Roca-Felter et al., 2012]. In separate analysis of malaria admissions among children aged less than six months it was observed that admission rates rose between 2001 and 2007 [Larru et al., 2009].

These additional data from routine HMIS or more detailed hospital-based studies suggest that observations made in the preceding sections suggesting no major changes in malaria transmission intensity between 2000 and 2010 are internally consistent with no change or increasing morbidity burdens during the same period.

4.8 Other parasite species

The current focus of control in Africa is justifiably *P. falciparum*, by far the most pathogenic of the five human malarias and contributes to over 95% of the world's mortality from malaria. However, it is not the only malaria parasite to affect man. *Plasmodium knowlesi,* the most recently discovered human malaria, has not been described in Africa. *Plasmodium vivax* is thought to have a restricted distribution in Africa owing to the refractory nature of duffy-negative red cells that lack a necessary receptor (Fy(a-b-)) for invasion. *Plasmodium ovale* and *P. malariae* have been reported in most regions of the world, however both parasites seem to be largely confined to sub-Saharan Africa and a few islands in the Western Pacific [Lysenko & Beljaev, 1969; Collins & Jeffery, 2005; Mueller et al., 2007]. There appears to be no duffy blood group restriction to infection for either of these parasites [Collins & Jeffery, 2005]. Recent genetic studies of parasite populations in Africa suggest that there may be more than one genetically distinct form of *P. ovale; Plasmodium ovale curtisi* (classic type) and *Plasmodium ovale wallikeri* (variant type) [Sutherland et al., 2010]. The non-falciparum human malarias are often susceptible to most antimalarial drugs including those that currently fail to treat *P. falciparum* [White, 2008], however most evade drug action as they are more often benign and/or relapse.

Plasmodium malariae is a relatively easy parasite to observe with microscopy owing to a distinctive pigmented band forms in host cells [Collins & Jeffrey, 2007]. Most *P. malariae* infections also share similar properties as *P. ovale* and are rarely uniquely associated with clinical events but persist for decades at very low parasite densities and have been associated nephritic syndromes [Hendrickse, 1980; Collins & Jeffery, 2005] and documented during biopsy work in Malawi [Brown et al., 1977]. While relatively uncommon, *P. malariae*'s true burden has never been formally quantified. There is some suggestion of a suppressive effect of *P. falciparum* on *P. malariae* and a parasite density regulatory effect of *P. malariae* on *P. falciparum* clinical infections [Black et al., 1994; Mueller et al., 2007]. While the mechanisms and epidemiological significance of these potential interactions require further confirmation

they might have a longer-term significance as prevalence of both parasites declines differentially with scaled prevention and treatment.

For *P. vivax* there are two dogmas that are not necessarily supported by any empirical data for sub-Saharan Africa. First, endemic *P. vivax* transmission is thought to be absent from much of the continent due to the presence of human genetic negativity for Duffy factor surface molecules required for invasion of *P. vivax* into red blood cells. Second, the dominant opinion has for many years been that *P. vivax* is clinically benign. There is a growing body of epidemiological and clinical evidence that suggests that *P. vivax* is far from benign directly causing, and not simply associated with, severe life-threatening disease, mortality and indirect consequences on pregnant women [Baird, 2007; Mendis et al., 2001; Price et al., 2007]. There is also growing epidemiological and molecular evidence that a parasite with characteristics of *P. vivax* is being transmitted among Duffy blood group–negative inhabitants in Kenya [Ryan et al., 2007], Congo [Culleton et al., 2009] and among travellers to central and west Africa [Gautret et al., 2001]. It would appear that vivax transmission is possibly routinely undetected and can persist in predominantly duffy-negative populations which may not be 100% refractive [Culleton et al., 2008; Rosenberg, 2007].

During the 1930s, *P. vivax* was widely described across Malawi. Community and school surveys at Mangochi, Thyolo, Blantyre, Zomba, Lilongwe, Mlange, Kota-Kota, Mzimba, Livingstonia and Chilwa Island all reported high prevalence of vivax during cross-sectional surveys [Nyasaland Protectorate, 1934-1937]. There was, and still is, a significant duffy-receptive Asian community living in Malawi who might have served as a small reservoir of susceptible populations contributing to transmission. Alternatively, microscopists during the 1930s mis-diagnosed *P. ovale* for *P. vivax* as there were no *P. ovale* descriptions within the same reports. Among 2922 slides taken from children aged 0-15 years during sentinel site surveys between 1934 and 1937, 5.6% were reported as harbouring *P. malariae* infections [Nyasaland Protectorate, 1934-1937]

No *P. vivax* infections were detected in slides taken from communities in the Kasungu Tobacco Project Area, Kawale School (Lilongwe Town) and the Rural Development Areas at Lilongwe, Karonga, Salima, and the Shire Valley in November 1973 [Cheyabejara et al., 1974]. Among the 587 children aged 2-10 years sampled at these six sites, eight (1.4%) were identified as harbouring *P. ovale* infections, representing 1.7% of all detected plasmodial species. *Plasmodium malariae* was however considerably more common, representing 133 infections (22%) or 29% of all plasmodial infections [Cheyabejara et al., 1974].

There are very few detailed, contemporary descriptions of asymptomatic parasite species descriptions in Malawi. In 2002, ten communities were investigated at Dedza and eight at Mangochi examining 2918 individuals aged over 6 months using microscopy and PCR; no vivax infections were reported. The prevalence of *P. ovale* at Dedza and Mangochi by PCR was 3.3% and 7.8% respectively; for *P. malariae* PCR prevalence in Dedza and Mangochi was 7.7% and 13.2% respectively [Bruce et al., 2008]. There were no major spatial disparities in risks or genotypes for *P. malariae* infections within and between Dedza and Mangochi [Bruce et al., 2011]. During a study of the aetiology of anaemia among pre-school children in Blantyre and

the surrounding communities (including Chikwawa) only one child had *P. ovale* (0.3%) and one child had *P. malariae* (0.3%) among 366 community controls [Calis et al., 2008]. At Chikhwawa district in 2003 entomological studies of *An. gambiae* s.s., *An. arabiensis* and *An. funestus* between 2002 and 2003 identified a single *An. gambiae* s.s. that was infected with both *P. falcparum* and *P. malariae* [Mzilahowa et al., 2012]. However, at six sites in Karonga district in 2010, 153 females of the *An. funestus* complex were analyzed for *P. vivax* and *P. falciparum* circumsporozoite protein by ELISA and of those collected during the dry season 1 of 15 (6.7%) were positive for *P. vivax* [Vezenegho et al., 2013]. Transmission of *P. vivax* cannot be excluded in Malawi.

Plasmodium ovale is rare, *Plasmodium malariae* is more common and its prevalence may be significantly under-estimated. *Plasmodium malariae* has a poorly defined disease burden but among Malawians [Brown et al., 1977] and non-immune travellers to Malawi [Hapuarachchi et al., 2008] glomerulonephritis has been attributed to this parasite. Comparing data from six sites in the 1970s with two sites in the 2000s there might be a suggestion that the prevalence of this parasite species is declining over long periods.

4.9 Malaria Seasonality

The malaria profile in Malawi has been characterized since the 1920s as acutely seasonal. Early investigations of the seasonal nature of dominant vectors [Lamborn, 1925] and the monthly incidence of parasite rates, spleen rates, clinical attacks and blackwater fever [Thomson, 1934] showed that the months of March to June were the worst months for malaria risk among the population, following acute rises in vector populations in February.

Relationships between climate, seasonal parasite transmission and disease outcomes are however, complex and have been poorly defined for many years [Gill, 1938]. There is a suggestion that areas with acute transmission represent settings that are more adapted to synchronized infections leading to higher host parasite densities [Mckenzie et al., 2001]. Acutely seasonal malaria exposure areas may lead to poorly “designed” immunization for new-born children, resulting in different disease-severity profiles compared to settings with equivalent annual parasite exposure more evenly distributed throughout a year (spaced immunization) [Carneiro et al., 2010; Greenwood et al., 1991].

The description of seasonality represents an important operational information platform to target the timing of vector control, most notably IRS and larval control operations, and the renewed interest in pulsed mass drug administration or restricted chemoprophylaxis in the Sahel, known as Seasonal Malaria Chemoprevention (SMC) [Cairns et al., 2012; WHO, 2012b].

The climate suitability maps developed by the MARA collaboration are based on the likelihood of stable transmission using a rules-based approach [Craig et al., 1999; Tanser et al., 2003; http://www.mara.org.za/] have never been used in Malawi as control tools. A more recent attempt at using empirical data to define extremes of seasonality for SMC have been published by Cairns and colleagues using Fourier processed daily rainfall data

[http://www.cpc.noaa.gov/products/fews/rfe.shtml] since 2000 and tested against monthly clinical incidence data from 55 sites across sub-Saharan Africa. The optimal model was one where 60% of annual rainfall occurred within 3 months and best fitted the seasonal clinical profiles of >60% of cumulative cases occurring in 4 consecutive months [Cairns et al., 2012]. Using this rainfall, profile areas with incidence patterns suitable for SMC were identified, with a sensitivity of 95.0% and a specificity of 73.5% [Cairns et al., 2012].

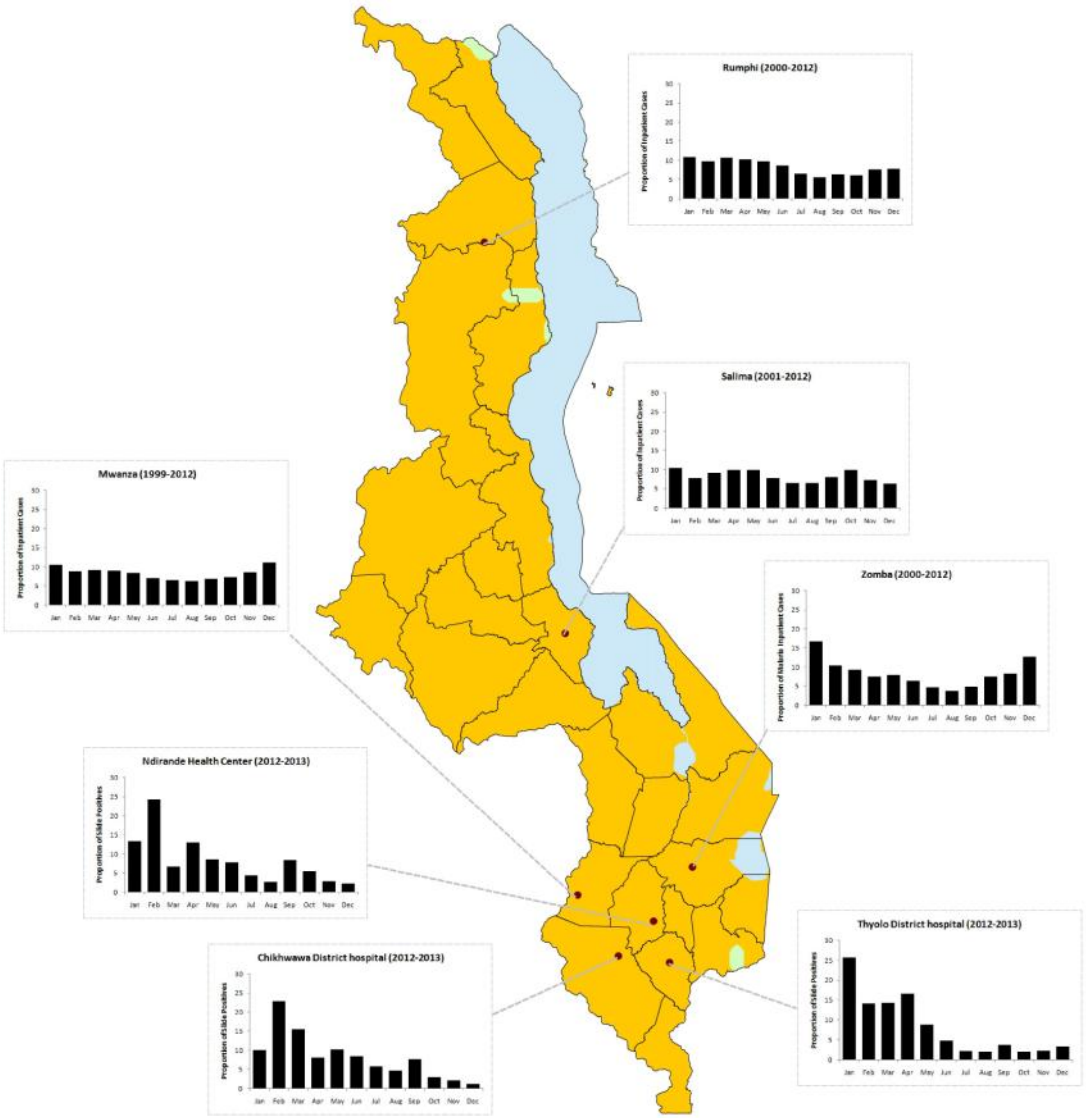
Here we have used daily rainfall estimates from the African Rainfall Estimates version 2 (RFE 2.0) dataset developed as a collaborative programme between NOAA's Climate Prediction centre (CPC), USAID/Famine Early Systems Network (FEWS). The RFE 2 gridded dataset combines weather gauge and satellite information on a near-real time basis to provide daily rainfall estimates over the African continent and is archived from January 2002 at 10 km spatial resolution [NOAA CPC, 2001; Novella & Thiaw, 2012]. To match work done by Cairns and colleagues, we have selected daily-accumulated rainfall data between 2002 to 2009 per 10 km pixel to define the maximum percentage of the total annual rainfall occurring in a period of consecutive months (Figure 4.8). Using these metrics all of Malawi appears to be suited to SMC strategies [Cairns et al., 2012].

Figure 4.8: Areas where 60% of annual rainfall falls within 3 continuous months (orange)

However, there is a sense that SMC would not be suitable in Malawi [D Ali, personal communication]. Malawi is coursed by perennial streams and rivers and the population located close to the lake experience transmission throughout the year. We have re-examined hospital admission data and slide positivity data from selected sites shown in Figure 4.9. These data

suggest that acute seasonal malaria is not as marked as might be expected from rainfall patterns. A different seasonal clinical pattern to the one predicted by Cairns et al. (2012) is seen and highlights the need to triangulate data in every country beyond simple rainfall pattern measurements. While there are rainfall-led patterns of risk these are not sufficiently temporally concentrated to signal the use of SMC in Malawi.

Figure 4.9: Monthly percentage of annual malaria paediatric admission data at four hospitals (Rumphi, Salima, Mwanza and Zomba) between 2000 and 2012 (Section 4.7) and three sites in southern Malawi (Thyolo, Chikwawa & Ndirande) where slide positivity collected monthly from febrile patients 2012-2013 [Blantyre Malaria Project, unpublished data].



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Chapter 5

Dominant malaria vectors in Malawi

5.1 Background

Africa is home to the most effective and efficient vectors of human malaria [Coluzzi, 1984]: *An. Gambiae s.s*, with its sibling, *An. arabiensis* [Coetzee, 2004; White, 1974], both form part of the *An. gambiae* complex which also includes the salt water tolerant, coastal species *An. melas* and *An. merus* [Gillies & Coetzee, 1987; Gillies & DeMeillon, 1968; Harbach, 2004; White, 1974]. Other members of the *An. gambiae* Giles complex are not regarded as dominant vectors because of their restricted, focal (*An. bwambae* [White, 1985]) or zoophilic nature (*An. quadriannulatus* A and *An. quadriannulatus* B [Coluzzi, 1984]), or because they cannot, by themselves, sustain malaria transmission in an area. In addition to the four dominant vector species (DVS) within the *An. gambiae* complex, large parts of Africa are also home to other DVS including the *An. funestus* Giles, *An. nili* and *An. moucheti*. Others such as *An. rivulorum, An. coustani and An. pharoensis,* although not considered DVS in Africa, appear to play a significant minor role as weaker, but nevertheless important vectors, in some selected areas [Kawada et al., 2012; Mwangangi et al., 2013; Wilkes et al., 1996].

All national malaria control programmes across Africa implement interventions aimed at reducing human exposure to infectious malaria vectors. These include insecticides on mosquito nets, applications of residual insecticides on household walls, or the targeting of larval stages of vectors to reduce vector abundance, survival and/or human-feeding frequency. However, the distribution of vector composition linked to their intrinsic behavioural bionomics and their resistance to currently available insecticides remains largely unknown, or under-emphasized, when planning vector control on national scales. Vector resistance to insecticides and behavioural adaptive changes accompanied by changing vector biodiversity pose real challenges to the future effectiveness of currently used vector control strategies [Ferguson et al., 2010; Gatton et al., 2013; Pates & Curtis, 2005; Ranson et al., 2011]. Furthermore, a lack of reliable entomological monitoring systems that capture all major relevant phenotypes and their effect on vector population dynamics on national scales limit capacity of malaria control programs to manage ongoing vector control efforts or adapt to changing vector behaviour and insecticide susceptibility [Govella et al., 2013].

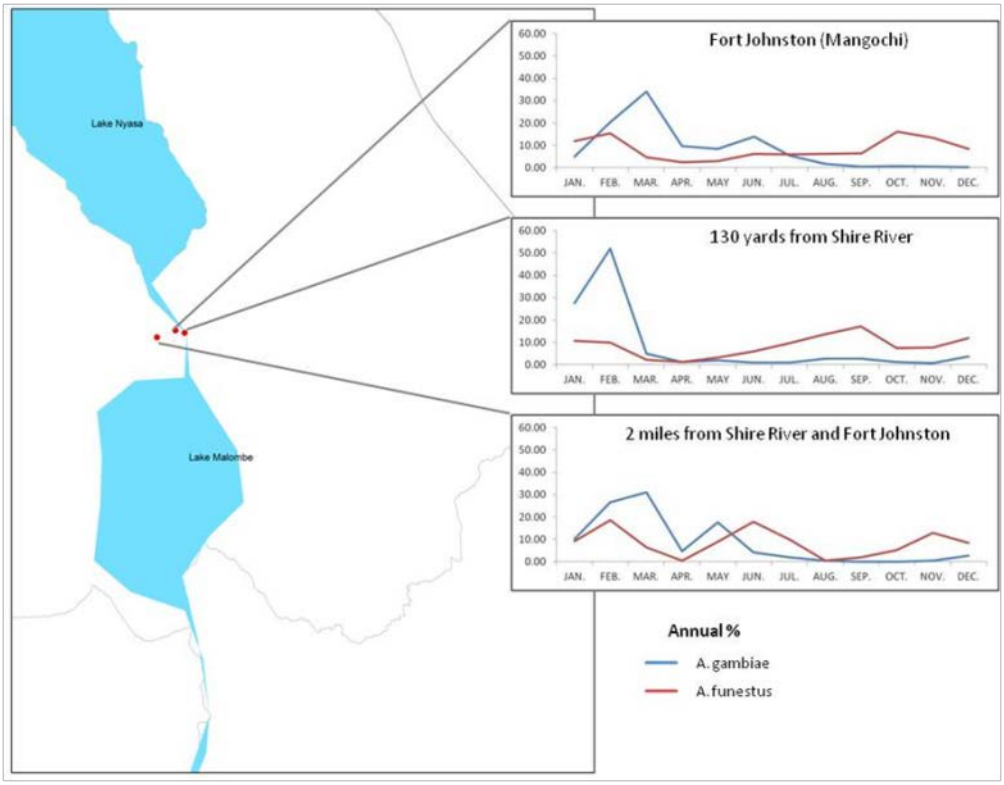
5.2 Historical vector surveillance

In 1921, WA Lamborn OBE, returned from German East Africa to Malawi where he became the Government entomologist until he retired from service, after an attachment to the army, in 1941. His extremely detailed annual reports were primarily focused on the descriptions and control of *Glossina* for sleeping sickness eradication. His first observations on malaria vectors in the protectorate were made in 1925. Here he described along the lake shores and lower altitudes a very seasonal occurrence of *Anopheles costalis* [Gambiae] "*...this anopheline was almost absent in the lower levels in the dry season but was overwhelmingly abundant by the late rains*" and *An. funestus*. At higher altitudes (Chowe 915 mASL) the dominant vector was *An. rhodesiensis* while *An. pretoriensis*, *An. funestus* and *An. gambiae* were rare. At even higher altitudes, at Dowa 1160 mASL), he was not able to locate any anophelines [Nyasaland Protectorate, 1925]. *An. rhodesiensis*, a day biting mosquito, was the subject of much

investigation and experimentation as a possible vector by Lamborn [Nyasaland Protectorate, 1938].

The acutely seasonal abundance of vectors was documented by Lamborn and he wondered where the mosquitoes went during the dry drought seasons in the hill regions. In May 1929, across the hills of the Shire Valley, he recorded 22 *An. gambiae*, 214 *An. funestus* and six *An. rhodesiensis* Theo adult females but not a single adult or larval stage in October and November the same year in the same locations (Figure 5.1) [Nyasaland Protectorate, 1925; Lamborn, 1925]. These seasonal patterns and differences between *An. gambiae* sibling species and *An. funestsus* were very similar to those described 70 years later in neighboring areas in Chikhwawa district [Mzilahowa et al., 2012]

Figure 5.1: Seasonal abundance of *An. gambiae s.l* and *An. funestus* in 1925 in Shire Valley [reproduced from Lamborn, 1925]



Cheyabejara et al. (1974) undertook a rapid entomological assessment at 27 sites across Malawi as part of a review of the malaria situation during a WHO mission in November 1973. The two most dominant vectors, as recorded during household spray catches and larval searches, were *An. gambiae* s.l and *An. funestus*. Other species identified as possible secondary, much more minor vectors included *An. rivilorum* (part of funestus complex), *An. rufipes*, *An. demeilioni*, *An. marshalli*, *An. maculipalpis*, *An. squamosus*, *An. zeimani* and [Cheyabejara et al., 1974]. Very few entomological investigations were undertaken, if any, during the 1980s, and it was not until 1991-1992 that reference is made to the dominance of *An. funestus*, *An. arabiensis* and *An.*

gambiae s.s from studies undertaken at 14 sites across Mangochi and Nsange districts; *An. gambiae* s.s. was found at only one site [Hawley et al., 1992]. The sporozoite infection rates ranged from 2 – 5 %, most blood meals were identified as emanating from the human host and the average Entomological Inoculation Rates (EIRs) were estimated to between 16 to 27 infective bites/person/year, although extrapolated from dry season investigations [Hawley et al., 1992].

5.3 Vector data assembly

The notion of mapping vector species was resurrected during the mid 1990s as part of the MARA/ARMA project [Coetzee et al., 2000]. There have been several recent attempts to model the distributions of DVS in Africa using sparse data and climatic determinants notably, temperature, soil moisture and other environmental drivers of vector species presence and abundance [Lindsay et al., 1998; Moffett et al., 2007; Sinka et al., 2010; Lunde et al., 2013a; Lunde et al. 2013b]. These model predictions have used different statistical approaches and different data sets and are hard to systematically compare.

The coincidental growth of geo-located databases of vector species has, however, provided some unique resources for countries to access, augment and adapt to local planning needs; notably AnoBase [http://skonops.imbb.forth.gr/], VectorBase [https://www.vectorbase.org], MARA/ARMA collaboration [https://www.mara.org.za], Walter Reed Biosystematics Unit (WRBU) Mosquito Catalog [http://www.mosquitocatalog.org], Malaria Atlas Project (MAP) [http://www.map.ox.ac.uk], and the Disease Vectors database [https://www.diseasevectors.org]. The database on insecticide resistance, the Arthropod Pesticide Resistance Database (APRD) [http://www.pesticideresistance.org/], covers a large variety of arthropods, but only reports instances of occurrence of resistance, without any precision on geographic location nor actual data. The African Network for Vector Resistance (ANVR) was established in 2000, and amongst its objectives was the important goal of improving dissemination of resistance data [ANVR, 2005]. Over the last 10 years, a database has been developed to store the results of resistance monitoring activities by ANVR members. This database has now been integrated for open access with the launch of IRBase [Dialynas et al., 2009].

The most comprehensive available, geo-coded species-specific data is currently held on the MAP database [Sinka et al., 2010]. We also re-ran on-line searches of medical literature databases including PubMed, Google Scholar and Web of Science using search terms “Anopheles AND Malawi“ for all study publications after December 1970 and post the last searches undertaken by MAP. Finally, we contacted a number of research and control partners working in Malawi to assemble unpublished information on DVS occurrence and resistance monitoring; notably those working on IRS projects supported by PMI, the Malaria Alert Centre (MAC) and the International Centers of Excellence for Malaria Research (ICEMR) which is under the College of Medicine and the Innovative Vector Control Consortium (IVCC).

Each study site was geo-coded using methods described in Section 4.3.3. Data abstracted from each report included the start and end of the entomological survey, species identified at complex or species member levels, methods of sampling (animal bait catches, bed net traps, CDC light traps, human landing catches, indoor resting searches, pyrethrum spray catches, exit traps, larval searches), methods of species detection (PCR, Chromosome Banding Sequences, Morphology, DNA probes) and the full citation source. For older survey data, it is recognized that there is a degree of taxonomic ambiguity, for example the *An. gambiae* complex was only fully categorised in 1998 and *An. quadrimaculatus* species B designated a separate species after this date [Harbach, 2004; Hunt et al., 1998]; furthermore the exact composition of the *An. funestus* complex remains unclear [Costantini et al., 1999], although sibling species from the complex have been described in Malawi [Spillings et al., 2009; Vezenegho et al., 2013]. In addition, we developed a database on recorded insecticide susceptibility testing.

5.4 Species occurrence and bionomics

The final database contained 145 site/time specific reports of DVS occurrence. The majority of information was provided from unpublished sources (56%) and not available on current open access databases [www.map.ox.ac.uk]. We were able to geo-locate all survey locations. The earliest reports were in 1973 and the most recent were in 2013. 98 (68%) survey-site locations were sampled in or after 2000. Sibling species composition of the *An. gambiae* complex was not provided for 38 (23%) of survey locations where the complex was identified and these are therefore not shown in Figures 5.2a and 5.2b. Figures 5.2 show the distribution of the sampled DVS since 1973[20] and a brief description of their classical bionomics.

The *Anopheles funestus* group is ubiquitous across Malawi. The dominance of *An. funestus* in the southern region exemplified by detailed studies in Chikwawa district in 2002; of all *Anopheles* collected 77% were *An. funestus*, 11% *An. arabiensis* and only 2% *An. gambiae* s.s. [Merelo-Lobo et al., 2003]. Using PCR, recent studies at sites across Karonga district identified several sibling species of the *An. funestus* group and *An. rivulorum*, all dominant indoor feeding vectors, and new *An. funestus*-like vector [Vezenegho et al., 2013].

[20] With a complete spatial and temporal database it is possible to develop a more mathematical approach to defining species distribution in Malawi with the geo-located species data and Boosted Trees Regression methods [Elith et al., 2008].

Figure 5.2: Maps of *An. gambiae s.s.*, *An. arabiensis*, and *An. funestus* locations sampled across Malawi between 1973 and 2013 and their bionomics

***a*. *Anopheles gambiae s.s*:** *Anopheles gambiae* s.s larvae typically inhabit sunlit, shallow, temporary bodies of fresh water such as round depressions, puddles, pools and hoof prints. This aspect of their bionomics may allow members of the *An. gambiae* complex to avoid most predators, and the larvae are able to develop very quickly (circa 6 days from egg to adult under optimal conditions). *An. gambiae* s.s has been reported from habitats containing floating and submerged algae, emergent grass, rice, or 'short plants' in roadside ditches and from sites devoid of any vegetation. It is considered to be highly anthropophilic, with many studies finding a marked preference for human hosts, typically feeds late at night and is often described as an endophagic and endophilic species, i.e. biting and resting mostly indoors. The species is considered to be one of the most efficient vectors of malaria in the world.

b. Anopheles arabiensis: *Anopheles arabiensis* is considered a species of dry, savannah environments or sparse woodland. Evidence is growing of a more ubiquitous range of *An. arabiensis* across Africa. Its larval habitats are generally small, temporary, sunlit, clear and shallow fresh water pools, although *An. arabiensis* is able to utilize a variety of habitats including slow flowing, partially shaded streams, large and small natural and man-made habitats, turbid waters and there are reports of larval identification in brackish habitats. *Anopheles arabiensis* is described as a zoophilic, exophagic and exophilic species but has a wide range of feeding and resting patterns, depending on geographical location. This behavioural plasticity allows *An. arabiensis* to adapt quickly to counter indoor residual spraying control as well as insecticide-treated bednets showing behavioural avoidance of sprayed surfaces depending on the type of insecticide used. Blood feeding times also vary in frequency; peak evening biting times can begin in the early evening (19:00) or early morning (03:00). This species usually has a greater tendency than *An. gambiae s.s.* to bite animals and rest outdoors.

c. Anopheles funestus: A typical *An. funestus* larval habitat is a large, permanent or semi-permanent body of fresh water with emergent vegetation, such as swamps, large ponds and lake edges. *An. funestus* is a highly adaptable species, allowing it to occupy and maintain its wide distribution and utilise and conform to the many habitats and climatic conditions. *An. funestus* is considered to be highly anthropophilic with a late-night biting pattern (after 22.00 hours). Endophilic resting behaviour is also commonly reported, and these characteristics are responsible for rapid disappearance of this vector following expanded indoor residual spraying and insecticide-treated nets. Compared to other dominant vector species in Africa, *An. funestus* shows fairly consistent behaviour (generally anthropophilic and endophilic) throughout its range. In the absence of insecticide use, the endophilic resting behaviour of *An. funestus* combined with a relatively high longevity, makes it as good a vector, or better in some areas, as *An. gambiae s.s*.

5.5 Resistance

The two single base substitutions in the sodium channel commonly referred to as knockdown resistance (*kdr*) mutations confer cross-resistance to DDT and pyrethroids and are associated with resistance in *An. gambiae* s.l populations [Ranson et al., 2011]. The gene mainly responsible, the *1014F* alleles (West), are at high frequency in West Africa [Santolamazza et al., 2008]. Presently, 40 malaria endemic countries have reported pyrethroid resistance [Gatton et al., 2013; WHO, 2012]. Recent studies outlined evidence to support claims of behavioural changes with *An. gambiae, An. funestus* and other dominant species to reflect exophagic feeding preferences. LLINs and IRS act as contact irritants driving vectors to rest outside human dwellings. Anthropophilic species such as *An. gambiae* complex are reported more frequently biting outdoors during the early hours of the evening when people are usually out socialising [Mwangangi et al., 2013; Gatton et al. 2013].

There is growing evidence of escalating insecticide resistance among anopheline vectors in Malawi (Figure 5.1). In 2002, bioassay results showed that *An. arabiensis* was susceptible to pyrethroids and organophosphate but exhibited reduced susceptibility to DDT in Chikwawa district [Mzilahowa et al., 2008]. Widespread resistance to pyrethroids (deltamethrin, permethin and lambdacyhalothrin) and bendiocarb (carbamate) was described among the *An. funestus* group by 2009 Nkhotakota, Chikwawa, Mangochi and Zomba districts) [Wondji et al., 2009], including Likoma Island [Hunt et al., 2010], but variable sensitivity to organochlorines (DDT) at several sites [Wondji et al., 2012]. Likewise there were variable results between insecticide classes between districts for results using *An. gambiae* s.l. [Wondji et al., 2012] but definite evidence of resistance among *An. gambiae* s.l at Davide (Nsanje district), Nchalo (Chikwawa district) [Wondji et al., 2012] and Liwonde National Park [Pemba et al., 2009]. Resistance in the *An. funestus* group was identified in 2010 in Karonga district to pyrethroids (Delatamethrin) and carbamates (Bendiocarb) but not organochlorines (DDT) [Vezenegho et al., 2013].

Further studies between 2010 and 2011 across the country continue to confirm reduced susceptibility among the *An. funestus* group to pyrethroids (lambdacyhalothrin, deltamethrin and permethrin) in Chikwawa, Mangochi, Dedza, Salima, Nkhotakota and Nkahata Bay districts [unpublished data]. The Organophosphate, malathion, was however, fully sensitive when tested against the *An. funestus* group in these districts and the *An. gambiae* complex, although less prolific, showed higher sensitivity against all classes in most districts. Behavioural tolerance studies are currently underway at MAC in two districts of Karonga and Nkhata Bay in northern Malawi to explore phenotypic changes in vector host preferences or feeding time changes in the face of sustained IRS or ITN use.

As a result of this high level of insecticide resistance mainly to pyrethroids, there has been debate on which insecticides to use for IRS. In 2011, the NMCP with support from PMI decided to use pirimiphos-methyl (an organophosphate) for IRS in Nkhotakota district to replace pyrethroids, however the costs of this insecticide led to the withdrawal of PMI support to Nkhotakota district. PMI did continue to provide technical assistance to the program, although

the program opted not to continue to spray in Nkhotakota without PMI support. The NMCP continues to use pyrethroids across this country. In 2013, the plan was to use alpha-cypermethrin for IRS in Karonga, Salima and Chikwawa districts against high pyrethroid resistance in *An. funestus* populations seen in Chikwawa and Salima districts.

Table 5.1: Evidence of insecticide resistance among anopheline vectors between 2007-2012

District	Start	End	Insecticide Class	Insecticide Type	Vector Species	Resistance Status
Balaka	2009	2009	Pyrethroids	Deltamethrin	gambiae sl	Confirmed resistance
Blantyre	2010	2011	Pyrethroids	Lamdacyhalothrin	funestus	Sucpetibile
	2010	2011	Pyrethroids	Permethrin	gambiae sl	Possible resistance
Chikwakwa	2007	2007	Organochlorines	DDT	gambiae sl	Sucpetibile
	2007	2007	Organophosphates	Malathion	gambiae sl	Sucpetibile
	2007	2007	Pyrethroids	Permethrin	gambiae sl	Sucpetibile
	2007	2007	Pyrethroids	Deltamethrin	gambiae sl	Sucpetibile
	2007	2007	Organochlorines	DDT	gambiae sl	Confirmed resistance
	2009	2010	Carbamates	Bendiocarb	gambiae sl	Sucpetibile
	2009	2010	Pyrethroids	Deltamethrin	gambiae sl	Sucpetibile
	2009	2010	Pyrethroids	Lamdacyhalothrin	gambiae sl	Confirmed resistance
	2009	2010	Pyrethroids	Permethrin	gambiae sl	Possible resistance
	2009	2010	Organophosphates	Primiphosmethyl	gambiae sl	Sucpetibile
	2009	2010	Carbamates	Bendiocarb	funestus	Confirmed resistance
	2009	2010	Pyrethroids	Deltamethrin	funestus	Confirmed resistance
	2009	2010	Pyrethroids	Permethrin	funestus	Confirmed resistance
	2009	2010	Pyrethroids	Lamdacyhalothrin	funestus	Sucpetibile
	2009	2010	Organochlorines	DDT	funestus	Confirmed resistance
	2010	2011	Organophosphates	Malathion	funestus	Sucpetibile
	2010	2011	Pyrethroids	Lamdacyhalothrin	funestus	Possible resistance
	2010	2011	Pyrethroids	Permethrin	funestus	Possible resistance
	2010	2011	Carbamates	Bendiocarb	funestus	Confirmed resistance
	2012	2012	Organochlorines	DDT	funestus	Sucpetibile
	2012	2012	Pyrethroids	Permethrin	funestus	Confirmed resistance
	2012	2012	Carbamates	Propoxur	funestus	Confirmed resistance
	2012	2012	Organochlorines	Dieldrin	funestus	Possible resistance
	2012	2012	Organophosphates	Fenithrothion	funestus	Sucpetibile
Dedza	1973	1973	Organochlorines	DDT	funestus	Possible resistance
	2010	2011	Pyrethroids	Permethrin	funestus	Confirmed resistance
	2010	2011	Pyrethroids	Deltamethrin	funestus	Confirmed resistance
	2010	2011	Pyrethroids	Lamdacyhalothrin	gambiae sl	Confirmed resistance
	2010	2011	Carbamates	Bendiocarb	funestus	Confirmed resistance
	2010	2011	Organophosphates	Malathion	funestus	Sucpetibile
Karonga	2010	2011	Pyrethroids	Lamdacyhalothrin	gambiae sl	Sucpetibile
	2010	2011	Carbamates	Bendiocarb	funestus	Confirmed resistance
	2010	2011	Pyrethroids	Deltamethrin	funestus	Confirmed resistance
	2010	2011	Organochlorines	DDT	funestus	Sucpetibile
	2011	2011	Pyrethroids	Permethrin	gambiae sl	Sucpetibile
	2011	2011	Pyrethroids	Deltamethrin	gambiae sl	Sucpetibile
	2011	2011	Organochlorines	DDT	gambiae sl	Sucpetibile
	2011	2012	Carbamates	Propoxur	funestus	Confirmed resistance
	2011	2012	Pyrethroids	Lamdacyhalothrin	funestus	Confirmed resistance
	2011	2012	Pyrethroids	Permethrin	funestus	Confirmed resistance
	2011	2012	Organophosphates	Malathion	funestus	Confirmed resistance
	2011	2012	Organochlorines	DDT	funestus	Confirmed resistance
	2011	2012	Carbamates	Bendiocarb	gambiae sl	Confirmed resistance
	2011	2012	Pyrethroids	Permethrin	gambiae sl	Confirmed resistance
Kasungu	1973	1973	Organochlorines	DDT	gambiae sl	Possible resistance

District	Start	End	Insecticide Class	Insecticide Type	Vector Species	Resistance Status
Likoma	2010	2010	Carbamates	Bendiocarb	funestus	Confirmed resistance
	2010	2010	Pyrethroids	Deltamethrin	funestus	Confirmed resistance
	2010	2010	Pyrethroids	Permethrin	funestus	Confirmed resistance
	2010	2010	Carbamates	Propoxur	funestus	Confirmed resistance
	2010	2010	Organophosphates	Malathion	funestus	Sucpetibile
	2010	2010	Organophosphates	Fenithrothion	funestus	Sucpetibile
	2010	2010	Organophosphates	Primiphosmethyl	funestus	Possible resistance
	2010	2010	Organochlorines	DDT	funestus	Sucpetibile
	2010	2010	Organochlorines	Dieldrin	funestus	Sucpetibile
Machinga	2009	2009	Pyrethroids	Deltamethrin	gambiae sl	Possible resistance
	2010	2011	Pyrethroids	Permethrin	funestus	Confirmed resistance
Mangochi	2009	2010	Pyrethroids	Permethrin	funestus	Confirmed resistance
	2010	2011	Organophosphates	Malathion	funestus	Sucpetibile
	2010	2011	Pyrethroids	Deltamethrin	funestus	Confirmed resistance
	2010	2011	Pyrethroids	Lamdacyhalothrin	funestus	Confirmed resistance
	2010	2011	Carbamates	Bendiocarb	funestus	Sucpetibile
Mchinji	2009	2010	Pyrethroids	Permethrin	gambiae sl	Possible resistance
Ntchisi	2010	2011	Organophosphates	Primiphosmethyl	funestus	Sucpetibile
Nkhata Bay	2009	2010	Pyrethroids	Deltamethrin	funestus	Sucpetibile
	2009	2010	Pyrethroids	Deltamethrin	gambiae sl	Sucpetibile
	2009	2010	Pyrethroids	Lamdacyhalothrin	funestus	Confirmed resistance
	2009	2010	Pyrethroids	Permethrin	funestus	Confirmed resistance
	2009	2010	Pyrethroids	Permethrin	gambiae sl	Sucpetibile
	2009	2010	Organochlorines	DDT	funestus	Confirmed resistance
	2009	2010	Organochlorines	DDT	gambiae sl	Sucpetibile
	2010	2011	Carbamates	Propoxur	funestus	Sucpetibile
Nkhotakota	2009	2010	Carbamates	Bendiocarb	funestus	Confirmed resistance
	2009	2010	Pyrethroids	Deltamethrin	funestus	Confirmed resistance
	2009	2010	Pyrethroids	Lamdacyhalothrin	funestus	Confirmed resistance
	2009	2010	Pyrethroids	Permethrin	funestus	Confirmed resistance
	2009	2010	Organochlorines	DDT	funestus	Sucpetibile
	2010	2011	Organophosphates	Malathion	funestus	Sucpetibile
Nsanje	2009	2010	Pyrethroids	Permethrin	gambiae sl	Confirmed resistance
Rumphi	2012	2012	Pyrethroids	Lamdacyhalothrin	funestus	Confirmed resistance
	2012	2012	Carbamates	Propoxur	funestus	Confirmed resistance
	2012	2012	Pyrethroids	Permethrin	funestus	Confirmed resistance
	2012	2012	Pyrethroids	Deltamethrin	funestus	Confirmed resistance
	2012	2012	Carbamates	Bendiocarb	funestus	Confirmed resistance
	2012	2012	Organophosphates	Malathion	funestus	Sucpetibile
	2012	2012	Organochlorines	DDT	funestus	Confirmed resistance
Salima	2009	2010	Pyrethroids	Permethrin	gambiae sl	Possible resistance
Zomba	2009	2010	Pyrethroids	Permethrin	funestus	Possible resistance

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Chapter 6

Summary, conclusions and recomendations

6.1 Background

The current global financial crisis will constrain international donors and national governments to provide long-term malaria control funding. This has led to a call for a much stronger evidence-based business case to effectively utilise limited resources. Such evidence platforms require layers of information in time and in space.

The lack of any systematic malaria epidemiological intelligence in Malawi was highlighted during the malaria programme review in 2010. In this report we address key knowledge gaps though a synthesis of data on malaria infection, dominant vector species, resistance, and intervention coverage. These data, and the products of modelled data, we hope will provide the context upon which the Malawian government can build its future control strategies and access development assistance.

6.2 Malawi's malaria epidemiology

We have assembled geo-coded repositories of community-based parasite prevalence and dominant vector species occurrence. Parasite prevalence data have been used within novel model-based geo-statistical frameworks to predict the intensity of malaria transmission in 2000 and 2010 across each of the 28 health districts used for sub-national planning.

Predictions for 2000 and 2010 show that the transmission intensity of *P. falciparum* is largely meso-endemic or higher (*Pf*PR_{2-10} >= 50%) across the country with some important variance within this range. The intensity of *P. falciparum* transmission appears not to have changed significantly despite a decade's investment in transmission control (Figures 4.3a and 4.3b) and remains very similar to patterns of malaria risk described since the 1930s (Section 3.2).

The mean population weighted childhood parasite prevalence (PA*Pf*PR_{2-10}) across Malawi in 2000 was 38% and in 2010 it was 43%. In 2010, we predicted that 28% of the population, were living in areas where the *Pf*PR_{2-10} was 50% or greater compared to 17% in 2000. The most intense transmission conditions are prevalent along Lake Malawi in the Central and Southern regions (Figure 4.3c). Few districts have realized a reduction in malaria risk during the 2000-2010 interval.

The lack of any substantial reduction in parasite exposure over the decade 2000-2010 is supported by an examination of hospital admission data (Section 4.7; Figure 4.7) and less perfect routine HMIS data (Section 4.7; Figure 4.5).

Why has there been so little change? This is beyond the scope of the present descriptive report but is a fundamental question that requires a careful handling of data on actual coverage of vector control, changing access to efficacious treatments, emerging resistance in vectors to insecticides, household economic data and climatology. What we have presented in this report should form the substrate for further enquiry by national academics and partners (**Recommendation 1**).

The current focus of control is on the most pathogenic of the human malarias in Africa, *P. falciparum*. However, Malawi has an interesting epidemiology of other species including the definitive presence of *P. vivax* transmission (Section 4.8) and evidence of a declining prevalence of *P. malariae* (Section 4.8). The co-infection, epidemiology and clinical profiles of these "other" parasites deserve further investigation (**Recommendation 2**).

The significant, cosmopolitan presence of *Anopheles funestus* group has been described across Malawi (Figure 5.2c). Understanding the ecology of a mosquito species and its behaviour has important implications for the success and or failure of control. Malawi is data poor with respect to detailed inventories of DVS and more importantly descriptions of their bionomics and how these might be changing in the face of wide-spread insecticide use.

Insecticide resistance have been a seen as threats to sustainable, effective control for many years. A point of concern today is that resistance has now been documented for pyrethroid, organochloride and carbamate insecticide classes across many districts in Malawi (Section 5.5; Table 5.1). The database assembled and Chapter 5 will be shared with NMCP to assist in the planning of future vector surveillance and resistance monitoring and serve as a template database for further updates.

Detailed investigations should be established longitudinally of vector species composition, bionomics and the molecular and bioassay susceptibility testing of insecticides at fixed sentinel sites across Malawi (**Recommendation 3**).

The seasonality of malaria transmission in Malawi had been well described since the 1930s. Using rainfall concentration indices developed to support the targeting of Seasonal Malaria Chemoprevention (SMC) suggest that the entire country would be suited to this approach to disease prevention in childhood. However, on further analysis (Section 4.9), it appears that despite acutely seasonal rainfall, clinical disease is more evenly spread across a 12 month cycle (Figure 4.9), presumably because of the presence of perennial breeding sites along the lake shore and river basins. This highlights that one index does not fit all situations and for SMC the 60% rainfall in three continuous months may not have equivalent applications in Southern Africa compared to the Sahel. It would be advisable to examine in more detail the seasonality of transmission and disease concentration before recommending SMC as a control option in Malawi (**Recommendation 4**).

6.3 Changing patterns of intervention coverage

The focus of national malaria strategies for the first decade after 1990 was on improving treatment and access to treatment. Over the years Malawi has employed various initiatives to improve treatment access including expanding IMCI and community based IMCI and iCCM (Section 3.7.6.3), expanding retail sector access (Section 3.7.6.3) and attempts to enhance drug supply and training of formal health service personnel in facilities nationwide (Section 3.7.6.2 &

3.7.6.3). Despite these initiatives to improve treatment access, the proportion of fevers treated promptly with an ACT remains low (Section 3.7.6.3).

Malawi was the first country in Africa to abandon failing CQ as a first line therapeutic in favour of SP, but was one of the last countries to abandon SP in favour of an ACT, only fully implemented as a policy change in 2008 (Section 3.7.6.2). In 2011, there was a shift from presumptive treatment to diagnosis and treatment but this is characterized by poor coverage (Section 3.7.6.4 & 3.8.4).

Social marketing and private sector distributions of ITN dominated the delivery approaches for this important vector control strategy up to 2003, when heavily subsidized ITN were made available through health facilities (Section 3.6.3). ITN were later offered free of charge to children and pregnant women from 2007. In 2006/7 free-mass campaigns were used to begin to improve coverage nationwide, notably amongst the poorest (Section 3.7.3.1). In 2008, the first nationwide free-mass campaign was launched.

We have used national household survey data within a small area estimation model (Section 3.7.3.2; Annex A.1) to examine the changes in reported ITN/LLIN use of all persons living in each of the 28 heath districts between 2000 and 2010 (Figure 3.7). Changing coverage from 2000 to 2010 Progressive but slow. By 2012, things had changed dramatically (Figure 3.9) however, only six districts had more than 50% of their inhabitants protected by an ITN after the mass campaign in 2012 (Karonga, Nkhotakota, Salima, Ntcheu, Neno, Phalombe) four of which were part of the initial pilot for universal coverage in 2010 to 2011. It is important to point out that the 2012 MIS was undertaken in April and May, while the Mass campaign was carried out in May to June the same year so coverage following the mass campaign is likely t be higher but there is no data to make these predictions. Nevertheless, operational and programmatic research is urgently required to understand why individuals are unprotected by an LLIN in Malawi (**Recommendation 5**).

IRS was first launched in a few areas of Malawi using BHC wettable powder (Gammexane) in 1956, but this campaign lasted only a few years owing to population resistance to spray teams, funds running out and insecticide resistance (Section 3.3). IRS returned as a malaria control tool in 2007 in one district using the pyrethroid lambda-cyhalothrin (Section 3.7.3.3). However, as was the case fifty years earlier, resistance has emerged in the vector population to most classes of insecticides, except organophosphates (Section 5.5) and funds are dwindling to sustain any further expansion. To date no decisions have been made on the future of IRS in Malawi. All available evidence on transmission impact, resistance and costs of combined versus single intervention (LLIN and/or IRS) must be tabled for an urgent evidence based review (**Recommendation 6**).

6.4 Attributing intervention coverage to change in burden

The political and donor commitment to malaria control in Malawi has been remarkable. The fact that ITN coverage in young children has increased from 15% in 2004 to 56% by 2012 is a

substantive achievement. Childhood mortality has also declined over the last decade (Figure 2.3).

The Lives Saved Tool (LiST) model makes various assumptions about the fraction of all deaths due to malaria, based on very few verbal autopsy studies, and impact size based on a few randomized control trials in Africa [Korenromp, 2012]. It does not account for the coverage effect-sizes necessary to achieve reductions in disease incidence nor the difference in effect size bade don starting transmission intensity [Smith et al., 2009; Griffin et al., 2010, Snow & Marsh, 2002]. We have not been able to show any significant effects of an incomplete ITN coverage on either transmission intensity or hospitalization. Two things are worth noting: a) the impact of scaled ITN coverage on disease and transmission might only become apparent post 2013[21]; and b) whatever the effects, ITN and/or IRS coverage must increase substantially to witness substantive changes in both transmission and disease [Smith et al., 2009; Griffin et al., 2010].

6.5 Monitoring future change

6.5.1 Maintaining national malaria data archives

A huge effort has gone into identifying malariometric survey data undertaken over the last 30 years in Malawi. These data have been carefully checked, geo-coded and stored in relevant databases. These represent important national resources for future work and investigations by control and academic communities within Malawi. The metadata describing these databases is provided as part of this report. Information is not static, data gaps exist, and new data are needed to chart the changing malaria epidemiology.

Sustaining a nationwide network of parasite, vectors and resistance surveillance needs to be prioritised within the NMCP. Warehousing, up-dating and checking further iterations of the data and creating access to the data demands a commitment and capacity within the NMCP. Creating this dedicated capacity requires greater investment in skills, equipment and finances. Ways in which this might be created as a national academic and MoH partnership should be explored with bi-lateral donor agencies. A plan of action should be developed, costed and institutionalized to make this happen (**Recommendation 7**).

6.5.2 Monitoring the future epidemiological transition

During the 1930s the colonial government in Malawi invested in undertaking detailed investigations of the health status of its population, often as part of what we could call today "sentinel sites" (Section 3.2). It was not always clear, however, how this medical data were used to guide health policy. Today there are several sentinel sites operating in various capacities including the Karonga DSS, Chikwawa rMIS, MAC sentinels, PMI sentinels and hospital data sites (Sections 3.7.5, 3.7.6.1, 4.5). As was the case over 80 years ago, it is not clear how these rich

[21] There is a tentative suggestion that disease risks are beginning to change in 2012 (Section 4.7; Figures 4.7)

data sites provide information in a harmonized way to guide and shape national health policy. This requires a strong leadership from the NMCP to establish mechanisms and a forum to share data, discuss the implications of observations and set new operational research agendas (**Recommendation 8**).

We have made our predictions in this report to 2010, a decade following the launch of RBM[22]. Predictions after 2010, for example to 2014/2015, are necessary but require much more data post-2010 for these to be of adequate precision. The MIS planned for 2014 will provide additional data to predict years after 2010, and further improved if malaria parasitaemia measures are included in the DHS planned for 2015 (**Recommendation 9**).

Although both the MIS and the DHS provide valuable information on infection prevalence and intervention coverage at national scales, they are inadequately designed to provide reliable spatial data on the more granular needs of mapping infection risks or intervention coverage at district levels. National household sample surveys are also expensive. Cheaper and higher resolution sampling strategies are available and need further exploration, these include rapid sampling of school children[23] [Brooker et al., 2009; Gitonga et al., 2010; 2012], the possibilities of using data already generated as part of screening for malaria by the National Blood Transfusion Service and ensuring that there are no missed opportunities across other national surveys that might be targeted to measuring other sector important variables such as access to banking services[24], education or nutrition[25].

A plan of action to piggy-back other surveys, harness existing data from other sources such as the NTBS and develop more rapid school based surveys will guarantee more data and lower cost for future sub-national modelling exercises (**Recommendation 10**).

In an ideal world, a fully operational and complete HMIS would provide reliable estimates of disease risk per district in Malawi. However incomplete records are a common feature at the facility level and routine reporting systems often do not include all individuals. However the use

[22] To improve the signal and predictions for 2010, we have used the data from the 2012 MIS. In this respect the contemporary map does reflect the influence of 2012 MIS data on the 2010 estimates with the effect greater where the 2012 data dominates. Additionally, plots of the moving average annual *Pf*PR trend from the raw data do not shows a decreasing trend over the period 2010 and 2012.

[23] Undertaken in the 1930s in Malawi and resurrected as part of Save the Children surveys of school health in Malawi in 2012

[24] In Kenya, the Financial Services Deepening Trust mounted a large national, sample survey in 2009 to look at access to money and were requested to include questions on household ownership of ITNs. This cost the malaria programme only US$ 5000 and increased the amount of household data two-fold

[25] In Somalia, the Food and Agricultural Organizations food security surveys included RDTs for malaria as a rapid means of increasing malariomenric data using existing survey instruments and personnel working under difficult conditions in hard to reach areas. The opportunity cost was minimal and the result was Somalia is one of the most malaria data rich countries in the sub-region [Noor et al., 2012].

of IDSR and HMIS data from a relatively small country with only circa 600 health facilities can be improved substantially to what we have presented here (Figure 4.5).

Model based geo-statistics are designed to handle incomplete data in time and space. Recently work in Namibia has shown the utility of these methods through combinations of incomplete monthly data on malaria slide positivity, household survey data on health facility use during fevers, a geo-coded health facility data base and high resolution population density maps [Alegana et al., 2012; 2013]. These data exist for Malawi (Population Section 2.8, Health Facilities Section 2.10.3, reported data Section 4.7 and national household survey data) and similar modelling exercises are possible to improve the precision and reliability of routine data (**Recommendation 11**).

6.6 Future prospects

There is a strong political commitment from the President's office to control and eventually "eliminate" malaria. The President recently stated that "*More than ever, this is the time to renew our efforts to ensure that we reach each and every child, woman, and man in this country with these life-saving interventions. Malawi is poised to achieve its goals in this fight against malaria. I am counting upon all of us to reaffirm our commitment to making malaria a thing of the past in Malawi*" [RBM, 2013]. Because elimination has been voiced as a possible ambition, the NMCP recently convened a stakeholders meeting to discuss the possibility of creating malaria free zones in Malawi. Current data suggest that this is an ambitious target, any future elimination strategy will depend heavily on a credible epidemiological evidence platform, a technical feasibility assessment and a long-term financial plan [Moonen et al., 2010b].

Meanwhile, Malawi has committed itself to "*halve malaria mortality and morbidity by the year 2010 with further reduction of morbidity and mortality figures of 2001 by 75% by 2015".* The likelihood of achieving strategic ambitions depends critically on securing adequate finances to meet the commodity and implementation needs of these ambitions. Clearly Malawi still has a long way to go to achieve levels of intervention coverage likely to impact on transmission in most of the country. Substantial resources haves been targeted towards IRS and ITNS yet results show limited evidence of al reduction in infection prevalence but these data are weak and with limited contemporary data.

Over the next 5 to 10 years, the NMCP will have to create the business case for effective inclusion of malaria prevention and control, this needs data and data that feed into planning and into impact evaluation to track progress. Thus a culture of data driven solutions will become the new norm.

Some of the new strategies currently in the pipeline include parasitological diagnosis of all fevers, improving access to rectal artesunate for pre-admission severe malaria cases in hard to reach areas and the possible re-introduction of DDT. A recent parliamentary committee on health led to a helpful public debate on whether DDT should be considered for IRS. The South-East African Malaria Eradication Project, including the Federation was formed in 1959. A

particular threat to Southern Rhodesia's elimination ambitions were migrant entry points from Nyasaland and Portuguese East Africa (Mozambique). More recently, the notion of cross-border collaboration has been re-introduced by the RBM's Southern African Regional Network involving Malawi, Mozambique and Zambia [RBM, 2012]. The careful monitoring of cross-border threats is particular important if the future ambitious targets of sustained control or zoned elimination are to be achieved.

Effective planning of malaria control is critically dependent on a reliable understanding of the epidemiology and epidemiological transition of the disease which form the foundation of any effective national malaria strategy planning cycle. Any new targets or intervention strategies demand data. Malawi is poised to create a revived culture of national data ownership and use, to set the framework for future evidence-based evaluations and planning and provide the necessary leadership for current ambitions for sustained control and eventual elimination failing which it will be difficult to realise these ambitious targets.

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Annexes

Annex A.1: Survey data with information on ITN utilisation and Bayesian mapping procedures

A 1.1 Bayesian geo-additive regression models

The presentation of ITN coverage data is often limited only to the lowest sampling precision estimates of national surveys, districts in the case of Malawi. Here, we use the properties of intervention coverage at geo-coded cluster levels combined data within a regression framework using a geo-additive semi-parametric mixed model constructed within a Bayesian framework [Kammann & Wand, 2003]. A fully Bayesian approach based on Markov priors was employed that uses MCMC techniques for inference and model checking [Fahrmeir & Lang, 2001; Lang & Brezger, 2004] where the classical linear regression model forms are as follows

$$y_i = w_i'\gamma + \varepsilon_i, \qquad \varepsilon_i \sim N(0, \sigma^2), \qquad \text{(Equation A.1.1)}$$

for observations (y_i, w_i), $i = 1,....,n$, on a response variable *y* and a vector *w* of covariates assume that the mean $E(y_i | w_i)$ can be modeled through a *linear predictor* $w_i'\gamma$. In our application to ITN coverage no covariate was used. The geographical small-area information was given in form of a location variable *s*, indicating the areal unit to which predictions of ITN coverage are to be made. In our study, this geographical information is given by the health districts of Malawi. Attempts to include such small-area information using district-specific dummy-variables would in our case entail more than 100 dummy-variables and using this approach we would not assess spatial inter-dependence. The latter problem also cannot be resolved through conventional multilevel modeling using uncorrelated random effects [Goldstein, 1999]. It is reasonable to assume that areas close to each other are more similar than areas far apart, so that spatially correlated random effects are required.

To overcome these difficulties, we replace the strictly linear predictor through a *geo-additive predictor*, leading to the *geo-additive regression model*

$$y_i = f_{spat}(s_i) + \varepsilon_i \qquad \text{(Equation A.1.2)}$$

here, f_{spat} is the spatial effect $s_i \in \{1,...,S\}$ labelling the districts in Malawi. Regression models with predictors as in (2) are sometimes referred to as geo-additive models.

In a Bayesian approach unknown functions f_j and parameters γ as well as the variance parameter σ^2 are considered as random variables and have to be supplemented with appropriate prior assumptions. In the absence of any prior knowledge we assume independent diffuse priors $\gamma_j \propto const, j=1,...,r$ for the parameters of fixed effects. Another common choice is highly dispersed Gaussian priors.

Several alternatives are available as smoothness priors for the unknown functions $f_j(x_j)$ [Fahrmeir & Lang, 2001; Fahrmeir et al., 2004]. We use Bayesian (Penalized) – Splines,

introduced by Eilers and Marx in a frequentist setting. It is assumed that an unknown smooth function $f_j(x_j)$ can be approximated by a polynomial spline of low degree. The usual choices are cubic splines, which are twice continuously differentiable piecewise cubic polynomials defined for a grid of k equally spaced knot *p* on the relevant interval $[a,b]$ of the x-axis; written in terms of a linear combination B-spline basis functions $B_m(x)$,

$$f(x)=\sum_{m=1}^{l}\beta_m B_m(x) \qquad \text{(Equation A.1.3)}$$

These basis functions have finite support on four neighbouring intervals of the grid, and are zero elsewhere. A comparably small number of knots (usually between 10 and 40) is chosen to ensure enough flexibility in combination with a roughness penalty based on second order difference of adjacent B-spline coefficients to guarantee sufficient smoothness of the fitted curves. In our Bayesian approach this corresponds to second order random walks

$$\beta_m = 2\beta_{m-1} - \beta_{m-2} + u_m, \qquad \text{(Equation A.1.4)}$$

with Gaussian errors $u_m \sim N(0,\tau^2)$. The variance parameter τ^2 controls the amount of smoothness, and is also estimated from the data. More details on Bayesian P-Splines can be found in Lang and Brezger (2004). Note that random walks are the special case of B-Splines of degree zero.

For the spatially correlated effect f_{str} (s), s = 1, … S, we have chosen Markov random field priors common in spatial statistics [Besag et al., 1991]. These priors reflect spatial neighbourhood relationships. For geographical data one usually assumes that two sites or regions *s* and *r* are neighbours if they share a common boundary. Then a spatial extension of random walk models leads to the conditional, spatially autoregressive specification

$$f_{str}(s) \mid f_{str}(r), r \neq s \sim N(\sum_{r\in\partial_s} f_{str}(r)/N_s, \tau^2/N_s) \qquad \text{(Equation A.1.5)}$$

where N_s is the number of adjacent regions, and $r \in \partial_s$ denotes that region r is a neighbour of region s. Thus the (conditional) mean of $f_{str}(s)$ is an average of function evaluations $f_{str}(s)$ of neighbouring regions. Again the variance τ^2_{str} controls the degree of smoothness. For a spatially uncorrelated (unstructured) effect f_{unstr} a common assumption is that the parameters $f_{unstr}(s)$ are i.i.d. Gaussian

$$f_{unstr}(s) \mid \tau^2_{unstr} \sim N(0, \tau^2_{unstr}) \qquad \text{(Equation A.1.6)}$$

Variance or smoothness parameters τ^2_j, *j=1,...,p, str, unstr,* are also considered as unknown and estimated simultaneously with corresponding unknown functions f_j. Therefore, hyper-priors are

assigned to them in a second stage of the hierarchy by highly dispersed inverse gamma distributions $p(\tau^2_j) \sim IG(a_j,b_j)$ with known hyper-parameters a_j and b_j. For model choice, we routinely used the Deviance Information Criterion (DIC) as a measure of fit and model complexity [Spiegelhalter et al., 2002].

A.1.2 Model selection

The spatial effects were modelled through the Markov random field (MRF) prior with penalized splines (P-spline) with second-order random walk penalty. With MRF prior, it was possible to predict ITN coverage in districts with no coverage data based on information of neighbouring districts. Two model forms were explored: a spatial model with district as random effect and with MRF priors (Model A); and geo-spline model with weights applied as inverse proportional to the distance of the centroids of neighbouring districts (Model B). Table A.2.1. Summarises the comparison of the DIC and prior sensitivities for the two models.

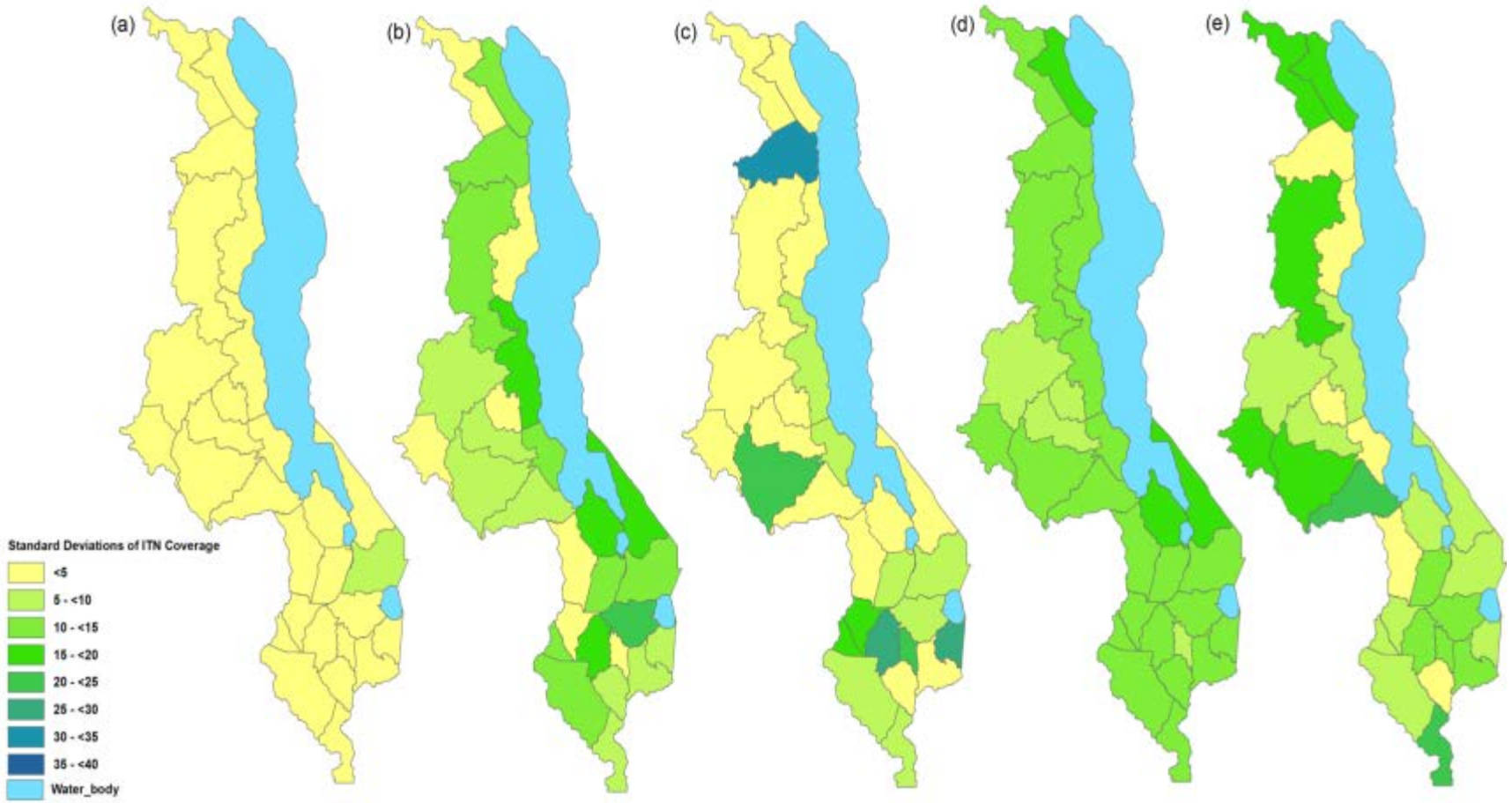
Table A.1.1 Summary of the DIC & sensitivity analysis of the choice of spatial priors for model selection

Hyper-parameters	Year	Diagnostics	Spatial With MRF	Spatial With geo-spline
a=1, b=0.005	2000 DHS	Deviance	543.8	538.2
		pD	20.2	21.1
		DIC	584.3	580.5*
a=1, b=0.005	2004 DHS	Deviance	498.8	499.4
		pD	22.3	22.5
		DIC	543.3*	544.3
a=1, b=0.005	2006 MICS3	Deviance	538.5	536.0
		Pd	20.8	21.3
		DIC	580.1	578.7*
a=1, b=0.005	2010 DHS	Deviance	498.0	502.7
		pD	23.6	21.3
		DIC	545.3	545.3
a=1, b=0.005	2012 MIS	Deviance	505.1	500.1
		pD	22.6	22.2
		DIC	550.4	544.6*

Models with asterisks (*) is the best.

The results indicated for the year 2004 (Model A) was most accurate and for 2000, 2006 and 2012 the geo-spline provided the best fit (Model B). For the year 2010, there was no difference between the two models. In addition to the sensitivity analysis (Table A.3.1), the standard deviation (SD) of the mean ITN coverage predictions per district were computed for each year with higher values of the SD indicating greater uncertainty (Figure A.3.1).

Figure A.1.1: Standards deviations of mean ITN coverage predictions in Malawi for the years: a) 2000; b) 2004; c) 2006; d) 2010; and e) 2012



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Annex A.2: Parasite prevalence model development

A.2.1 *Pf*PR$_{2\text{-}10}$ Model specification

A Bayesian hierarchical spatial-temporal model was implemented through SPDE approach using R-INLA library [R-INLA, 2013] to produce continuous maps of *PfPR*$_{2\text{-}10}$ at 1 × 1 km spatial resolution using data ranging from 1960-2011. The continuous indexed Gaussian Field (GF) with covariance function was represented as a discretely indexed random process, that is, as a Gaussian Markov Random Field (GMRF) [Rue & Held, 2005; Lindgren et al., 2011; Cameletti et al., 2012]. This is where an explicit link between GF and GMRF formulated as a basis function is provided through SPDE approach [Lindgren et al., 2011; Bolin & Lindgren, 2011; Simpson et al., 2012a; 2012b]. The solution for SPDE can be expressed as

$$(k^2-\Delta)^{\alpha/2}(\tau x(u)=W(u),\quad u\in\square^d,\quad \alpha=v+d/2,\quad \sigma^2-\Gamma(\mathrm{v})(\Gamma(\alpha)(4\pi)^{d/2}k^{2v}\tau^2)^{-1}$$
$$k>0, v>0 \qquad \text{(Equation A.2.1)}$$

This SPDE is a Gaussian random field with Matérn covariance function where W, is the spatial Gaussian white noise, Δ is the Laplacian, α controls the smoothness of the realization and τ controls the variance. The link between Matérn smoothness v and variance σ^2 is $\alpha=v+d/2$ and $\sigma^2-\Gamma(\mathrm{v})(\Gamma(\alpha)(4\pi)^{d/2}k^{2v}\tau^2)^{-1}$, where d is the spatial dimension [Lindgren & Rue, 2013]. An approximation of this SPDE can be solved using a finite element method (FEM), which is a numerical technique for solving partial differential equations [Lindgren et al., 2011]. In this case, the spatio-temporal covariance function and dense covariance matrix of the GF are replaced by a neighbourhood structure and a sparse precision matrix respectively and together define a GMRF. A GMRF can be described as a spatial process that models spatial dependence of data observed at a spatial unit like grid or geographical region and it can be expressed as $u=(u_1\ldots\ldots,u_n)'$ with $u\sim(\mu,Q^{-1})$. This is an n-dimensional GMRF with mean μ and a symmetrical positive definite precision matrix Q computed as the inverse of the covariance matrix [Cameletti et al., 2012]. Thus the density of u is given by

$$\pi(\mathrm{u})=(2\pi)^{-n/2}\left|Q\right|^{1/2}\exp(-\frac{1}{2}(\mathrm{u}-\mu)'\,\mathrm{Q}(\mathrm{u}-\mu)) \qquad \text{(Equation A.2.2)}$$

The sparse precision matrix Q offers computational advantage when making inference with GMRF. This is because the linear algebra operations can be performed using numerical methods for the sparse matrices which results in a considerable computational gain and this is further enhanced by using INLA algorithm for Bayesian inference [Rue & Held, 2005; Rue et al., 2009; Cameletti et al., 2012]. The infinite-dimensional Gaussian Random Field (GRF) is replaced with a finite-dimensional basis function representation

$$x(u)=\sum_{i=1}^{n}\psi_i(u)w_i \quad , \qquad \text{(Equation A.2.3)}$$

where w_i represents the weights and Ψ_i are piece-wise linear basis functions defined on a triangulation of the domain with n nodes which are defined as mesh in the code [Lindgren et al., 2011]. The basic functions are deterministic and are defined by each node in the triangulation while the stochastic property of the process is determined by the weights. The model used in this paper assumed non-stationary GRFs because environmental phenomena which are known to influence *PfPR*$_{2\text{-}10}$ are non-stationary in nature and therefore the distribution of *PfPR*$_{2\text{-}10}$ is non-stationary [Daly et al., 1994]. This non-stationary model was made possible by the flexible nature of SPDE models which allows modification of the SPDE rather than the covariance function to obtain the GRFs with other dependence structures other than the stationary Matérn covariance. The stationary isotropic Matérn covariance function, between locations u and v in $\mathbb{R}^d$ is expressed as

$$C(u,v) = \frac{\sigma^2}{2^{\nu-1}\Gamma(\nu)}(k\|v-u\|)^{\nu} K_{\nu}(k\|v-u\|) \ , \qquad \text{(Equation A.2.4)}$$

Where K_V is the modified Bessel function of the second kind, $\|\cdot\|$ denotes the Euclidean distance and order $\nu > 0$. $k > 0$ is a scaling parameter and σ^2 is the marginal variance. For the stationary model, k and ν are constant in space. The parameter k is linked to the range p by the empirically derived relationship $p = \sqrt{8}/k$. k, here can be described as the range parameter presiding over the spatial dependence structure of the GRF [Lindgren et al 2011]. For the non-stationary, τ and k space-dependent covariance parameters are introduced as functions of the spatial location u, $u \in D$, where D is the spatial domain. Therefore the modified SPDE becomes

$$(k(u)^2 - D)(t(u)x(u)) = W(u) \ , \ u \in \mathbb{R}^2 \qquad \text{(Equation A.2.5)}$$

where x is a non-stationary GRF because τ and k vary by location and as the consequence the variance and correlation range vary by location. The non-stationary described above is defined on the mesh because it controls the local distance metric in the manifold. $\log \tau(u)$ and $\log k(u)$ can be defined as the sum of the basis function, where the basis functions $\left\{B_i^{(\cdot)}(\cdot)\right\}$ are smooth over the domain of interest.

$$\log(k^2(u)) = \sum b_i^{(k^2)} B_i^{(k^2)}(u) \ \text{ and } \ \log(\tau(u)) = \sum \beta_i^{(\tau)} B_i^{(\tau)}(u) \, , \qquad \text{(Equation A.2.6)}$$

Using this SPDE approach, the overall hierarchical space-time binomial and zero-inflated binomial models of the prevalence to malaria parasite were used denoted by

$$y(s,t) = z(s,t)\beta + \xi(s,t) + \varepsilon(s,t) \, , \qquad \text{(Equation A.2.7)}$$

This model is characterised by a GF ***y(s, t)*** built from covariate information ***z(s, t)***, measurement error ***ε(s, t)***, and a second order autoregressive dynamic model for the latent process ***ξ(s, t)*** with spatially correlated innovations ***ω(s, t)***. The *Pf*PR$_{2\text{-}10}$ survey data were modelled as realizations of this spatial process (random field) changing in time. These realizations were used to make inference about the process and predict it at desired

locations and at a specified time. This is where $y(s_i,t)$ was the realization of a spatial-temporal process representing the *Pf*PR$_{2\text{-}10}$ at the community location s_i, where $i=1...n$, and year t_j where $j=1...m$, $z(s_i,t_j)=(z_1(s_i,t_j)\dots z_p(s_t,t_j))$ represents fixed effect from the covariates for cluster s_i at time t_j, $\beta=(\beta_1\dots,\beta_p)'$ is the coefficient vector, $\varepsilon(s_i,t)\sim N(0,\sigma_\varepsilon^2)$ is the measurement error defined by the Gaussian white noise process, and $y(s_i,t_j)$ is the predicted posterior mean prevalence of the plasmodium parasite in cluster i at time j. In the model formulation the large scale component that depends on the covariates is defined as $Z(s_i,t_j)\beta$ while the measurement error variance or the nugget effect is σ_e^2. The realization of state process or the unobserved level of *Pf*PR$_{2\text{-}10}$ in this case is defined by $\xi(s_i,t_j)$ as a spatial-temporal GRF that changes in time as a second-order autoregressive function.

The prior for the SPDE model by default are Gaussian. In the latest version of SPDE function, the default priors are chosen heuristically to match the spatial scale of the MeSH domain. The user can override the defaults by supplying a "hyper" parameter [Lindgren, 2013]. This is normally suitable when the dataset lacks enough information for the likelihood to fully identify the parameters for the prior distribution. In this paper the SPDE default priors were sufficient for the model.

A.2.2 Constructing a suitable MESH

A finite element representation is used to outline the GRF as a linear combination of basic functions defined on a triangulation of the domain, say D. This is achieved by subdividing D into non-intersecting triangles meeting in at most common edge or corner, thus a *mesh*. The GRF in the triangulation is given by Equation (SI 3.3), where n is the total number of vertices, $\{\psi,(s)\}$ are the basis functions and $\{\omega_l\}$ are normally distributed weights [Lindgren et al., 2011; Cameletti et al., 2012].

The mesh function (*inla.mesh.create.helper*) in INLA is used to create a Constrained Refined Delaunay Triangulation (CRDT). The overall effect of the triangulation construction is that, if desired, one can have smaller triangles, and hence higher accuracy of the field representation. However, this will have an effect on the computation of the model. There is therefore a need to balance the number of triangles and the computation time required. If the data points (cluster coordinates) are used to construct the mesh, a cut-off value (specified in the function represents the maximum distance in which data points are represented by a single vertex. If the boundary of the area domain is used to construct the mesh, (i.e using the function points.domain=border), then the mesh is constructed to cover the border of the domain using restrictions provided in other arguments. But if both data points and area domain (boundary) are used the restrictions are combined. In this model, the mesh was constructed using the boundary of the area domain. This method produces a mesh with regular size of triangles. A cut-off value was specified to avoid building many small triangles around *Pf*PR$_{2\text{-}10}$ input locations. A reasonable offset value was used to specify the size of the inner and outer extensions around the data locations. The maximum edge value was used to specify the maximum allowed triangle edge lengths in the inner domain

and in the outer extension. The inner maximum edge value was made small enough to allow the triangulation to support representing functions with small enough features, and typically smaller than the spatial correlation range of the model. Therefore this value was adjusted to fit the range of the area domain in the model.

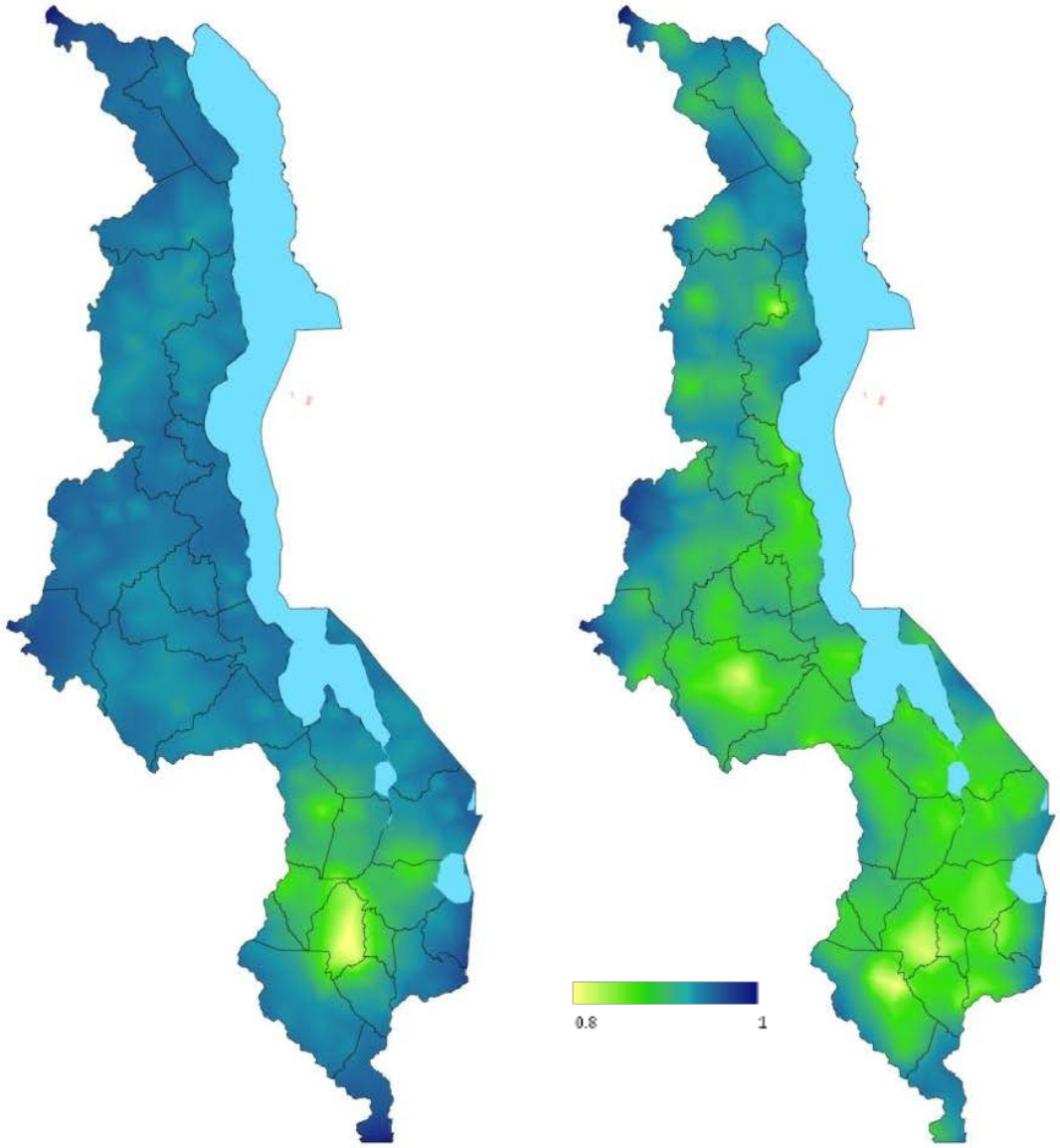
A matrix was then constructed to link the *PfPR*$_{2\text{-}10}$ input locations to the triangles on the mesh defined by ŋ* as $\eta^* = A(x + 1\beta_0)$ and in the inla code in the following *inla.spde.make. A* function. This makes each row in the matrix to have three non-zero elements since every data point is inside a triangle and the corresponding columns are expected to have non-zero elements. In order to obtain a square matrix for the model, the response was linked to the index of the random field, where the length of the index vector was the same as the length of the projection matrix. In order to estimate the intercept, the stack function introduces a vector of ones in the matrix and this is removed in the formula by putting [-1] [Lindgren, 2013].

A.2.3 Prediction accuracy

The standard deviation is a measure of the variability or dispersion of an expected value of a variable from its mean. High/low standard deviations indicate that data points are far/close to the mean. In scientific measurements it can be used as a measure of uncertainty. Of particular importance is the distance of the SD from the mean. This is because the absolute value of the standard deviation could be both because of uncertainty but also a function of generally high base (mean) values of the measure under consideration. In this study, the distance (number) of the standard deviations of the mean *Pf*PR$_{2\text{-}10}$ were computed for the years 2000 and 2010. 2010 predictions were more accurate than 2000, however, both predictions were highly accurate with no areas where predictions were made at greater than one SD. For purposes of display we have shown gradations of less than 1 SD in Figure A.1.1.

Figure A.2.1: Standard deviation maps from posterior distributions of predicted mean *Pf*PR $_{2-10}$ for a) 2000; and b) 2010: darker blue the less precise the predictions; however all predictions highly accurate with all predictions being made within one SD.

a) b)



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Annex A.3: Covariates selected and tested for PfPR modeling

A3.1 Temperature

Temperature plays a key role in determining the transmission of human malaria [Lunde et al., 2013; Beck-Johnson et al., 2013]. Laboratory experiments have shown that high temperatures (> 34^{o}C) lead to almost 100% larval mortality and at lower temperatures (< 16 ^{o}C) they were unable to produce viable adults [Bayoh & Lindsay 2003; 2004]. The mortality of the anopheles mosquitoes also increase sharply at ambient temperatures approaching 40°C [Muirhead-Thompson, 1951; Kirby & Lindsay 2004]. Temperatures of between 25°C and 30°C are considered optimum for *P. falciparum* sporogony [Molineaux, 1988]. It is on the basis of these biological relationships that we have assembled two temperature metrics in order to test their statistical relationships with *Pf*PR_{2-10}. *The annual mean temperature* surface was developed from monthly average temperature raster surfaces at 1×1 km resolution which were downloaded from the WorldClim website [http://www.worldclim.org]. These surfaces were produced from global weather station temperature records gathered from a variety of sources for the period 1950-2000 and interpolated using a thin-plate smoothing spline algorithm, with altitude as a covariate, to produce a continuous global surface [Hijmans et al., 2005; Figure A3a]. The *Temperature Suitability Index* (TSI) was developed as a quantitative value of optimal *P. falciparum* sporozoite development [Gething et al., 2011]. The TSI model uses a biological framework based on the survival of vectors and the fluctuating monthly ambient temperature effects on the duration of sporogony that must be completed within the lifetime of a single generation of Anophelines. The TSI is constructed using long-term monthly temperature time series [Hijmans et al., 2005] and represented on a scale of increasing transmission suitability, from 0 (unsuitable) to 1 (most suitable) (Figure A3b).

A3.2 Proxies of suitable conditions for larval development (precipitation and vegetation)

Rainfall, combined with suitable ambient temperatures, provides potential breeding environments for *Anopheles* vectors while humidity is associated with vector longevity. Normally, proxies of rainfall such as precipitation and vegetation are used in malaria risk predictions [Schalermann et al., 2008]. This is because actual rainfall data, typically collected from weather stations, are sparse throughout Africa [Hijmans et al., 2005]. Monthly mean precipitation raster surfaces at 1 × 1 km resolution were downloaded from the WorldClim website [http://www.worldclim.org/] and used as a proxy for rainfall compiled over a similar period and weather as for mean temperature surfaces [Hijmans et al., 2005; Figure A3c]. These monthly surfaces were summed to generate a synoptic annual mean precipitation surface and re-sampled 5x5 km resolutions.

For vegetation, Fourier–processed EVI, derived from the MODerate-resolution Imaging Spectroradiometer (MODIS) sensor imagery and available at approximately 1×1 km spatial resolution [Scharlemann et al., 2008] was used to develop an annual mean EVI surface. EVI is an index of intensity of photosynthetic activity and ranges from 0 (no vegetation) to 1 (complete vegetation) (Figure A3d). EVI, compared to the more commonly used Normalised Difference Vegetation Index (NDVI), is developed from satellite imagery of higher spatial and

spectral resolution and corrects for some distortions in the reflected light caused by the particles in the air as well as the ground cover below the vegetation [NASA].

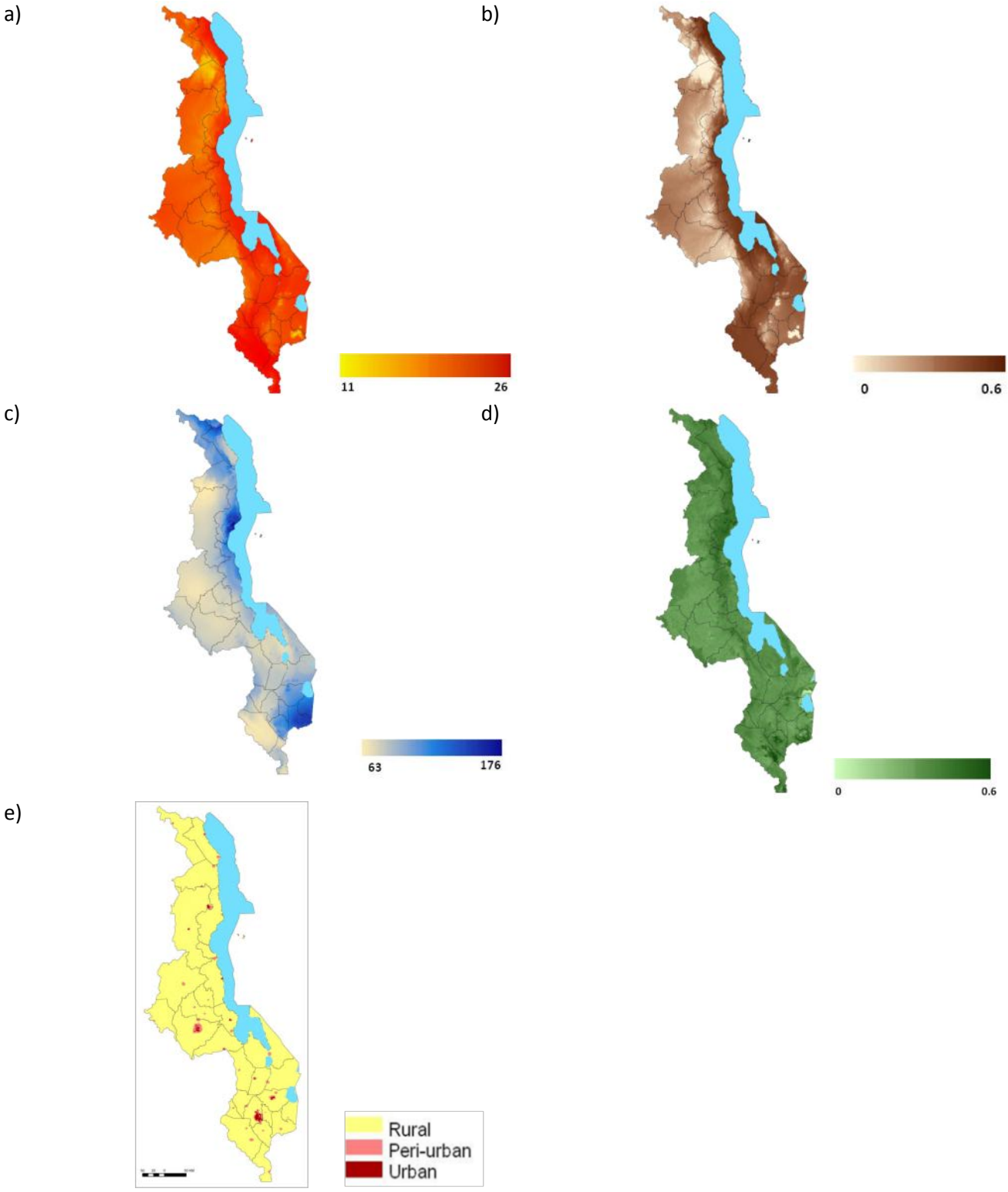
A3.3 Urbanization

The availability of optimum environments for the development of the malaria transmitting anopheline populations become limited in urban areas resulting in reduced vector density, biting rates and transmission intensity. Overall malaria infection rates are lower in urban compared to rural areas of Africa [Hay et al., 2005]. To develop a consistently defined surface of urbanisation, information from the GRUMP [Balk et al., 2006] and the Afripop project [www.AfriPop.org; Linard et al., 2012] was used (Section 2.9). Urban areas were defined as locations with a density of more than 1000 persons per km^2 with the rest of the GRUMP urban extent defined as peri-urban (Figure A3e).

A3.4 Pre-processing covariate grids

There were internal lake-coastline spatial mismatches between the various assembled raster grid covariates due to the various geographic idiosyncrasies and projection problems of the source data. A process of carefully rectifying these spatial shifts was undertaken before the covariates selection process began to minimise any potential errors. The population surface was used as the template for correcting the distortions because it had a much closer match with the defined national administrative boundaries. Reconciliations were undertaken using the *Raster-to-Point Conversion* Tool in ArcGIS 10.1 (ESRI Inc., USA) and overlaid exactly on the template grid using the *shift* tool in ArcGIS 10.1.

Figure A3: Climate and environmental covariates tested for Malawi malaria prevalence model: a) mean ambient air temperature; b) Temperature Suitability Index; c) precipitation; d) EVI; e) urbanisation



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