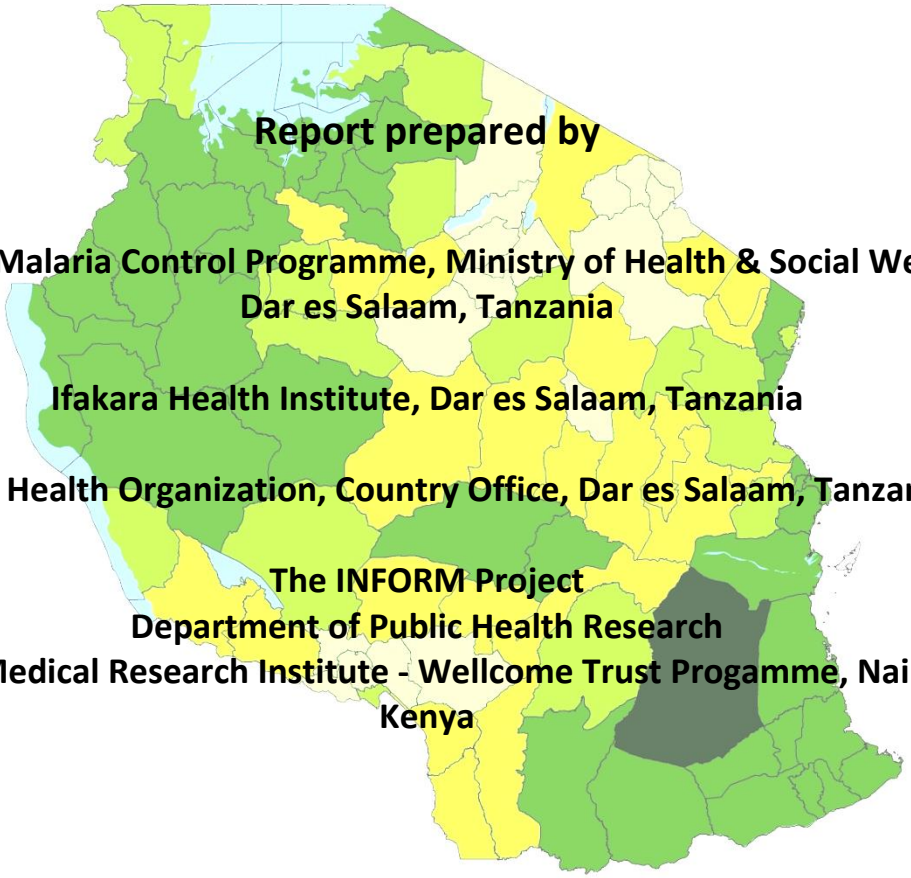
NATIONAL MALARIA CONTROL PROGRAMME

ROLL BACK MALARIA

An epidemiological profile of malaria and its control in Mainland Tanzania



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Abbreviations

ACTs	Artemisinin-based Combination Therapy
ADDOs	Accredited Drug Dispensing Outlets
AFRO	WHO Regional Office for Africa
AIS	AIDs Indication Survey
AJOL	African Journals Online
ALMA	African Leaders Malaria Alliance
ALu	Artemether-lumefantrine
AMFm	Affordable Medicines for Malaria
ANC	Antenatal care
ANVR	African Network for Vector Resistance
APRD	Arthropod Pesticide Resistance Database
AVHRR	Advanced Very High Resolution Radiometer
BHC	Benzene-hexachloride
BIC	Bayesian Information Criteria
BS	*Bacillus sphaericus*
BTI	*Bacillus thurigiensisvarisraelensis*
CCM	Chama Cha Mapinduzi
COMMIT	Communication and Malaria Initiative in Tanzania
CPC	Climate Prediction Centre
CRDT	Constrained Redinaed Delaunay Triangulation
DCW	Digital Charts of the World's Population places
DDT	Di-chlorodiphenyl-trichloroethanein
DEET	Diethyl toluamide
DFID	Department for International Development
DHMT	District Health Management Team
DHS	Demographic and Health Surveys
DIC	Deviance Information Criterion
DSS	Demographic Surveillance System
DVS	Dominant Vector Species
EA	Enumeration Area
EA-MVB	East African Malaria & Vector Borne Diseases Inst
EAC	East African Community
EANMAT	East African Network for Monitoring AM Treatment
EIR	Entomological Inoculation Rate
EVI	Enhanced Vegetation Index
FAO	Food and Agricultural Organization
FELTP	Field Epidemiology and Laboratory Training Program
FEM	Finite Element Method
FEWS	Famine Early Systems Network
GAUL	Global Administrative Unit Layers
GDP	Gross Domestic Product
GF	Gaussian Field
GIS	Geographic Information Systems
GLWD	The Global Lakes and Wetlands

GMEP	Global Malaria Eradication Programme
GMRF	Gaussian Markov Random Field
GPS	Global Positioning Systems
GRUMP	Global Rural-Urban Mapping
HMIS	Health Management Information Systems
IDSR	Integrated Disease Surveillance and Response
IEC	Information Education and Communication
IGME	Inter-agency Group for Child Mortality Estimation
IHI	Ifakara Health Institute
IMCI	Integrated Management of Childhood Illnesses
IMR	Infant Mortality Rate
INFORM	Information for Malaria Project
INLA	Integrated Nested Laplace Approximations
IPTi	Intermittent Presumptive treatment of infants
IPTp	Intermittent preventive treatment in pregnancy
IRS	Indoor residual house-spraying
ITN	Insecticide treated nets
IVMC	Integrated Vector Malaria Control
JICA	Japan International Cooperation Agency
KINET	Kilombero Net project
LLIN	Long-lasting insecticide treated nets
LST	Land Surface Temperature
M&E	Monitoring and Evaluation
MAP	Malaria Atlas Project
MAPE	Mean Absolute Predication Error
MARA	Mapping Malaria Risk in Africa
MBG	Model Based Geo-Statistics
MCMC	Markov Chain Monte Carlo
MDA	Mass drug administration
MEDA	Mennonite Economic Development Associates
MeSH	Medical Subject Heading
MIS	Malaria Indicator Survey
MODIS	Moderate-resolution Imaging Spectroradiometer
MOHSW	Ministry of Health & Social Welfare
MPE	Mean prediction error
MPR	Malaria Programme Performance Review
MRF	Markov Random Field Prior
MRU	Medical Research Unit
NATNET	National Insecticide Treated Nets Program
NBS	National Bureau of Statistics
NDVI	Normalized Difference Vegetation Index
NGO	Non-governmental organization
NMAC	National Malaria Advisory Committee
NMCP	National Malaria Control Programme
NMRI	National Institute of Medical Research
NMS	National Malaria Strategy Plans

NOAA	National Oceanic and Atmospheric Administration
OA	Open Access
ODA	Overseas Development Assistance
PA*Pf*PR_{2-10}	Population adjusted *Pf*PR_{2-10}
PCR	Polymerase Chain Reaction
PEHI	Package for Essential Health Interventions
PfR_{2-10}	*Plasmodium falciparum* parasite rate corrected to 2-10 yrs
PHC	Population and Housing Census
PMI	President's Malaria Initiative (USA)
PMORALG	Prime Minister's Off – Regional Admin & Local Gov
PSI	Population Services International
RBM	Roll Back Malaria
RDTs	Rapid Diagnostic Test
RFE	Rainfall Estimate
RHMT	Regional Health Management Team
RTI	Research Triangle International
SAM	Service Availability Mapping
SD	Standard Deviation
SDA	Seventh Day Adventist
SMARTNET	Tanzania's nationwide Strategic Social Marketing
SMC	Seasonal Malaria Control
SP	Sulphadoxine-Pyrimethamine
SPDE	Stochastic Partial Differential Equations
SRTM	Shuttle Radar Topographic Mission
TANU	Tanganyika African National Union
TMS	Tanganyika Malaria Service
TNVS	Tanzania National Voucher Scheme
TPC	Tactical Pilotage Charts
TSI	Temperature Suitability Index
U5M	Under five Mortality Rate
UMCP	Urban Malaria Control Program
UN	United Nations
UNDP	United Nations Development Programme
UNICEF	United Nations International Children's Emergency Fund
USAID	United States Agency for International Development
WHO	World Health Organization
WRBU	Walter Reed Biosystematics Unit
WWF	World Wildlife Funds

Executive summary

This report is a product of a collaboration between the Tanzanian National Malaria Control Programme, the Ifakara Health Institute and the INFORM Project, Department of Public Health Research of the KEMRI-Wellcome Trust Programme in Kenya.

The report serves as a review of critical epidemiological features of malaria over the last decade within the context of both historical and current malaria control activities. 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 council levels necessary for federal resource allocation.

The review 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.

This work has highlighted a number of key observations as useful inputs to the new malaria strategic plan, which is currently being developed. Observations that will have implications for the design of future malaria control in Tanzania include the following:

- There has been a greater than 50% reduction in predicted mean population-adjusted parasite prevalence in children aged 2-10 years (PA*Pf*PR_{2-10}) across Tanzania between 2000 and 2010. The proportion of Tanzania's population living in areas of intense transmission (PA*Pf*$PR_{2-10} \geq 50\%$) has declined from 11.6% to only 2.3% by 2010. While only 30% of Tanzania's population lived in areas where transmission would be regarded as hypo-endemic in 2000, by 2010 almost 60% of Tanzanian's were living under these conditions.

- Dramatic declines in malaria transmission intensity have not been witnessed everywhere; areas that have been resistant to the epidemiological transition are located in the Southern and parts of the North Western regions of Tanzania. Revised vector control coverage targets and possibilities of seasonal drug-based prevention should be considered options for future control in these areas.

- Modeled predictions of LLIN use by 2012 indicate that 64% of all Tanzanians were sleeping under an LLIN. Approximately 5 million people were protected by IRS. However, there are significant differences between districts in LLIN coverage and no district to date has achieved "universal coverage."

- Reports suggest that *Anopheles arabiensis* has become more ubiquitous across the country since 2000 and in some regions *An. funestus* has emerged as a highly significant vector despite a widely held view that *An. gambiae* s.s. is the dominant vector. Biological insecticide resistance and behavioral adaptations by dominant vectors has emerged in the face of wide-spread insecticide use.

This work was made possible because of the generosity of many researchers, institutes and control agencies working in Tanzania who are prepared to share their survey data collected over the last three decades. The databases are by their very nature opportunistic, but their application within an analytical framework is clearly valuable.

The NMCP recognizes the need to move from a position of opportunistic data collection to a pro-active, regular surveillance of parasite prevalence, vector distributions and intervention coverage. This will form the basis of future evaluation metrics and form the basis of a "live" mapping product to gauge success, gaps and opportunities to decide on priority interventions based on scientific evidence in malaria control investment nationwide.

Chapter 1

Introduction

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. 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 most 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 ($Pf\text{PR}_{2\text{-}10}$), 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].

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. These future business cases must be grounded in the best possible 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 (NMS) plans 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. Several maps of malaria risk were used to define the epidemiology of malaria in Tanzania as part of their MPR in 2012. However in conclusion the MPR states as one of its recommendations that there is a need to "*update the national*

malaria epidemiological maps to enable targeting and reflection of impact of interventions" [NMCP, MoHSW, 2012].

The United Republic of Tanzania was one of the first recipients of Global Fund support for malaria in Africa. The Republic has two ministries of health supporting mainland Tanzania and the Islands of Zanzibar. Zanzibar has a unique history of malaria control and elimination and began to receive separate ODA against different control ambitions from 2006. We focus only on Mainland Tanzania in this report.

Tanzania continues to receive significant ODA for malaria control ambitions. The future of control on mainland Tanzania will depend on a carefully defined set of evidence-based objectives, based upon past, present and future predictions of epidemiological conditionsto target future populations for intervention packages. In 2013 the National Malaria Control Programme (NMCP), in collaboration with its partners, began developing a revised mid-term strategic plan to cover the period 2014-2019.

In support of the MPR recommendation, here we present a review of several key epidemiological features of malaria and service coverage using geo-coded data assemblies, model-based geo-statistical models and context narrative. The final report is a source of meta-data to accompany the analysis and serve as part of a more integrated data series for future up-dating and analysis by Tanzanian and regional partners.

The work is a collaborative effort between the NMCP of the Ministry of Health and Social Welfare, the WHO country Office, the Ifakara Health Institute and the INFORM Project of the Deaprtment of Public Health Research of the KEMRI-Wellcome Trust programme in Nairobi, Kenya. Funding has been provided by the Department for International Development – UK, The Wellcome Trust, UK and the Ifakara Health Institute.

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Chapter 2

Country context, administration, population distribution and health service provision

2.1 Country context

Tanzania has a 900 km eastern seaboard along the Indian Ocean and is bordered by Kenya and Uganda to the north, Rwanda, Burundi and the Democratic Republic of the Congo to the west, and Zambia, Malawi and Mozambique to the south. The 947,300 km², that mainland Tanzania occupies, makes it one of the largest countries in Africa. The country has a mountainous region in the northeast, including Mount Kilimanjaro (6,000 m) and the Usumbara mountains (2,440 m). To the north and west are the Great Lakes of Lake Victoria and Lake Tanganyika. Central Tanzania comprises a large plateau (central plateau, southwest plateau and Masai steppes) at *circa* 1,000 m above sea level, with plains and arable land where most of the country's major rivers drain into forming swamps and marshes. Over 25% of Tanzania's land mass is occupied by protected game reserves including Africa's largest protected area, the Selous Game Reserve, and the reserves of the Ngorongoro Crater, Serengeti, Mikumi, Rungwa, Ruaha, Uwanda, Mahale, Arusha, Tarangire and Lake Manyara.

Tanzania is one of the oldest known inhabited areas on Earth with fossil evidence at Olduvai of early humans dating back over two million years [Morrell, 1996]. The Bantu-migration began approximately 2,000 years ago followed much later by Nilotic pastoralists during from the 18th century [Kelsby, 1977; Curtin et al., 1995]. Trading migrants from the Arab peninsula began to establish settlements along the coast from the 9th century as part of what became the *Swahili Corridor* linking East Africa to the Arabian Peninsula, Europe and China [Horton, 1989].

In the late 19th century, Imperial Germany occupied the regions that are now mainland Tanzania, Rwanda, and Burundi and was incorporated as German East Africa, with their original base at Bagamoyo. Following the First World War, the League of Nations charter designated the area a British Mandate, with the north-west territories ceded to Belgium, governed as Rwanda and Burundi.

In 1954, Julius '*Mwalimu*' (The Teacher) Nyerere formed the Tanganyika African National Union (TANU) that sought national sovereignty for Tanganyika and finally brought to an end British rule and independence in December 1961. Tanganyika and Zanzibar united in 1964, following the end of Arab rule on the Islands, to form the United Republic of Tanganyika and Zanzibar and the same year renamed the United Republic of Tanzania. Nyerere pursued policies in line with Pan-African Socialism, promoted KiSwahili as a single national language, nationalized banks and major industries, actively supported the movements against racial oppression in South Africa and Zimbabwe, led the overthrow of Uganda's Dictator Idi Amin in 1979 that cost Tanzania an estimated US$ 1 million per day, and attempted to unify the 125 ethnic groups across Tanzania through a philosophy of *ujamaa* or brotherhood [Bell, 1986]. Despite a strong social ambition, Nyerere's policies led to a financial crisis during the 1970s, and Tanzania had to borrow heavily from the International Monetary Fund during the 1980s. Nyerere retired as president in 1985 and was succeeded by the President of Zanzibar, Hassan Ali Mwinyi, of the Chama Cha Mapinduzi (CCM) Party who oversaw political reforms and a transition to a market economy, necessary as a result of the economic collapse following centralized economic management. Benjamin Mkapa, the CCM candidate, was elected president in 1995 and served two terms with policies aimed at

reducing poverty, expanding economic growth and abolishing corruption. In December 2005, Jakaya Mrisho Kikwete was elected as the current serving president also from the CCM party.

In 1996, the official capital of Tanzania moved from Dar es Salaam to Dodoma, where Parliament is located. Dar es Salaam, however, remains the principal commercial city of Tanzania and the location of most government institutions, including the Ministry of Health and Social Welfare (MoHSW). Dar es Salaam has a major strategic significance as a seaport for its landlocked neighbours.

2.2 Economy & Poverty

Foreign exchange is largely raised through tourism and revenues earned from the export of gold, coffee, cashews, manufactured products, cotton and cloves. Tanzania's present economic performance is highly rated by the World Bank, with growth rates over 6% in 2011 and 2012, and a decline in the fiscal deficit 2011/12 for the first time in four years to 5% of Gross Domestic Product (GDP) [World Bank, 2012]. Tanzania is a member, with Kenya and Uganda, of the East African Community (EAC), established in 1999 as a treaty to revive a union that had collapsed in 1977. The EAC Treaty provides a legal framework for regional development, economic policy cooperation, trade and political coordination. Tanzania is also a Southern African Development Community member, cooperating with its southern neighbors in regional economic development projects.

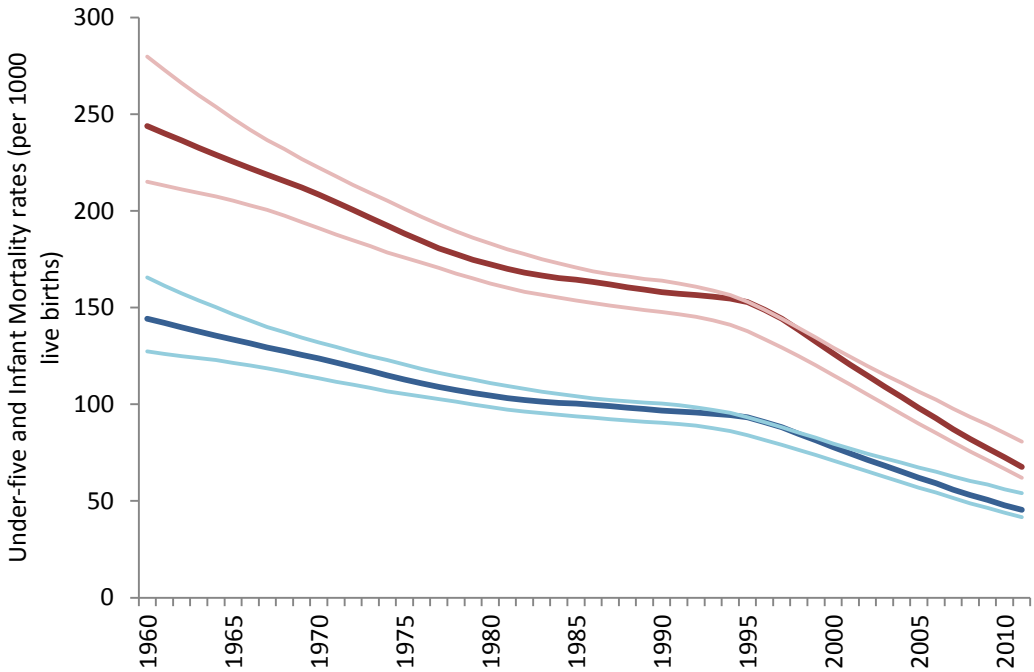
2.3 Child survival

Civil registration was made compulsory in Tanzania in 1967 [Ominde, 1974]. However, its coverage is incomplete and therefore unsatisfactory as a source of demographic statistics. The absence of reliable 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) and used combinations of weighted LOESS regression techniques to fit smoothed mortality trends to estimate mortality between survey periods using combinations of sample survey data (Demographic and Health Surveys (DHS), and Multiple Indicator Cluster Surveys (MICS) and World Fertility surveys) and census data [UNICEF-IGME, 2011]. The IGME estimates of under-five mortality (the probability of dying between birth and the fifth birthday) and infant mortality (number deaths in the first year of life per 1000 pregnancies) for Tanzania between 1960 and 2011 are shown in Figure 2.1. Substantial declines in both infant and under-five mortality were witnessed from 1960 through to the mid-1980s when modeled household survey data show the stagnation of progress coincidental with the emerging HIV epidemic, declining efficacy of antimalarial drugs and a period of economic austerity. By the mid-1990s Infant and child mortality began to decline significantly. The declines between

1999 and 2004 have been attributed to improvements in Tanzania's health system, including doubled public expenditure on health; decentralization and sector-wide basket funding; and increased coverage of key child-survival interventions, such as integrated management of childhood illness, insecticide-treated nets, vitamin A supplementation, immunization, and exclusive breastfeeding [Masanja et al., 2008]. The recent 2012 national household DHS suggests that under-five mortality (U5M, 5q0) in the last five year period was 81 per 1000 live births and infant mortality (IMR, 1q0) was 51 per 1000 live births [NBS, 2011].

Figure 2.1: Under-five mortality rates (red) and Infant mortality rates (blue) per 1000 live births for Tanzania, 1960 to 2011 [UNICEF-IGME, 2011]



Legend: Under-five mortality rates (red) and Infant mortality rate (blue) per 1000 live births Tanzania, 1960 to 2011. All rates are defined as per 1000 live births [UNICEF-IGME, 2011]. For IMR and U5M, 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).

2.4 Defining health service administration-planning units

Over time, governments across Africa have embraced decentralization. Tanzania began its process of decentralized health service provision soon after independence and formally from 1972, using a blue print developed by McKinsey & Co. of New York on decentralized management across all ministries [Nsekela & Nhonoli, 1976]. The aim was to promote people's participation in planning processes as well as to facilitate local decision-making [MRA & LG, 1998].

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 diminished value [Omumbo et al., 2013]. Defining the second and third level administrative regions within each country poses perennial problems as these routinely change and are different for different national administrative purposes (e.g. census units don't always correspond to health planning units or political constituency units).

Mainland Tanzania is divided into regions and district councils. Councils are divided into four to five divisions and each division has three to four wards. Five to seven villages form a ward. The council is the most important administrative and implementation authority for public services including policies of the MoHSW [Ministry of Health 2003a; 2003b; Ministry of Health & Social Welfare, 2008] and consequently those of the NMCP as embodied in the current National Malaria Strategic Plan [NMCP, 2008]

The administrative councils and regions have increased in number in recent years: the 2012 census includes 25 regions, 159 councils of wich 125 district councils (mainly in rural settings), 12 town, 29 municipal and 3 city councils (mainly in urban settings). These digital boudnaries are not yet avialble and will beused in furture mapping exercises (Chapter 7). In order to define health administrative units, we have used as a reference the information given on the 'District health in Tanzania' developed by the Health Sector Reform Secretariat in 2010. This provided spatial information on 119 councils across 21 regions of mainland Tanzania. We then compared this with a standard internationally used second level administrative boundary map developed by UN agencies under the direction of the Food and Agriculture Organization (FAO), referred to as the Global Administrative Unit Layers (GAUL) and dated 2008. The GAUL database maintains global layers with a unified coding system at country, first (e.g. regions) and second administrative levels (e.g. districts) which are updated annually and is freely available to the public [http://www.fao.org/geonetwork/srv/en/].

For the purposes of malaria risk mapping, or mapping sub-national access and coverage of interventions, a decision was required to merge the urban councils that are located inside rural councils. These pose several spatial epidemiological modeling and interpretation challenges when attempting to interpolate information in space across contiguous areas. We have therefore used the GAUL layers for districts where these match exactly, have adapted GAUL to match the MoHSW defined district margins where these were different from GAUL (Sumbawanga Rural and Uyui) and have removed 14 urban council boundaries to be merged with their rural neighbors for the urban-rural pairs at Dodoma, Iringa, Bukoba, Kigoma, Moshi, Lindi, Musoma, Mbeya, Morogoro, Mtwara, Sumbawanga, Songea, Shinyanga and Singida. In addition we have combined the two municipal districts in Mwanza city (Nyamagana & Ilemela) into a single geographical unit as their independent orientation would make interpolated quantities of risk or coverage difficult. The urban councils of Arusha and Tabora were merged with their respective rural neighborhoods of Arumeru in Arusha region and Uyui in Tabora region for similar reasons (Figure 2.2). Consequently the number of district entities without urban "islands" was 102 (Figure 2.3). We return to the definition of urban extents, suitable for urban malaria control in Sections 2.6 and 4.3.2.

Finally, GAUL margins of the unnamed district assigned as the water body Lake Rukwa, was edited in part at its northwest boundary with Sumbawanga District and its southwest boundary with Mbozi to align with the zero value pixel edge of population grid so that the entire district would assume population pixels with a value of zero when overlaid with the population grid. Consequently, in the WWF water bodies' shapefile (a hybrid of Global Wetlands and Lakes Database I and II), the location of Lake Rukwa was edited to completely extend within the boundary of the above unnamed district assigned to it in GAUL. All merging was done in ArcGIS version 10.0 (ESRI, Inc., Redland, CA, USA).

Figure 2.2: Areas merged from urban "islands" (pink) to be combined with wider surrounding district areas (yellow) to form contiguous health administrative units for malaria risk mapping in Tanzania.

Figure 2.3: Final 102 resolved health districts/councils within 21 Administrative Regions used in the present report

It should be noted that the 2012 census re-defined regional and district council boundaries. At the time of analyzing the data and writing the report we had not obtained the current official shape files for these revised demarcations. However, future iterations of the boundaries and better reconciled population data will be possible during the next iteration of the report in 12 months time.

2.5 Population growth and distribution

The first census was undertaken in 1921, the year that the Belgians transferred Kigoma district to Tanganyika, with a total estimated population of 4.34 million people [http://www.populstat.info/Africa/tanzanic.htm]. The next census was in 1931 and enumerated a total of 5.06 million people. Both early censuses, however, focused on non-African populations and used “counts” to enumerate the African population [Kuncyzinski,

1948]. The 1948 national census used modern demographic methods for the first time following the formation of the East African Statistical Department. The Tanganyika Territory 1948 census, across all eight administrative regions, enumerated 7.5 million people. The 1957/58 census recorded a total population of 8.79 million people in Tanganyika.

The population of mainland Tanzania according to census years post-independence were 11.96 million in 1967, 17.04 million in 1978, 22.46 million in 1988 and 33.46 million in 2002. Inter-censal annual growth rates have been approximately 3% since the 1970s [NBS, 2013]. According to the 2012 national census the total population of mainland Tanzania is currently 43.63 million people occupying 9.1 million households and an annual growth rate of 2.7% [NBS, 2013]. UN median variant projections for Tanzania project that the population in 2050 will be in excess 138 million people and by 2100 over 300 million [UNPD, 2011].

Tanzania is a large country with one of the most over-dispersed population settlement patterns in Africa. It is essential that population counts are matched at much higher spatial resolutions to disease risks, especially as with malaria when these risks are themselves, highly spatially over-distributed. Recently spatial modeling 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 varying, and often low, spatial resolutions [Linard et al., 2010; 2012; www.afripop.org]. In brief, a dasymetric modeling technique [Mennis, 2009] was used to redistribute population counts within the 18,421 spatially enumeration areas (EA) (Figure 2.4) used during the 2002 national census and land cover data sets derived from 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 or arid deserts 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 resolutions. The population distribution datasets were projected to 2000 and 2010 using United Nations (UN) national rural and urban growth rates [UNDP, 2011] and made to match the total national population estimates provided by the UN Population Division [UNDP, 2010] for these years. The resulting population density map is shown in Figure 2.5.

The age and sex composition of the population for the 18,421 spatially mapped enumeration areas was also obtained from the 2002 census. For each enumeration area, the proportion of women of child-bearing age and the proportion children under 5 years were extracted and used to adjust the spatial total population datasets in order to produce gridded population distribution of these most vulnerable categories of people.

It is worth noting that the micro-data collected during the 2012 national census is expected to be released sometime later in 2013 and these would help improve population distribution modeling, age-sex compositions, projected populations per gridded count and definitions of urbanization.

Figure 2.4: 18,421 enumeration area boundaries (2002) [Openmicrodata, 2013] and protected areas using the 2010 World Database on Protected Area [WDPA, 2013].

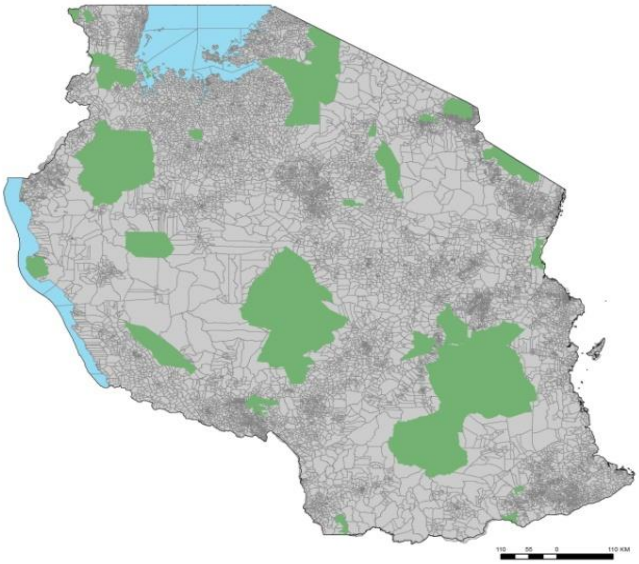
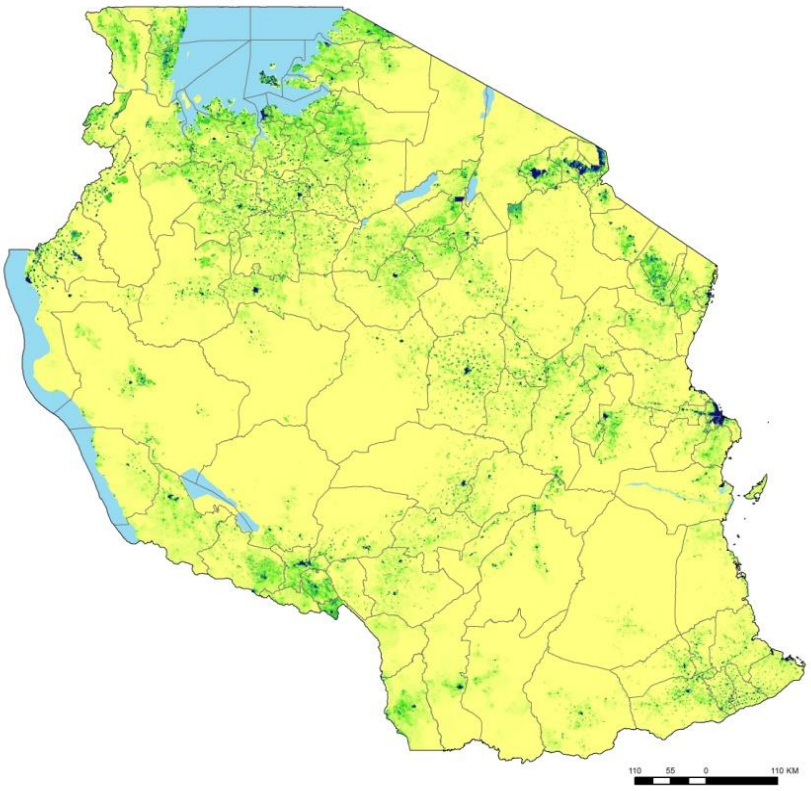


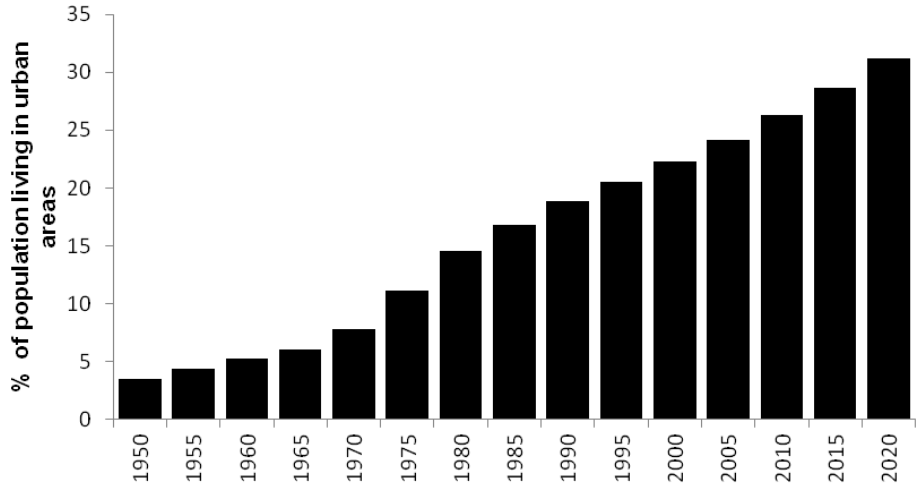
Figure 2.5: Modeled population density projected to 2010 using methods described in the text and represented as increasing density as shown in legend below. Ranging from zero to c. 44,000 per km^2



2.6 Urbanization

The proportion of the population living in urban areas has increased with each census year from 5% in 1967, 13% in 1978, 21% in 1988 and 27% in 2002. In 2012, Dar es Salaam accounted for 10% of mainland Tanzania's population. This is recognized as an increasing burden on already over-whelmed public services and social infrastructure in urban settings. The UN's World Population Prospects 2012 models project Tanzania's urban population to grow to over 30% by 2020 (Figure 2.6)

Figure 2.6: Percentage of population residing in urban areas of Tanzania between 1950 and 2020 [UN, 2012]

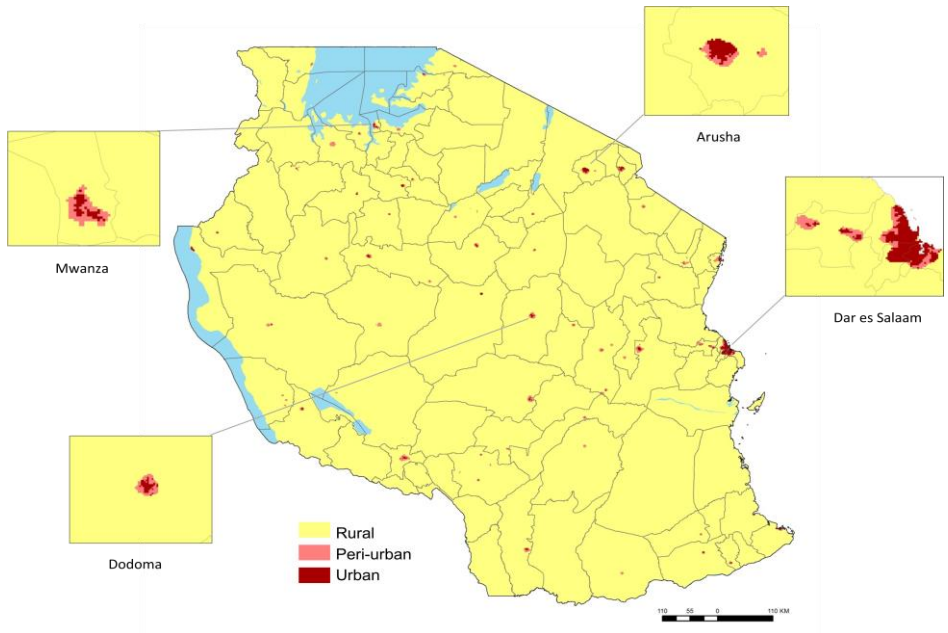


During the 2002 household and population census, the National Bureau of Statistics (NBS) defined all regional and district headquarters as "urban areas" [NBS, 2006; Muzzini & Lindeboom, 2008; UN, 2011]. The boundaries of these headquarters were defined by the Village Act (1975) and Urban Ward Act (1976) that divides the entire country into urban and rural wards. Some wards adjacent to urban boundaries are also included as urban areas if they were determined to have "urban characteristics" defined by: a) minimal level of size-density criterion; b) have specialist functions that are mainly non-agricultural with many inhabitants engaged in nonagricultural occupations; c) if many buildings in the ward were used for non-domestic purposes (shops, garages, places of entertainment or factories). Although no specific numerical values of size and density is given, the decision of inclusion or exclusion of such wards in urban areas is made by the District/Regional Census Committees. A category of "mixed wards" is defined where the entirely ward can be characterized as urban or rural in which case the District/Regional census committee determines which EAs in such wards should be considered urban.

These national definitions of urban settlements are vague and potentially inconsistent across the country. We have therefore 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 the AfriPop project [Linard et al., 2012]. GRUMP urban extent grids distinguish urban and rural areas based on a combination of NOAA's Night-time lights dataset [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., 2006] while settlements data sources include ESRI's Digital Chart of the World's Populated Places (DCW), Tactical Pilotage Charts (TPC) from Australian Defense Imagery and Geospatial Organization and some LandSAT-derived polygons [Balk et al., 2004; CIESIN, 2004]. 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-light' 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 was greater than 5,000 persons were classified as urban with the rest of the grid define 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 2.7).

Figure 2.7: Urban and peri-urban settlements in Tanzania (see text for definitions and derivation)



2.7 Health facility 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 [Osisobe, 1989; Boerma & Stansfield, 2007; WHO, 2008]. 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 to 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 [Bullen et al., 1996; Gatrell & Markku, 1998] but there

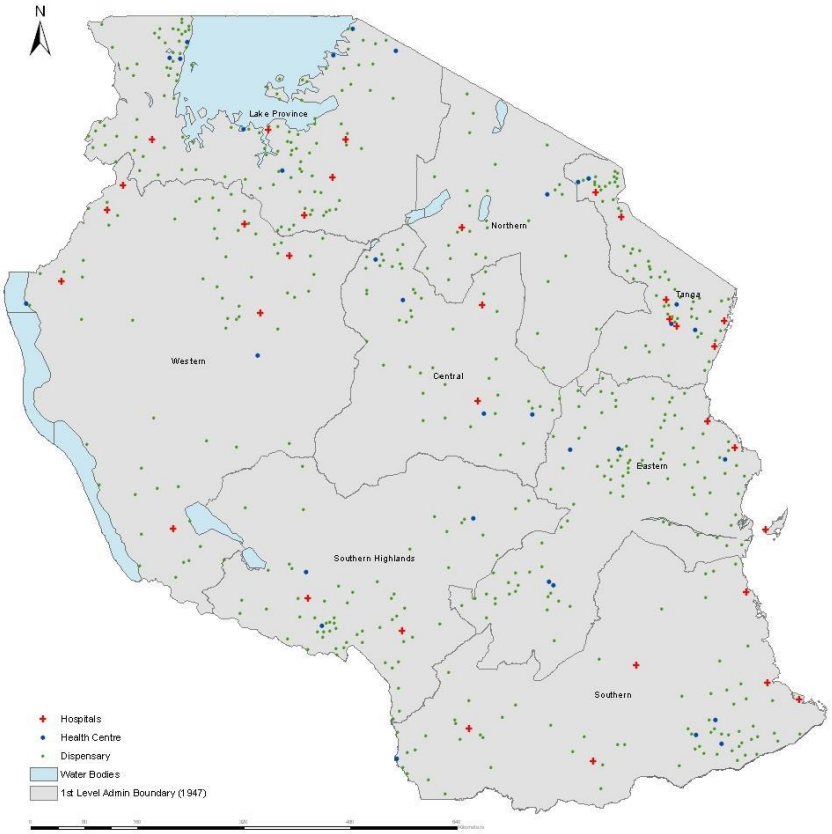
are few examples of their development and operational use in resource poor settings in Africa [Noor et al., 2004; 2009; Kazembe et al., 2007; Lozano-Fuentes et al., 2008].

In 1877, the first missionary hospital was built at Mamboya near Mpwapwa by Church Missionary Society (CMS) [Beck, 1970; Mwaluko et al., 1991]. By 1892, the military government and German missionaries collaborated as informal partners in the formation of formal medical care where missionaries supplemented the government by dealing with rural areas [Beck, 1970]. In 1897, Ocean road hospital and Sewa Haji hospital (started by Indian trader) were opened in Dar-es-Salaam. Ocean road hospital was exclusive to the Europeans and the staff included Robert Koch and Gustav Giemsa; while Sewa Haji hospital served Arabs, Indians, civil servants, African military troops, and "natives" [Clyde, 1962]. Under John Shirecore, the British post First World War Chief Medical Officer, medical training schools and research centres were established and more hospitals and rural dispensaries constructed. By 1934, there were 100 registered and 58 licensed physicians out of which 51 registered practitioners and 53 licensed were in government service providing mainly curative care while the rest were in mission practice [Nsekela et al., 1976]. After the Second World War, the medical department reorganized the health services under a five-year medical plan labelled “Exercise Crystal Ball”. [MOHL, 1961; Clyde, 1962].

The first health facility map developed for Tanzania was in 1947 [Government of Tanganyika, 1947]. The map provided positions of nine Provincial Medical Headquarters, 14 medical officers stations, 25 hospitals maintained by the colonial government, 44 dispensaries maintained by the government, 344 “native authority” hospitals or dispensaries, 18 mission doctors stations, 147 hospitals or dispensaries maintained by the mission sector, six industrial firms maintaining hospitals with doctors and two without doctors. This paper map was scanned and imported into *ArcMap 10.1* for geo-referencing and on-screen-digitization of each of the 608 facilities. We recoded the facilities into Hospitals (Provincial medical headquarters/ Government hospitals/ industrial hospitals); Health Centres (medical officers/ mission doctors station); and finally dispensaries (native authority/ mission hospitals or dispensaries). The distribution of services is shown in Figure 2.8

Following independence there was a rapid development of rural health services. By 1980, it was estimated that about 45% of the population lived within 1 km of a health facility, 72% within 5 km and 93% within 10 km. For the last 20 years the national health system has been based on decentralized services to local government authorities in line with the principle of ‘*decentralization by devolution*’. The MoHSW and the Prime Minister’s Office, Regional Administration and Local Government (PMO-RALG) are jointly responsible for the delivery of public health services. The central MoHSW is responsible for policy formulation and development of guidelines to facilitate policy implementation. The Office of the Regional Administrative Secretary, under PMO-RALG, interprets these policies and monitors their implementation in the districts they supervise using regional health management teams. The district/council health management team is responsible for council health services including dispensaries, health centres and district hospitals.

Figure 2.8: Distribution of health facilities in 1947 by the principal governing administrative boundaries in the 1940s [Reproduced from Government of Tanganyika, 1947]



Since the 1990s the health system has been arranged as a pyramid. The lowest level of fixed service delivery, the village health post owned by the village government and are manned by village health workers, to the dispensary within a ward serving between 6,000-10,000 people manned by a Clinical Assistant or Clinical Officer with a minimum of three years training, who also supervises the village health workers; to the health centre which can provide both inpatient and outpatient services, staffed by an Assistant Medical Officer or Clinical Officer, assisted by approximately eight other health workers serving a population of between 50,000-80,000 people; the district hospital, located in every district/council, providing curative and preventive services, training and referral services from lower health facilities, serving an average population of 250,000 people. The District Medical Officer is located at the district hospital and is the chairperson of the District Health Management Team (DHMT) and Secretary to the District PHC Committee. The hospital has medical officers, nurses, pharmacists, laboratory technicians, radiographers, health officers and health secretaries. Finally at the apex of the health system there are 17 regional and four specialist hospitals. Regional hospitals are located in each region except Dar es Salaam, Mbeya and Coast regions and provide referral services from district hospitals; the regional medical officer heads the Regional Health Management Team (RHMT). The four consultant and specialised hospitals are Muhimbili Medical Centre in Dar es Salaam; Bugando Medical Centre in Mwanza, Kilimanjaro Christian Medical Centre in Moshi and Mbeya Referral Hospital in Mbeya. In addition there are two specialised hospitals, Mirembe Mental Hospital in Dodoma and Kibong'oto Tuberculosis Hospital in Moshi.

Faith-based organizations and the for-profit private sector are part of the health-service delivery system. The government has supported the work of voluntary agencies through substantial subsidies. It is estimated that voluntary agencies run about 40% of all health facilities and provide 40% of hospital beds. The private organizations also provide care in health centres and dispensaries, although to a lesser extent. Since the government re-legalized private medical practice in 1991, the non-subsidized private sector has grown considerably, predominantly in the urban areas.

In 1996, a total of 4,910 health facilities were recorded by the Ministry of Health and services managed by government, mission and Non-Government Organization (NGO) sectors. The composition of facilities included 205 hospitals, 318 health centres, and 4,387 dispensaries and 4,508 village health posts. A Service Availability Mapping Survey (SAM) was carried out between December 2005 and February 2006 in Tanzania by the MoHSW and WHO that estimated that the total number of facilities has increased to 5,552 [MoHSW, 2007].

The MoHSW have recently updated their national master health facility database which is available on-line at the Online Health Facility Registry [http://hfr.ehealth.go.tz; accessed 6th March 2013]. This we have assumed is a reasonable representation of audited clinical facilities in Tanzania for 2012/13. Information on facility registry ID, name and location of the facility (district, ward, municipal council), service level (hospital, health centre, dispensary), management (private, NGO, mission or government) and the status (operating, closed, proposed site etc) was abstracted into a single excel file. We identified 57 structures that were duplicates and these were removed; in addition we noticed that the labeling of provider was incorrect in several instances with Seventh Day Adventist (SDA) labeled government, these were changed to faith-based providers. We excluded 285 facilities that were labeled “closed” or “not operating”; 511 structures that were labeled dental clinics, eye clinics, maternity homes, physiotherapists, mental clinics, youth centres or other specialist and teaching facilities that were unlikely to be providing routine curative services; and 588 facilities labeled as being private. The latter are significant providers of curative services but as with previous audits of master health facility lists in Kenya, Somalia and Uganda these are often under-represented in MoHSW registries, located in urban centres, accessible only to those able to afford services, unregulated and do not often feature in antimalarial and net distribution supply management systems. We have retained all facilities under the umbrella of “public” facilities that are managed by NGOs and mission groups; these are often included in MoHSW commodity distribution systems. The final public sector facility database contained 6256 facilities; including 217 hospitals, 563 health centres and 5476 dispensaries. 663 of the facilities did not have a label of who provided the service, 4767 were labeled as managed by the government and 826 managed by faith based groups, voluntary organizations or NGOs. We have therefore undertaken a rapid cross-referencing exercise with other available digital sources to geo-code the master list.

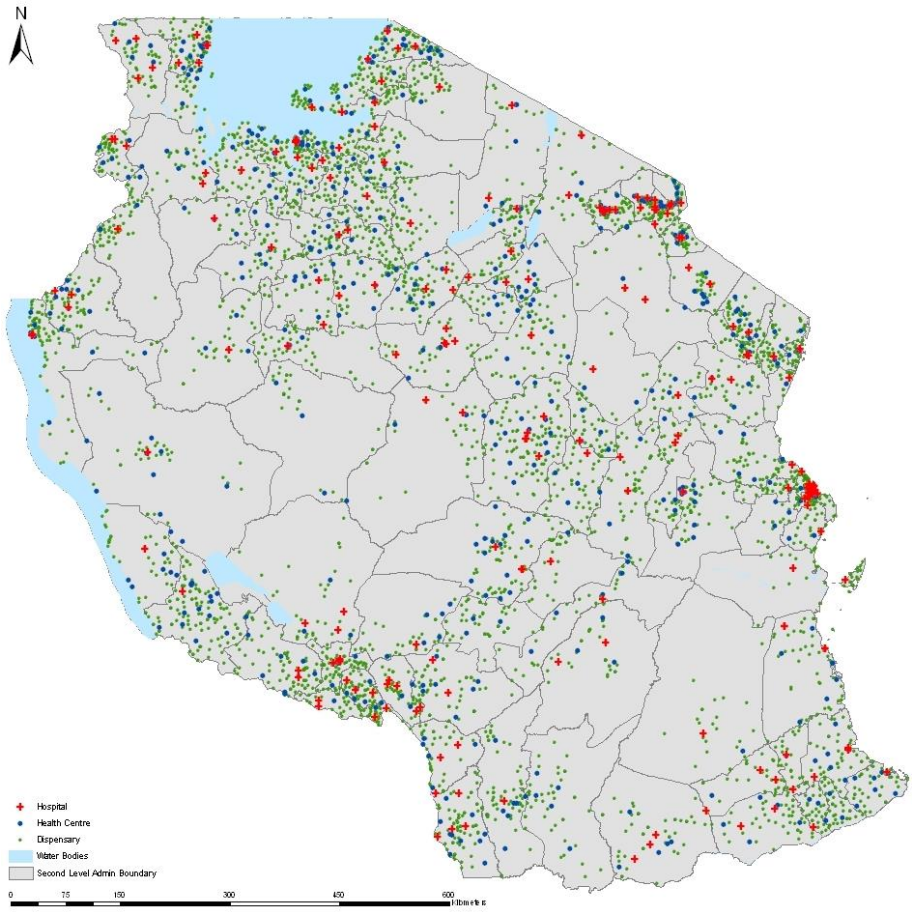
At present only a few facilities on the master list have geo-coordinates. We have therefore undertaken a rapid cross-referencing exercise with other available digital sources to geo-code the master list.

First, we obtained a number of Global Positioning System (GPS) data sets that have been recently assembled and relate to the locations of health service providers these included: a) the distribution database developed by the NGO Mennonite Economic Development Agency (MEDA) for the mass-campaigns of net distributions between 2008 and 2012 covering 4442 facilities nationwide; b) the sentinel site facility database developed by the Ifakara Health Institute (IHI) as part of support to the NMCP in tracking health and malaria indicators and provided GPS coordinates for 2778 public facilities; c) a database of 731 GPS coordinates collected by Research Triangle International (RTI) across the Kagera, Mara and Mwanza regions bordering Lake Victoria in October 2012 as part of their Indoor Residual Spraying campaigns; d) a database developed for the SMS for life project in collaboration with John Snow Inc. that had detailed cell phone numbers for service providers at each facility and the coordinates of 3026 facilities; it is not clear how coordinates were developed for these facilities. The RTI and SMS databases did not provide information on level of service provision (dispensary etc) nor who provided the service (government etc) but did have facility name, region and district. Databases were used in the following order MEDA, IHI, RTI and SMS for Life accepting the first set of longitudes and latitudes from the first database before using the subsequent database to identify missing facilities per district.

Coordinates were checked with the health administrative boundary map described in Figure 2.3 to locate those facilities that were in the wrong administrative boundary. In addition points along the coastline were checked using the GAUL 2008 coastline shape file. 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 selection tool in ArcGIS 10.1 (ESRI, USA) to identify facility coordinates that fell slightly off the coastline, 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 6256 public facilities we geo-located 2109 using the MEDA database, 1657 using the IHI database, 182 using the RTI database and 96 using the SMS database. We were able to identify 896 coordinates from the MoHSW web-site but do not know whether these are GPS and 308 using combinations of Encarta, Google Earth, and GeoNames to the nearest village equivalent name within the same ward location and 208 using other online digital gazetteers [https://gistdata.itos.uga.edu]. 948 (15%) remained un-positioned after exhausting all available geo-location sources. These should be located using national resources and contacts. The location of 216 hospitals, 523 health centres and 4569 dispensaries is shown in Figure 2.9.

Figure 2.9: Distribution of geo-coded hospitals, health centres and dispensaries managed as part of the public sector (government, faith-based, voluntary or NGO).



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Chapter 3

100 years of malaria control in Tanzania

3.1 Malaria control under the German administration: 1890-1914

Herrmann von Wissmann was appointed the first imperial commissioner for German East Africa in 1888 and he included on his general staff two medical doctors [Beck, 1977]. Considerable efforts were made by the German Medical Administration to control malaria in areas they settled across Tanzania before the First World War. Malaria control in Dar es Salaam started in the 1890s and was initially focused on larval mosquito control. The urban expansion of Dar es Salaam was managed by the colonial administration that actively selected development sites and regulated building standards along racial lines (Africans, Asians and Europeans). The population of Dar es Salaam in 1900 was estimated to be 20,000 people and in 1913, the town was divided in two: the European quarter along the beach and the "native" (African, Arabs and Asians) were settled in houses further inland. Environmental works targeted at larval control such as oiling, swamp drainage and general sanitation improvement were introduced as early as 1901, principally in the European settled areas, and undertaken by staff of the General Sanitary Authority using guidelines of the *Gesundheits Commission* [Tanganyika Medical & Sanitary Department, 1926; Owen, 1933; Bang et al., 1973; Beck, 1977; Castro et al., 2004]. However, the presence of permanent swamps across the town sustained multiple mosquito breeding sites and vector control efforts proved too ineffective and considered too costly [Ruge, 1907; Ollwig, 1912; Bangs et al., 1973].

The focus of the anti-malarial campaigns in Dar es Salaam changed to malaria parasite control through quinine administration, first proposed by Professor Robert Koch in 1899. Mass administration of quinine under the German administration began in 1901 led by Dr Ollwig, the director of the special unit on malaria. All infected cases found through blood examination of all Africans, Indians and Arabs employed or living within European quarters or in adjacent areas were treated with 1 gram of quinine on the 9^{th} and 10^{th} day for two months [Ollwig, 1912; Orenstein, 1914; Clyde, 1967]. The proportion of infected people decreased from 74% in 1902 to 35% of the population in 1904 across Dar es Salaam; a 50% reduction [Ruge, 1907]. The "*blood sterilization"* campaign was taken over by the German military in 1904 until the First World War [Ruge, 1907; Ollwig, 1912; Clyde, 1967; Castro et al*.,* 2004]. Limited staff numbers and the mobility of the Dar population made it difficult to maintain a mass drug administration programme [Pomeroy, 1920]. With many inhabitants and visitors escaping treatment, the malaria programme gradually returned to targeted vector control, including a German ordinance for mosquito extermination that provided legal sanctions for the destruction of ponds, vessels, tins, and other sources of standing water from 1913 and led by Dr AJ Orenstein, the Colony's newly appointed malaria specialist [Pomeroy, 1920; Orenstein, 1914; Clyde, 1967; Castro et al., 2004]. These efforts were abandoned during the second half of 1914 at the start of the First World War.

3.2 British colonial malaria control: Between the wars

During the First World War, the location of quinine stores played a strategic role, for the British and German forces. The Germans used low-dose prophylactic prescriptions of quinine using supply chains from production sites at their research centres at Amani and Mpwapwa, with over 1000 kg of quinine used during the war; conversely the British only used quinine as a means of treating hospitalized patients [Clyde, 1962; Strachan, 2001].

Following the war and the establishment of a British colonial administration, anti-malarial measures were designed by Dr WA Lamborn, head of the Sanitary Branch of the Tanganyika Medical Department. Across Dar es Salaam control continued to be directed at the mosquito through oiling and drainage construction; malaria was made a notifiable disease in from 1921 [Colonial Development Fund, 1935]. In 1920 the Sanitation Branch comprised of two Medical Officers of Health, five European Sanitary Superintendents, 18 Native Sanitary Inspectors and 741 Sanitary Laborers; incurring 1.4% of the total government expenditure across the Territory. Mosquito nets were supplied by the government to all European and Asian officials who required them in 1922 and during this year over 138,000 tablets and 1,300 ampoules of quinine were issued from the medical stores for prophylactic and curative purposes. Nevertheless the annual report for 1922 reported that malaria morbidity in this population remained excessive [Tanganyika Medical & Sanitary Department, 1922].

In 1921 some concerns were raised about the possibilities of anopheles breeding in the crowns of coconut palms in Dar es Salaam and elsewhere in the Territory [Haworth, 1924]. This led to correspondence between Dr RR Scott, Director of Medical Services, Professor Balfour at the London School of Hygiene and Tropical Medicine and the Governor on whether to chop down the palm groves [Balfour, 1924; 1925]; finally supervised larval catches proved the original observations to be invalid and palm groves across Tanzanian towns were saved.

As early as 1925 doubts were voiced about the value of routine reported malaria statistics for the territory; "*Malaria in its different forms continues to provide the largest number of cases attending government hospitals. The number of native patients seen any year cannot be taken as an index of the malarial incidence during that period. The personality of the individual medical officer, the degree of intelligence of the local inhabitants and spread of education resulting in the appreciation of the value of European medicines are all factors which have to be taken into account*". It added that "*The majority of European non-officials, especially if living at any distance from a government station would certainly not call in a medical officer to treat an uncomplicated case of malaria*" [Tanganyika Medical & Sanitary Department, 1925]. In 1929 the annual medical report further highlights the inadequacies of routine statistics "*..the majority of cases of malaria are treated as out-patients are not diagnosed by blood examination..*" and that many of "*.. these cases may be attributed to other causes*" [Tanganyika Medical & Sanitary Department, 1929]. During 1929, among 390 deaths registered in Dar es Salaam among the African population 86 (22%) were recorded as "malaria" including malaria (2), cerebral malaria (3) and *Homa* (81) – the latter being a non-specific Swahili term used to define a febrile illness [Tanganyika Medical & Sanitary Department, 1929].

During 1925, it was noted that there had been an increase in the routine work undertaken by the different health officers to eradicate mosquito breeding places through the use of sanitary inspectors. But with some exasperation, the Director of Medical Services, Dr JO Shircore, notes that "*considerable numbers of the urban population of the townships in the territory who do little or nothing to prevent mosquito breeding on their premises, heavier fines are needed to convince habitual offenders of the errors of their ways*" [Tanganyika Medical & Sanitary Department, 1925].

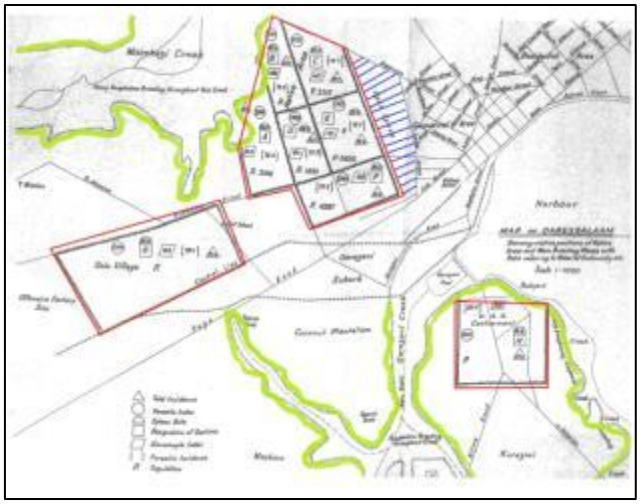
Throughout the 1920s and early 1930s the emphasis was on protecting urban settlements occupied by Europeans, including Dar es Salaam, Lindi, Bukoba, Tanga, Moshi, Kigoma, Mwanza, Morogoro and Tabora using brigades of "mosquito boys" established first by the British Royal Army Medical Corps. These brigades were tasked with periodically inspecting each part of a town to identify and destroy mosquito breeding sites through oiling (using various mixtures of road tar oil, kerosene and castor oil), draining swamps, maintaining the free flow of engineered drains and filling up holes and depressions [Tanganyika Medical & Sanitary Department, 1922; 1926; 1929; Colonial Development Fund, 1935]. For example Dr R Nixon, the resident sanitation officer at Tanga in 1927 reported that during the year 458,459 tanks, barrels, pits and wells had been inspected for larvae and 143,963 premises inspected for adult mosquitoes [Tanganyika Medical & Sanitary Department, 1927]. Nixon goes on to describe a largely mosquito free environment in the central European sectors of Tanga with anopheline infestation confined to the native fringes of the town. Also in the late 1920s Paris green was used on a limited scale and the introduction of larvivorous fish were tested [Tanganyika Medical & Sanitary Department, 1926; Owen, 1933].

The Malaria Research Unit (MRU) was established in August 1931 with support from the Colonial Development Fund (built near Koch's Medical Laboratory and the site of the present-day Government Chemist). The MRU was headed by the first Malaria Research Officer, Dr R Mackay. A similar unit was established later at Tanga between 1933 and 1936 and managed by Dr D Bagster Wilson and his wife, Margaret [Wilson, 1936a]. Much of the work of the Tanga station of the MRU was dedicated to very detailed survey descriptions of malaria infection and morbidity among communities in Tanga town, Gombero and the Pare mountains which led to Wilson's view of the challenges faced by interrupting the natural course of acquired functional immunity [Wilson, 1936b; 1939]. Bagster and Margaret Wilson re-visited Gombero village almost 30 years following their first surveys. Of note was that anopheline household densities were considerably higher in 1960 compared to 1934 but that malaria prevalence and parasite density in young children was lower in 1960 compared to 1934, which they hinted might have been a result of the wider scale availability and use of chloroquine with time [Wilson & Wilson, 1962]. The MRU in Dar es Salaam and Tanga operated on approximately £6,000 per annum and continued operations up to the start of the Second World War when malaria control and research were taken over by the military [Hocking, 1947].

Notable during the 1930s were the significant grants made by the Colonial Development Fund (equivalent to DFID today) to the engineering and environmental control of malaria in Dar es Salaam [Mackay, 1938; Clyde, 1967]. £34,330 from the fund was used in malaria control activities in Dar es Salaam between 1932 and 1936 that included engineering and drainage works at Mzimbazi, Gerezani and Kurasini creeks, developing protective zones from European settlement (Figure 3.1) and routine surveillance of mosquito larvae [Colonial Development Fund, 1935; Tanganyika Medical & Sanitary Department, 1937; Mackay, 1938]. Importantly, in relation to equivalent resources today, £27,000 was provided by the Colonial Development Fund in 1937 to provide a detailed epidemiological evaluation of the urban malaria control project [Tanganyika Medical & Sanitary Department, 1937]. 1935 saw the introduction of British ordinance Number 40 for mosquito extermination providing for

penalties aimed at controlling mosquito breeding was enacted in 1935 [Tanganyika Medical & Sanitary Department, 1937].

Figure 3.1: Map showing areas of Dar es Salaam under malaria surveillance in 1935. Anopheles breeding sites are shown using a green line while native dwelling with a red line. Adapted from Colonial Development Fund (1935).



In 1933 the Colonial authority released a guide on the prevention and cure of malaria in which it outlined the seriousness of malaria and how to prevent the disease with the proper use of a mosquito net, the recommended prophylactic and treatment doses of plasmoquine, quinine, atebrin and a combination treatment of quino-plasmoquine and how to destroy larval breeding sites using oil and kerosene. In its opening gambit the pamphlet states "*The measures to be taken to secure protection, then, can only be decided after carefully considering the circumstances: it will readily be understood that the measures which would be taken to protect the inhabitants of a compact town with a prosperous trading population able to afford money to carry out essential drainage works on the outskirts would not be suitable for a scattered community living in the swamps of the Rifiji delta: so everyone who wishes to protect himself against this expensive and fatal disease must consider the facts as they apply to his own case, and so decide what measures of protection are going to secure for him the greatest degree of protection for the least expenditure* [Tanganyika Territory, 1933]. This represents perhaps the earliest recognition in Tanzania that the design of malaria control must be driven by an understanding of the epidemiology and the cost-effectiveness of intervention.

The role of Sanitary "policemen" began to change by the 1940s to include rural communities and with more emphasis on education rather than punitive strategies. The Director of Medical services in 1940, Dr P Sneath, stated that "*I believe a new view point is necessary with respect to the outlook and training of the European health inspector whose duties must be essentially concerned with* [the] *rural population. In my opinion, he requires to be an exponent of the educational aspects of preventive medicine in the rural communities and not a sanitary policeman. To that end he should have training as an epidemiologist, who is in a position to determine the prevalence of the common diseases, who knows the means of preventing these diseases and has the knack, not of merely telling people what should be*

done to prevent them, but of showing or supervising the means of doing what is necessary and seeing it done" [Tanganyika Medical & Sanitary Department, 1940].

3.3 Malaria control post-second world war to independence: 1946-1961

In 1946 the Director of Medical Services emphasized in his annual report that "*past antimalarial activities here* [Tanzania] *appear to have involved an inextricably complex combination of field and research activities, wherein the latter have tended to over-shadow the former. Now because of the great fund of knowledge accumulated from Allied War experience, the primary objective of the Territorial malaria control policy may be summarized as an attempt to sort and apply what is already known to the malaria problems in the organized communities of the Territory and to reserve both applied and fundamental research as subject of inter territorial and extra territorial undertaking and direction, with such collaboration as will bear on the objective*" [Tanganyika Medical Department, 1946]. In essence, saying that he was keen to see less research and more operational action.

Following the Second World War, dichlorodiphenyltrichloroethane (DDT) and dieldrin were introduced for purposes of indoor residual house-spraying (IRS) [Anon, 1955]. There were pilot approaches using aerial spraying with dieldrin granules over swamps and creeks in Dar es Salaam early in 1956 [Tanganyika Medical Department, 1957; Yeo & Wilson, 1958]. These new vector control approaches were again largely limited to urban settlements and accompanied continued approaches to vector control using larvicides, environmental management and the introduction of chloroquine and paludrine as prophylactics in selected populations including school children [Tanganyika Medical Department, 1950; 1955; 1957].

In 1948, Dr Bagster Wilson, described the Territory as "*….generally regarded as consisting of a few islands in which malaria is slight or absent set in a sea of intense transmission*"; Wilson however recognized the significance of a changing urban malaria status since the turn of the century and adds "*There are now quite a number of concentrations of population, in towns or industrial undertakings in which, although the area may be small, a considerable population is being protected by European activity…*" [Tanganyika Medical Department, 1948].

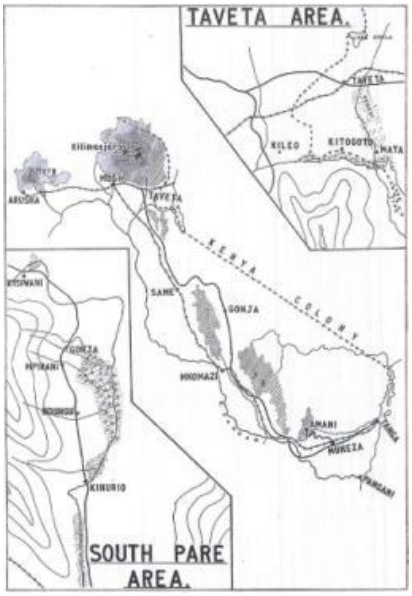
The East Africa Malaria Unit was established at Muheza in 1949, under the directorship of Dr DB Wilson with an annual budget of £9,000 provided by the Colonial Development & Welfare Scheme, but did not become fully functional until it moved to Amani in 1951. The unit changed its name in 1954 to the East Africa Institute of Malaria and Vector Borne Diseases (EA-MVBD), operating on an annual budget of approximately £28,000. Staff from the Tanganyika Malaria Service (TMS) joined the unit at Amani in 1952, headed by Dr David F Clyde, with two entomologists, five malaria field officers and 35 malaria assistants responsible to national control efforts. The TMS moved from Amani to Morogoro in 1959. By 1961 when Tanzania became independent, malaria control operations by the TMS were being undertaken in 68 townships.

By the end of the 1950s, the EA-MVBD was responsible for several pilot control schemes based on IRS with dieldrin, gammexane or DDT, larviding, drug based prophylaxis and mass drug administration at various localities including: Ukonga International airport, Kitangare,

sugar estates at Arusha Chini, Mbulu valley, Mpanda, Marvera, the Rift Valley settlement scheme at Mto-wa-Mbu ("malaria river") near Lake Manyara, Mtwara in Southern Province, the Sisal station at Mlingano and most significantly the projects at Pare-Taveta on the border with Kenya [Tanganyika Medical Department, 1955; 1957; 1959].

The Pare-Taveta Malaria pilot scheme was financed by the Colonial Development and Welfare Fund and with contributions from the East African governments. The project was conducted by staff from the EA-MVBD unit assisted by personnel provided by the World Health Organization (Drs CC Draper and A Smith). The site chosen was Pare district in Tanganyika and Taveta district in Kenya and these combined areas represented an important diversity of malaria risks within a single geographical region from hillfoot villages to swampy lowland villages (Figure 3.2). Between July and November 1955 the first dieldrin indoor spraying cycle was completed, protecting 13,000 houses and a population of 45,000. The project lasted for approximately five years and costs per round of spraying averaged £1.15 per person protected.

Figure 3.2: Location of Pare-Taveta dieldrin IRS pilot scheme 1955-1958 [EA-MVBD, 1960]



The IRS program achieved a rapid and immediate reduction in *An. gambiae* s.l household densities after the first spray round in South Pare and Taveta, and the virtual elimination of *An. funestus*, only to return five years after the cessation of spraying. May-June infant parasite rates declined from 40% in 1954 to 2% in 1958 at the South Pare swamp villages with a corresponding rise from 56% to 89% among comparison villages at Kiloza [EA-MVBD, 1960]. Overall infection prevalence in children below the age of 10 was reduced from 60% to 5% as a result of spraying over 3.5 years and was associated with a halving of infant and under-five mortality [Smith & Draper, 1959; Draper & Smith, 1960]. This was a phenomenal success but was seen as a failure to interrupt transmission in line with expectations of the Global Malaria Eradication Programme. Spraying ceased in 1958 and within several years, transmission had returned to its original intensity and mortality experiences among young children witnessed a rebound [Pringle & Matola, 1967].

By the end of the 1950s malaria outside of pilot project areas and urban centres, continued to plague the majority of the population. The 1959 annual report of the Medical Department states "*there are few communities whose life is not affected by this disease. It continues to figure very prominent in the returns from all hospitals and cerebral forms with substantial mortality have not been uncommon*" [Tanganyika Medical Department, 1959].

3.4 Post-independence malaria control to the launch of RBM: assembling the evidence

After the country's independence in 1961, the activities of the TMS began to decline and the malaria assistants and orderlies were integrated into urban health organizations within their towns. The TMS assumed an advisory and executive responsibility with headquarters in the Ministry of Health, Dar es Salaam, under the continued leadership of David Clyde. To a large extent spraying, larval source reduction and disease surveillance came to an end with a few exceptions, notably continued work in Dar es Salaam where in 1963 larviciding covered 73 km^2 across the city [Clyde, 1967; Castro et al., 2004]. A project was launched between 1961 and 1965 to examine the role of 0.3% chloroquine medicated salt sold through shops at Mto wa Mbu [Clyde et al., 1963; Clyde et al., 1964]. Despite a remarkable reduction in infection prevalence by 1965 (0% in children aged less than 5 years) this programme was stopped on WHO recommendations for fears of resistance [Clyde, 1967].

Malaria research continued under the TMS until the establishment of the National Institute of Medical Research (NIMR) in 1979 as a parastatal organization under the Ministry of Health [http://www.nimr.or.tz] and its first Director General was Professor Wen Kilama. An important affiliate of NMIR was the Swiss Tropical Institute's research centre at Ifakara in Morogoro region, established by Dr Rudolf Geigy in 1949, became associated with NMIR in 1991, and were responsible for the first synthetic malaria vaccine trial in Africa, S*Pf*66 [Alonso et al., 1994]. The Ifakara Health Research and Development Centre (IHRDC) subsequently become a nationally independent research centre in 1996 under Dr Hassan Mshinda and since 2008 it is now known as the Ifakara Heath Institute directed by Dr Salim Abdulla based in Dar es Salaam [http://ihi.or.tz].

The declining commitment to malaria-specific activities over the next two decades is evident in the estimated per capita expenditure on controlling mosquito vectors in Dar es Salaam: 1961 it was 8.14 Tanzanian Shillings (Tsh); by 1971 this had halved to 4.51 Tsh and by 1981 it was merely 1.9 Tsh [Kilama, 1994]. Adverse economic conditions during the 1970s resulted in the deterioration of the health system in many urban settings and malaria prevention was largely neglected with the exception of a few pilot approaches to chloroquine prophylaxis through village, ten-household Balozi leaders in North Mara [MacCormack, 1983; MacCormack & Lwihula, 1983].

Over the two decades following independence, the Tanzanian government focused efforts on building its broader health system, expanding its community based care based through village health workers. Throughout the 1970s and 1980s the focus of malaria was on presumptive treatment of fevers with chloroquine (CQ). CQ use post-independence increased dramatically. Several studies showed that approximately 1 in 4 people had recently taken CQ or had evidence of CQ in their urine by the 1980s and 1990s [Kilama, 1994; Hellgren et al., 1994]. The number of CQ tablets issued by the Central Medical Stores

rose from 102 million in 1975/76 to 300 million by 1980/81 [Kilama, 1994] in part a direct result of expanding community health worker needs to mount basic fever management services at the periphery but highlights the rising scale of CQ consumption during this period. Nevertheless, despite a growing access to antimalarials for fever management, the 1980s were a period where very little was done to prevent infection. At Muhumbili Medical Centre, in Dar es Salaam, 28% of all patients on the paediatric ward had malaria, 5% of whom presented with cerebral malaria [Msengi & Yohani, 1984].

In 1990 the Government launched the National Malaria Control Programme (NMCP) headed by Dr. Mfungo Marero to support the Malaria Operational Plan 1990-1995. Since then, the NMCP came under the Epidemiology and Disease Surveillance Section, whose head, reported to the Director of Preventive Services. The NMCP was supported by a National Malaria Advisory Committee (NMAC) which managed three technical committees: clinical, behavioral change and vector control. During this period, the NMCP began to reignite a broad health system awareness of malaria through workshops to engage Regional Primary Health Care Committees, health workers and laboratory staff. A series of revised guidelines were developed for diagnosis, treatment and referral of malaria cases and materials for Information Education and Communications (IEC) were produced.

3.4.1 Changing antimalarial drug policies

There was some debate on the presence of CQ resistance during the mid-1960s in areas where it had been used widely as a prophylactic [Clyde, 1967]. By 1966 there was no documented case of CQ resistant malaria in Tanzania. Pyrimethamine resistance, however, was detected in 1953 [Clyde & Shute, 1954] and spread without drug pressure (mono-therapeutic use had been stopped) appearing miles from its original focus [Kouznetsov et al., 1980]. Suspicions of reduced chloroquine sensitivity re-emerged in the late 1970s and early 1980s at sites where there had been a high CQ drug pressure as part of chemo-suppression campaigns [Onori et al., 1982; Draper et al., 1985].

Country wide *in vitro* and *in vivo* CQ sensitivity testing began in 1982 under the direction of NIMR. Alarming rates of delayed parasitological clearance and resistance following standard treatment courses of CQ began to emerge rapidly. This was documented in hospital admissions of malaria patients, asymptomatic school children and febrile out-patient attenders across the country [Kilimali & Mkutya, 1985; Mutabingwa et al., 1985; Irare et al., 1988; Huber et al., 1993; Fowler et al., 1993; Premji et al., 1994; Mshinda et al., 1996; Warsame et al., 1999]. By 1999 many sites had documented CQ clinical failure rates in excess of 40%.

In response to the alarming rates of CQ resistance and difficulties in assembling timely and relevant drug efficacy data for national ministry of health engagement, the East African Network for Monitoring Antimalarial Treatment (EANMAT) was founded in 1997. The purpose was to provide a network of sentinel sites across East Africa to assemble standardized, quality assured data and managed as a partnership between research/training institutes and Ministries of Health. Initially the network included Tanzania, Kenya and Uganda and later extended to Zanzibar, Burundi and Rwanda [EANMAT, 2001]. Funding was provided by the UK's Department for International Development (DFID) and the first chairman was from

NIMR, Dr Theonest Mutabingwa. The eight sites were established under the coordination of the NMCP. The sites include clinics at: Mkuzi, Chamwino, Masasi, Mlimba, Butimba, Kyela, Kigoma and Kibaha. Participating research/training Institutions managing the sites included: NIMR, IHRD, Muhimbili University of Health and Allied Sciences, Bugando Medical Centre and Kilimanjaro Christian Medical Centre. Data generated from this regional network was instrumental in advocating for a change from CQ to SP and subsequently to Artemisinin Combination Therapy (ACT) in the sub-region [Attaran et al., 2006] and led to changing the policy in Tanzania from CQ to SP in 2001 and from SP to artemether-lumefanthrine (ALu) in 2004 but implementation was delayed until drugs and training could be completed in December 2006.

Williams et al. (2004) in their analysis of the drug policy debate in Tanzania highlighted a drug policy meeting in May 1999 of scientists, clinicians and Ministry of Health representatives on the need to change policy in Tanzania and a quote from one of the scientists expressing concern at the delays in abandoning chloroquine "*We have evidence . . . yes! But the Ministry is saying we have no choice before us as SP is not going to last; SP is too costly and we have no money. So, let us go much longer* [referring to use of chloroquine]" [cited in Williams et al., 2004]. This highlights a challenging period for policy makers in the sub-region and how to interpret the complex resistance data and costs of drug policy change. It was not until August 2001 that the national drug policy was implemented to support the use of SP as first line therapy [Williams et al., 2004]. However, as expected, this was a short-lived effective policy as Tanzania soon faced the challenge of rapidly emerging SP resistance, already present when the country changed to SP [Ronn et al., 1996; Trigg et al., 1997; EANMAT, 2003]. Before 2000 two of six sentinel sites in Tanzania had reported combined early and late SP treatment failures of greater than 15% of treated children [EANMAT, 2003].

3.4.2 Establishing a national insecticide-treated bed net policy

Entomological, experimental hut studies on insecticide-treated bed nets (ITN) in Africa started during the early 1980s in Tanzania using materials impregnated with permethrin or diethyl toluamide (DEET) [Lines et al., 1985]. Several efficacy trials ITN followed over the next decade across Tanzania [Lyimo et al., 1991; Njunwa et al., 1991; Magesa et al., 1991;Njau et al., 1993; Curtis et al., 1996; Maxwell et al., 1999] and were undertaken against a background of ongoing larger community randomized controlled trials on ITNs against mortality in The Gambia, Kenya, Burkina Faso and Ghana [Lengeler, 2004]. Operational studies for ITN delivery strategies were conducted in Bagamoyo spearheaded by scientists from Muhumbili University with funds from USAID between 1991 and 1996. They used existing village health structures to create village bed net committees who sold subsidized nets to the community to generate a revolving fund [Makemba et al., 1995; Premji et al., 1995]. In 1996, a large observational, operational study was undertaken by the Ifakara Health Research Centre to examine the impact a large-scale social marketing campaign of ITN delivery in the Kilombero region covering 480,000 people [Schellenberg et al., 1999]. The KINET study showed rapid uptake of socially marketed nets [Schellenberg et al., 1999], significant protection against malaria infection [Abdulla et al., 2001] and mortality [Schellenberg et al.,2001] in young children. This was an influential study in setting a stage for ITN scaling up in Tanzania.

In 1999, a national ITN stakeholder conference was held in Dar es Salaam following the success of the KINET project. A larger stakeholder meeting followed, under the auspices of the Ministry of Health and PSI, to further consolidate the national strategy for scaling up ITNs. The National Insecticide Treated Net Campaign (NATNET) was launched under an "*enabling environment*" for multi-stakeholder investment including national manufacturers (mainly A to Z Textile Mills and SunFlag based in Arusha and Tanzania Textile Manufacturing Ltd in Dar es Salaam), private sector retailers, social marketing agencies, non-government partners and the government sector [Magesa et al., 2005; Njau et al., 2009a]. In 2000 the government zero-rated taxes and tariffs for mosquito nets and materials required for their manufacture [Starling & Njau, 2002]. For the next five years this strategy provided the framework for Tanzania's nationwide Strategic Social Marketing (SMARTNET) under the NATNET plan, based on subsidized nets to end users and implemented by PSI-Tanzania with overseas development assistance from the UK and Netherlands aid programmes. In November 2004, the Tanzanian National ITN Voucher Scheme (TNVS) was launched with funds provided by the Global Fund to selectively target pregnant women with highly subsidized nets available from 6,000 registered retailers. The scheme also provided a free insecticide re-treatment kit for infants who completed DPT3 and measles vaccination. In 2006, NATNETS expanded the TNVS to include infants as target vulnerable groups, through PMI support. The Ministry of Health sub-contracted the Mennonite Economic Development Associates (MEDA), a nationally registered NGO to manage all the logistics of the programme [Njau et al., 2009a; http://medatanzania.org/; De Savigny et al., 2012]. Tanzania probably has one of the most successful public-private partnerships in ITN delivery, involving local manufacturers and the public sector [Njau et al., 2009b]. All nets today have a single approved branding whether available in the private or public sectors. Between 2004 and 2012 the TNVS has delivered an estimated 9 million ITN.

3.4.3 Urban malaria control revisited

The other notable operational investigation of combined vector control during this period was the Dar es Salaam and Tanga Urban Malaria Control Project (UMCP) between 1988 and 1996. UMCP was an ambitious programme deploying IRS using Fenitrothion 40% wetable powder every 3-6 months (suspended in 1993 and 1994 due to lack of insecticides), selling over 180,000 subsidized ITN and reduction of breeding sites through environmental management, weekly larviciding (Pyriproxifen) and some reference to use of expanded polystyrene beads in closed water collection sites. The project might be seen as the third wave of concerted urban malaria control in Dar since 1900. Intervention implementation during the 1988 project was spatially stratified across Dar based on definitions of urban and peri-urban status, across the latter both IRS and ITN were introduced. The project received equipment, technical and operational expertise amounting to US$ 17 million from the Japan International Cooperation Agency (JICA) over the eight years. An additional US$ 2.7 million was provided by the Tanzanian Ministry of Health (13.4%), Dar es Salaam City Council (65.2%) and Tanga municipal council (21.4%). By 1996, malaria parasitaemia in school children aged 6-16 years fell markedly in the population covered [Yamagata, 1996]; however, the project ended because resources could not be found to sustain it by government or bilateral partners.

3.4.4 Epidemics

El Niño Southern Oscillation (ENSO) unstable climate conditions in the Pacific during 1997–1998 led to exceptional rainfall patterns across East Africa [McPhaden, 1999] resulting in several dramatic malaria epidemics across the sub-region. In Tanzania the El Niño epidemics were largely concentrated in the high altitude areas around Lake Victoria, notably Kagera, and the Usumbaras [Carlstedt, 1997; Lindsay et al., 2000; Wort et al., 2004]. Refugees from neighbouring countries in 1997 suffered heavily suffered heavily from the coincidence of exceptional transmission and having arrived from areas where immunity had not been acquired most notably at the Kibondo and Nduta camps in north-west Tanzania [Crowe, 1997].

3.4.5 The 1997-2000 National Malaria Strategy

In 1998, the WHO and US and other partners embarked on a major initiative to accelerate malaria control in the region [WHO, 1997]. Tanzania was one of the 20 countries selected in this endeavour and developed a National Malaria Strategy 1997-2000 which was termed the *Malaria Accelerated Plan of Action*. The strategy promoted a broad suite of vector control methods including detection and prevention of epidemics, case-management and malaria prevention in pregnancy and supporting initiatives such as behavioural change, monitoring and evaluation and research, based on WHO recommendations for control in Africa [WHO, 1993]. The overall goal was to "*contribute towards improving health and well-being of all Tanzanians especially those at risk*" while aligning to the broader health sector strategic plan [NMCP, 1997]. The target was to achieve a 50% reduction in case-fatality rates in hospitals by 2000, a 30% reduction in the incidence of malaria in the community and a 30% reduction in the incidence of severe life-threatening malaria among children under the age of 5 years. However, the plan lacked the details on how Monitoring and Evaluation (M&E) metrics would be measured. The role of the NMCP remained one of providing strategic direction in the development of policies, coordination of activities and provision of technical support and capacity building at the district level including advocacy and training of the District Management Teams.

In summary, the post-independence period of malaria control in Tanzania was one characterized by a rapid escalation in the presumptive use of CQ through an expansion of the formal health system, community-level primary care and a growing private sector. This was accompanied by a declining interest and investment in vector control. The general process of decentralization and expansion of the primary care health system was seen by some to herald the demise of Tanzania's malaria control efforts; Professor Wen Kilama states in an address in 1994 "*the excellent mosquito control programmes were suddenly disrupted with decentralization in 1972: fewer funds were allocated, some operational personnel had their services terminated, and proper records were not kept*" [Kilama, 1994]. Toward the end of the 1980s malaria control began to unravel in Tanzania as with many other areas of sub-Saharan Africa [Snow et al., 2012]. Chloroquine resistance became established and spread at alarming rate, epidemics led to high disease burdens in areas previously free of malaria and the funding necessary to undertake any systematic, nationwide vector control was conspicuous by its absence.

3.5 The decade of RBM 2000-2010

The launch of Roll Back Malaria (RBM) initiative in 1998 [Nabarro & Tayler, 1998] provided the Ministry of Health an opportunity to position malaria within the Health Sector Reforms. Thus malaria was interwoven with other health sector initiatives including the Package for Essential Health Interventions (PEHI) [NPEHI, 2000], the essential drugs supply, health information systems and primary health care packages. The reforms were also aligned to Millennium Development Goals [UNDP, 2003] and Tanzania's Development Vision 2025 launched in 1999 [http://www.tanzania.go.tz/vision.htm].

In 2000 malaria control, developed a tailor-made package for malaria planning and implementation for district managers. These were rolled out in all 114 districts at that time. In 2000, the NMCP staff consisted of three medical officers and four health officers, headed by Dr Alex Mwita, who served from 1997–2011. The programme was challenged by inadequate office space within the Expanded Programme of Immunization on the outskirts of Dar es Salaam at Mabibo. The programme was funded with less than US$ 150,000 to provide interventions throughout the country [Snow et al., 2010; RBM, 2012].

3.5.1 The 2002-2007 National Malaria Strategy

The development of the 2002–2007 strategic plan was based on a comprehensive situation analysis spearheaded by WHO [NMCP, 2002]. The goal was "*to reduce mortality and morbidity due to malaria in all 20 regionsof the country by 25% by 2007 and by 50% by 2010*" through the delivery of four strategic approaches: improved malaria case management, vector control through the use of ITNs, the control of malaria in pregnancy and malaria epidemic prevention and control. The strategy set all intervention targets to be 60% by 2007. The strategy was developed in the era of renewed international commitment and investment in malaria control. Such initiatives included commitments made by African Head of States during the Abuja Summit in [WHO, 2000], the Global Fund to fight against HIV/AIDs, Tuberculosis and Malaria in 2002, and the US Presidents Malaria Initiative in 2004. In 2004 the NMCP moved to a new office complex, next to NIMR headquarters. Human resources and technical assistance to the programme from bi-lateral and WHO sources was increased.

The biggest challenge facing the NMCP at the time was the very recent change from chloroquine to SP, particularly the effective implementation at all levels of health care delivery systems, the perceived side effects of the drug by providers. In the 2002-2007 strategy, the Ministry of Health and its partners recognised the importance of engaging the private sector in case management of malaria. This inlcuded strengthening the delivery of medicines though retail outlets, notably Accredited Drug Dispensing Outlets (ADDOs) [MSH, 2001; Goodman, 2004]. There was also a strong emphasis on community level integration of correct treatment of fever within the integrated management of childhood illnesses (IMCI) initiative, established in 1996 in Tanzania [Armstrong Schellenberg et al., 2004].

In 2002, Intermittent Presumptive Treatment in pregnancy (IPTp) using SP was introduced as part of a national policy to provide protection to pregnant women in their second and third trimesters through Focussed Antenatal Care (ANC). The target of this intervention was

to reach at least 60% of pregnant women by 2007. Scaling up the use of ITNs was the main vector control intervention advocated in this strategy using three interdependent delivery mechanisms; Establishment of the ITN Cell within the NMCP to provide overall coordination and monitoring of the NATNETs activities in the country from with financial support from the Swiss Tropical Institute (STI), the ITN voucher scheme and a contracted ITN social marketing campaign (SMARTNET) including managing delivery of insecticide treatment kits (section 3.4.2.).

The estimated cost of the strategy was approximately USD$ 76 million. Financial support for the strategy was mainly from Global Fund Round 1, the World Health Organization, PMI, DFID, the Netherlands Embassy and the Government. This financial support was progressively increased towards the end of the 2002-2007 strategy. In 2006 funding for malaria control was a staggering US$ 34.3 million and doubling in 2007 to US$ 67.8 million [Snow et al., 2010; RBM, 2012].

In order to monitor performance of the strategy, seven districts were selected as sentinel districts. The number of sentinel districts increased progressively from seven in 2001 to nine in 2003 and to 21 districts in 2005. Each sentinel district represented a region. A series of household and facility based surveys were carried out in 2001, 2003, 2005, 2006 and 2008 [NMCP, 2006]. In 2003, the first Annual Malaria Conference was held as a platform to discuss and evaluate implementation issues [MoH&SW, 2003]. All District Medical Officers (DMOs) and other partners participated. The meeting provided an opportunity to collect malaria annual reports from each district using a standardized format. Data collected was used to establish the NMCP database, which has been subsequently updated annually. The quality of the data in terms of completeness, accuracy and timeliness remain a challenge and the accuracy of assessing changes in trends of facility based malaria burden over the years remains sub- optimal.

Two national household surveys were undertaken during the period of this strategy: in 2004-05 [NBS, 2005] and in 2007-08 [TACAIDS, 2008]. By 2007 only 33% of children below the age of five and 24% of pregnant women used an ITN the night before the survey. This was a demonstrable improvement from 2005 when the corresponding coverage figures were 20% (children) and 19% (pregnant women), however between a quarter and a half lower in 2007-2008 than the national programme's ambition for 2007. Only 22% of pregnant women took two or more doses of SP during their last pregnancy in 2005, rising to only 30% by 2007-08. 51% of children who reported a fever in the last two weeks received an antimalarial on the same or next day in 2004-05; very few received chloroquine (1.7%), abandoned in 2001, but only 21.4% received SP the recommended first-line treatment in 2004-05, while 18% received amodiaquine. This poor access to SP was largely attributed to severe stock-outs of SP in health facilities in the period leading up to the introduction of ALu, although compensated by the wide availability of SP in shops. In 2007-08 fewer (34%) febrile children promptly received an antimalarial treatment during their illness; few children received SP (2.5%), abandoned in 2006, but only 14.2% of fevers received ALu on the same or next day of their illness, 18% of fevers continued to be treated with amodiaquine. These coverage data reveal the difficulties facing improved treatment access, some of the failings of reaching high ITN coverage using only social marketing and private sector strategies and the inevitable consequence of long periods of poor funding support.

In order to increase community awareness around all interventions, the Ministry engaged with several partners particularly NGOs such as Population Service International (PSI), COMMIT and Tanzania Alliance Against Malaria (TAANAM).

During the late 1990s early 2000s several studies were launched in Africa to examine the impact of Intermittent preventive treatment in infants (IPTi) involving the delivery of three treatment doses of an antimalarial drug, mainly SP, as directly observed therapy alongside routine vaccinations against DPT/OPV (at about 2-3 months of age) and measles (about 9 months of age) and given regardless of the presence of symptoms or parasitaemia. One pivotal trial was undertaken at Ifakara in Southern Tanzania between August 1999 and April 2000 [Schellenberg et al., 2001]. The trial demonstrated a 59% reduction in clinical episodes. These results prompted a larger effectiveness trial that began in 2005 in Southern Tanzania covering the districts of Nachingwea, Lindi Rural, Ruangwa, Tandahimba and Newala. The project was launched under the branded name of *Mkinge,* Swahili for protect and linked to awareness campaigns of "Protect your child from malaria." [Manzi et al., 2009; Schellenberg et al., 2011]. The trial reached coverage rates of between 47-76%, however intention-to-treat analysis of infection prevalence and infant survival were inconclusive [Schellenberg et al., 2010; 2011]. Despite WHO recommendations, Tanzania has not adopted this strategy.

3.5.2 The 2008-2013 National Malaria Strategy

In developing the 2008 -2013 strategy, the Ministry of Health & Social Welfare, in collaboration with partners, aligned the framework to the impetus of the Roll Back Malaria Partnership of Scale Up For Impact (SUFI) to achieve targets of universal coverage of 80% by 2010 and the Millennium Development Goals by 2015 [NMCP, 2008].

The 2008-2013 vision was that "*Tanzania becomes a society where malaria is no longer a threat to the health of its citizens regardless of gender, religion or socio-economic status*". The strategy included two main technical areas: a) Malaria diagnosis and treatment; and b) Integrated Malaria Vector Control both supported by improved M&E (including , operational research and epidemic early detection and response), community-based malaria control and behavioural change initiatives, and retaining a focus on decentralized support through regional and district capacity building around malaria control [NMCP, 2008].

The strategic plan 2008-2013 built upon the successes of the previous strategy embraced a new paradigm shift towards "*phased malaria elimination*" beginning with the reduction in the disease burden caused by malaria by 80% of those defined in 2007. This is probably the first time in the history of malaria control in Tanzania that elimination was proposed as a long-term strategy. The Honorable Minister for Health and Social Welfare, Professor David Mwakyusa, defends this ambition in the introduction of the national strategy "*Without an ambitious plan, we cannot come to grips with a ruthless enemy which malaria, indeed is. There is no doubt that with a combination of our efforts, of our friends' elimination should be around the corner"* [NMCP, 2008].

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The strategy includes two main technical areas: a) Malaria diagnosis and treatment; and b) Integrated Malaria Vector Control both supported by improved M&E (including sentinel sites, operational research and epidemic early detection and response), community-based malaria control and behavioural change initiatives, and retaining a focus on decentralized support through regional and district capacity building around malaria control.

There are significant changes in technical and strategic directions of malaria control interventions in the 2008-13 compared to the previous plan 2000-07. There was an emphasis on achieving universal coverage to attain 80% for all interventions by 2013. There was a much stronger, and clearly defined, emphasis on Integrated Vector Malaria Management (IVMC): in addition to ITN and IRS, larval control and environmental management in urban areas were added. This renewed emphasis followed a renaissance in successful malaria control in Dar es Salaam, the Urban Malaria Control Programme (UMCP). The UMCP was launched in 2004 by the Dar es Salaam City Council as part of routine municipal services involving community-level activities focused on larval breeding site identification/mosquito surveillance and fortnightly larviciding with environmental management by community-based resource persons [Fillinger et al*.,* 2008; Castro et al*.,* 2009; Chaki et al., 2011]. The average annual economic cost of the UMCP across 15 wards was estimated to be US$ 559,476 [Worrall & Fillinger, 2011]. Urban malaria control, based on this model, is now expected to scale up to other urban councils in the country by 2013 using *Bacillus sphaericus* (Bs,) and *Bacillus thuringiensis israelensis* (Bti). A factory, using Government of Tanzania infrastructure funding with technical support from the Government of Cuba is nearly completed at Kibaha, 40 km from Dar es Salaam and will have the capacity to produce 6 million litres of Bs and Bti per year.

IRS was re-introduced as part of vector control in the epidemic prone and high malaria endemic districts. Implementation started in 2007 in Muleba and Karagwe district, in Kagera region to prevent malaria epidemics using lambda-cyhalothrin 0.05% (ICON®); the operation targeted 100,000 households and managed by the international NGO Research Triangle Institute (RTI) [http://www.rti.org] in collaboration with NMCP, respective regional and district authorities. The intervention was expanded across the Kagera region in 2009 covering 450,000 households and by 2010 approximately 2.2 million people were protected by IRS. In 2010, it was further scaled up to include the two remaining lakeside regions of Mara and Mwanza targeting by 2010 over 1.25 million households and 6.5 million people. By 2011 the programme had successfully reached over 90% of households in 18 districts in the three regions contributing to a 67% reduction in malaria infection rates in children in sample villages [RTI, 2012; Mashauri et al., 2013; West et al., 2013]. Resistance to lambda-cyhalothrin has been detected in this area and Bendiocarb, a Carbamate, has been the insecticide selected from 2013 [Protopopoff et al., 2013]. More details of IRS coverage are provided in Chapter 6. This intervention is financially supported by PMI.

In recognition of the slow progress in achieving the targets for ITN coverage and use through the public-private initiatives, which mainly targeted vulnerable groups, the ITN strategy evolved to include a mass-campaign delivery mechanism. The paradigm shift from targeted ITN delivery to universal coverage involved an intensive policy dialogue between the government and malaria partners. However, the government ultimately succeeded in convincing the malaria fraternity that this was the direction that they deemed was

necessary to achieve universal coverage and ultimately reduce the malaria burden [Alex Mwita, personal communication].

Two mass LLIN "*catch-up*" campaigns were implemented in Tanzania between 2009 and 2011 during which a total of 24.6 million LLINs were distributed free of charge [Bonner et al., 2011; Koenker et al., 2013]. The two campaigns were some of the most successful and largest distributions of LLINs, resulting in Tanzania being one of the first African countries to achieve universal household ownership of at least one LLIN amongst all segments of the population. The first "*catch-up*" campaign was launched in 2009 and 8.7 million Long-lasting Insecticide treated Nets (LLIN) were distributed to children under five years. The campaign was jointly funded by the GFATM, World Bank, PMI, UNICEF, Government of Tanzania and the Swiss Development agnecy. The 2010 universal coverage campaign targeted all sleeping spaces not protected through the previous catch-up campaign and the TNVS. This was initiated in October 2010 and completed in November 2011, distributing 18.2 million LLINs, supported by the Red Cross Tanzania with funding from PMI [Renggli et al., 2013].

The TNVS campaign continues to form the bed-rock of the "*keep up*" campaign strategy, having delivered 9 million nets since 2004, but mass, catch-up campaigns have reduced some of the inequities in LLIN access. According to the national household sample survey in 2010 [NBS, 2011], ITN use by children aged less than five the night before the survey was 64%, double the estimates reported in 2007-08. The national household sample survey undertaken toward the end of 2011, showed that 72.3% of all children under the age of five were reported sleeping under an ITN the night before the survey [NBS, 2013]. The impact of these catch-up campaigns is clear; both campaigns cost of USD 160.2 million [Renggli et al., 2013]. Modelled district-level estimates of ITN coverage between 2000 and 2010-2012 are provided in Chapter 6.

Another observation in the new strategic plan was that providing efficacious and prompt treatment of fevers was a continuous challenge. Significant funds from the Global Fund Rounds 7 and 9 and PMI were dedicated to ensuring adequate supplies of ALu in the public sector and encouraging early models of delivery through the private, retail sectors. New approaches to better managing drug supply using mobile phone technology to eradicate stock outs in the public sector were sponsored by the Roll Back Malaria Partnership, Novartis Pharma AG, Vodafone, IBM, Malaria Medicines Initiative (MMV) and the NMCP between 2009 and 2010 and called *SMS for Life* [Barrington et al., 2010]. This pilot project was undertaken in the rural districts of Lindi, Kigoma and Ulanga and showed a sharp decline in stock-outs. As a result, PSI was contracted to conduct a national roll-out of the system through training Council management teams and health service providers.

The revised 2008-2013 strategy also promoted the use of diagnostics in the management of febrile illness. This was in-line with a growing recognition that relatively cheap and sensitive rapid diagnostics could be made available at the most peripheral levels of the health sector and that as vector control became more wide-spread asymptomatic infection prevalence would begin to decline [D'Acremont et al., 2009; Kahama-Maro et al. 2011], reversing the dogma that it was legitimate to consider all fevers as malaria across Tanzania and previously advocated as part of IMCI. As such standard treatment guidelines were changed in 2011 to support the use of rapid diagnostic tests (RDTs) and microscopy in the diagnosis of malaria

[MoHSW, 2011]. Although RDTs were introduced into the public sector facilities from 2011, wide scale distribution began in 2013. The NMCP has a specific objective to ensure that the proportion of laboratory confirmed “malaria” cases shall increase from 20% in 2007 to 80% by 2013. The introduction of RDTs as a means to change established health worker practices for fever treatment has not, however, been easy [McMorrow et al., 2008; Masanga et al., 2010]

The NMCP recognized the difficulties in reaching the majority of fevers with the recommended ALu, as only 14.2% of febrile children during the 2007-08 national household sample survey. As such it embraced a pilot initiative to increase availability through the private sector and was selected as one of 10 countries to participate in the Global Fund’s Affordable Medicines Facility for malaria (AMFm) initiative in 2009 [Global Fund, 2012; Tougher et al., 2012]. AMFm negotiated with manufacturers to reduce the price of their ACTs and then in-country national importers, wholesalers and retailers worked out an affordable profit margin to ensure quality assured ALu to consumers at the periphery through ADDOs, Part II drug stores and general shops, approximately $0.05 per tablet [Rutta et al., 2011]. A study was undertaken nested within the Kilombero and Ulanga district Demographic Surveillance System, managed by IHI [Hetzel et al., 2007], to examine longitudinally the availability, accessibility, costs and uptake of ALu both the private retail and public health sectors. The study showed improved access by households to ALu, no direct competition with the public sector, but no change in affordability [Alba et al., 2010]. Despite concerted efforts in the Kilombero-Ulanga and Rufiji DSS areas to improve access to ALu less than 50% of fever cases had access to an authorized ACT provider within 24 hours of fever onset by 2011 [Khatib et al., 2013]. The AMFm was a short-lived project and has not been recommended for further support in its current form by various international stakeholders [Talisuna et al., 2012]. Nationally only 21% of febrile children took ALu on the same day/next day of the illness starting in 2011/12; however an encouraging sign was that 25% of febrile children were reported as having been tested for malaria and it is conceivable that not all negative patients were treated with an antimalarial, making this indicator hard to interpret unless questions asked and analysed differently [NBS, 2013].

Finally, the strategic plans for 2008-2013 were accompanied by a very detailed Monitoring and Evaluation (M&E) plan [NMCP, 2009]. The plan covers the recommendations made by RBM’s MERG but provides a detailed outline of all possible data sources and how these will be integrated into a single platform, managed by the NMCP for them to monitor progress. As part of integrated management, the plan highlights the need to access more effectively the existing national routine data from Health Information and Management System (HMIS) and the Integrated Disease Surveillance and Response (IDSR) strategy including data collected on the numbers of malaria and anemia cases, provision of IPTp, bednet vouchers and iron/folate to ANC clients, and deaths related to malaria. However, the plan recognizes that in 2009 most cases were diagnosed on clinical grounds and not with any parasitological testing. With the introduction of RDTs, a plan to improve the quality of laboratory diagnosis, overall health system strengthening initiatives including an ongoing training of to a cadre of health staff embedded in the district health system as part of a two-year program known as the Field Epidemiology and Laboratory Training Program (FELTP), with support from PMI, the quality of confirmed malaria reports is expected to improve.

Recognizing the challenges of guaranteeing a perfect national HMIS, the NMCP established a network of health facilities to be used for tracking trends in malaria related morbidity and mortality at 15 sentinel health facilities in 2008, however from 2010 reporting dwindled as funding ended. On the other hand, NMCP collect information from population-based surveys, perform routine antimalarial drug efficacy assessments and entomologic surveillance from established sentinel sites. These are managed by the NMCP with collaborating partners including IHI, NIMR and others. The sentinel site data are expected to support other national data particularly the malaria indicator surveys as part of Demographic and Health Surveys (DHS) in 2014/15 and Malaria Indicator Surveys (MIS) in 2015/16.

In 2009, the NMCP had five medical doctors with post-graduate training in public health/ applied epidemiology, three environmental health officers, two environmental engineers, an M&E officer, a pharmacist, a laboratory technologist, a social welfare officer, a health administrator, accountants and support staff. In 2008 development assistance for malaria had risen to US$ 112.3 million, dropped to US$ 87.4 million in 2009 and disbursements rose again in 2010 to a remarkable US$ 137.9 million, a 100 fold increase in malaria funding when compared to 2002 [Snow et al., 2010; RBM, 2012]. The majority of the funding continued since 2003 to come from the Global Fund, with increasingly significant funding from PMI from 2006 and funds from the World Bank Booster Program in 2009.

3.6 The future

Tanzania has made important progress toward ensuring access to malaria control interventions over the last five years; however it has a long-way to go to reach, and sustain, a policy of universal coverage of effective curative services and prevention. Leveraging existing partnerships, including the private sector, and effective engagement of the community in malaria control will be essential components for the future of malaria control in Tanzania. The Permanent Secretary of the Ministry of Health and Social Welfare, Blandina SJ Nyoni, states in the RBM impact report "*Though Tanzania has made progress, it cannot yet claim victory and still, too many suffer from malaria. However, fewer children still die from malaria in Tanzania. To a great extent, the country's progress depends on how well it does in waking up the population to the fact that malaria is unacceptable, and so the saying: Zinduka! Malaria Haikubaliki (Wake up! Malaria is unacceptable)*" [RBM, 2012]. This community awareness campaign, launched in 2010, will be critical in creating a sustained demand for malaria control from the grass roots. It also requires a political commitment, and perhaps this is where Tanzania leads the continent in the strong advocacy provided by the President, Dr Jakaya Mrisho Kikwete, who has spearheaded the establishment of the African Leaders Malaria Alliance (ALMA) to promote a greater political awareness and what governments should contribute from domestic resources.

Making sure malaria is properly diagnosed, adequately treated and monitored will not be an easy task. This will require strengthening of the health system at all levels. At a time of global financial crisis ensuring adequate overseas development assistance will also be a challenge. In Tanzania's favour in 2013 the Global Fund announced that the country would be one of four high burden African countries to receive guaranteed sustained support. Nevertheless using an intelligent planning platform based on data will be necessary to

define priority national investment and monitor change. The following chapters in this report go some way to providing this provisional platform.

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Chapter 4

Mapping malaria transmission intensity

4.1 Previous malaria map use in Tanzania

4.1.1 Maps and malaria endemicity descriptions pre-independence

The first cartography of malaria risk in the country was produced as part of an Atlas by the Government of Tanganyika in 1956. This map was developed as a length of transmission, seasonality map, based on a combination of expert opinion and climatology [Figure 4.1a: Government of Tanganyika, 1956]. There is no evidence that this map was used in any empirical sense to guide control decisions at the time, but did represent an early recognition that all was not equal across the Territory.

From the early 1960s David Clyde and colleagues began to review the malaria situation for the various regions of the Territory [Clyde, 1962; Clyde & Msangi, 1963; Clyde & Mzoo, 1964; Clyde & Mluba, 1964; Clyde & Elibariki, 1965; Clyde, 1965]. This represented one of the first attempts to create an inventory of historical epidemiological data in Africa and summarized in Clyde's book on *Malaria in Tanzania* (1967). Using these data, a semi-qualitative description of malaria risk was based on endemicity classifications first developed at the 1958 WHO Kampala malaria in Africa conference based on spleen rates in children, later adapted to be classified according to parasite rates (PR) [Metseelar & Van Thiel, 1959]. Clyde and colleagues described four strata:

a) *Highly endemic zones* (PR in children> 50%) which included the coastal and sub-coastal plains, all the way to the foot of the Eastern Arc Range including Pare, Usambara and Nguu Mountains in the north east, Ukaguru, Ulugulu, Rubeho and Udzungwa Mountains of central and southern Tanzania, the shores of Lakes Nyasa, Tanganyika and Victoria, the plateaux of Tabora, Singida, and the Serengeti Plain. In total an area covering more than 50% of the country was defined as highly endemic.

b) *Mesoendemic zones* which included the Masai Steppe in the Rift Valley, the dry region which borders the Central Plateau (Dodoma), the foothills of Kilimanjaro between 850 and 1,250 m.

c) *Hypo-endemic zones* which included the mountainous regions of Pare, Usambara, Arusha, and Kilimanjaro (between 1,250-1,500 m) in the north, the fringe of Southern Highlands.

d) *Malaria-free* which included the high ground of Kilimanjaro (above 1,500 m), the part of the highlands to the west of Lake Victoria, the Njombe region highlands parallel to Lake Nyasa, the Iringa Region highlands of Mufindi and Udzungwa in the south.

This description malaria risk served as the basis of most impressions of malaria endemicity across mainland Tanzania for the next 30 years.

4.1.2 Malaria endemicity descriptions and maps used during National Strategic Plans 1997-2008

The 1997-2000 national malaria strategy [NMCP, 1997] did not present any malaria risk map, but did provide a narrative of malaria endemicity across the country, although none of these strata were used in any meaningful way to guide the selection of malaria interventions. The strata provided in the strategy were those largely developed in the 1960s, and while not traditionally anchored on parasite or spleen rates, the descriptions were again based on the duration of the malaria seasons as a proxy for endemicity classification:

> (a) *Hypoendemic* - with less than 3 months transmission: areas where transmission is low and normally the effects of malaria on the population are minimal except during epidemics; including areas above 2000 m and temperatures not exceeding 20°C (some parts in Mbeya, Iringa, Usambara mountain areas of Tanga and Kilimanjaro regions).
>
> (b) *Mesoendemic* - up to 3 months of transmission, including areas at higher altitudes along the East African Rift Valley or mountain areas with temperatures of 10^0c -20^0c and mean annual vapour pressures of 13-15 millibars; malaria may occur in epidemic forms when there are environmental and climatic changes (some parts of Arusha region such as those above the Rift Valley and Ngorongoro, Loliondo, Serengeti in Mara region, some parts of Kagera and Kilimanjaro regions).
>
> (c) *Hyperendemic* - 3 to 6 months of transmission in a year, intense but seasonal transmission and where the immunity is insufficient to prevent the effects of malaria on all age groups, with temperatures above 15°C and mean annual vapour pressures of 10-20 millibars (Dodoma, Singida, Ruvuma, Mbeya, Tabora, Shinyanga, Mwanza, Kigoma, Rukwa and some areas in Arusha region).
>
> (d) *Holoendemic* - 6 to 12 months transmission: perennial high transmission intensity, resulting in a considerable degree of immunity in all age groups, but particularly in adults (all regions of Tanzania mainland along the coast extending to as far as 160-240 kilometres inland, temperatures of 24-32°C year around and mean annual vapour pressures of 26-29 millibars (Coast, Lindi, Mtwara, Tanga, Dar es Salaam and Morogoro regions, other parts of some regions of North of Lake Nyasa and South of Lake Victoria).

The strategy raised some reservations over these strata because they were essentially developed over 30 years ago and that "*climate changes, environmental degradation and population migration are facilitating the changing pattern of malaria distribution in the country. This necessitates updating the existing epidemiological distribution of malaria in the country*".

The national malaria strategy of 2002-2007 repeats the same narrative used in the 1997-2002 strategy, again based on descriptions from the 1960s, but extends the classification of malaria seasonality more formally using the Mapping Malaria Risk in Africa (MARA) duration

of malaria seasons map to provide the epidemiological context for this five-year plan of action (Figure 4.1b). With this model the 2002-2007 strategic plan enumerated populations at risk as: a) over 6 months transmission, stable, perennial (coastal), 14 million people; b) 4-6 months stable seasonal transmission (central zone); 11.3 million people; c) 1-3 months strongly seasonal or epidemic (fringe highlands rift valley), 2.6 million people; and d) less than one month of transmission, epidemic or no malaria (highlands), 5.8 million people [NMCP, 2002].

The national malaria strategy proposed for the period 2008-2013 [NMCP, 2008] provides combinations of descriptive narratives and modelled maps of malaria risk. The narratives provided are based on descriptions used by the NMCP over the preceding decade, highlighting three important classifications a) Unstable, seasonal malaria, 20% of the country, largely in the arid central plateau; b) stable malaria with seasonal variations, southern part of the country has a single main rainy season (March-May), while northern and western Tanzania experience bimodal rainfall (November-January and March-May); and c) perennial malaria, the coastal fringe, southern lowlands, and regions bordering Lake Victoria, malaria transmission is stable with very high transmission intensities. The strategic plan provides two malaria risk maps: a) the MARA map of climate suitability (Figure 4.1c) and b) a smoothed, interpolated map of the proportion of out-patient childhood presentations that are due to malaria (Figure 4.1d). The later signals an important milestone in risk mapping, by integrating health information system data; however, explicit details of how this map was derived and the coverage of the input data were not provided.

4.1.3 Other mapped descriptions of malaria risk in Tanzania

None of the mapped presentations of malaria risk in Tanzania over the last 60 years have explicitly used parasite prevalence. David Clyde valued data on prevalence in his inventory of risk in Tanzania but could only provide a description of risk rather than a modelled presentation of prevalence. Parasite prevalence in children aged 2-10 years (*Pf*PR_{2-10}) has a predictable relationship to other, less frequently measured parameters of transmission intensity, notably the Entomological Inoculation Rate (EIR) and the Basic Reproduction Rate of Infection (R_o). As such values of *Pf*PR_{2-10} have recently been used to model control timelines to transmission reduction and the appropriate combinations of available interventions [Hay et al., 2008; Smith et al., 2009; Griffin et al., 2010] and a factor in the decision pathway to predict the likelihood of elimination [Cohen et al., 2010]. Importantly today it is possible to use mathematical models that interpolate across sparse data to provide quantities at locations where data are absent, known as model based geo-statistics (MBG) [Diggle & Ribeiro, 2007; see Section 4.3]. These techniques, nor the computing pre-requisites, were available to malariologists 60 years ago.

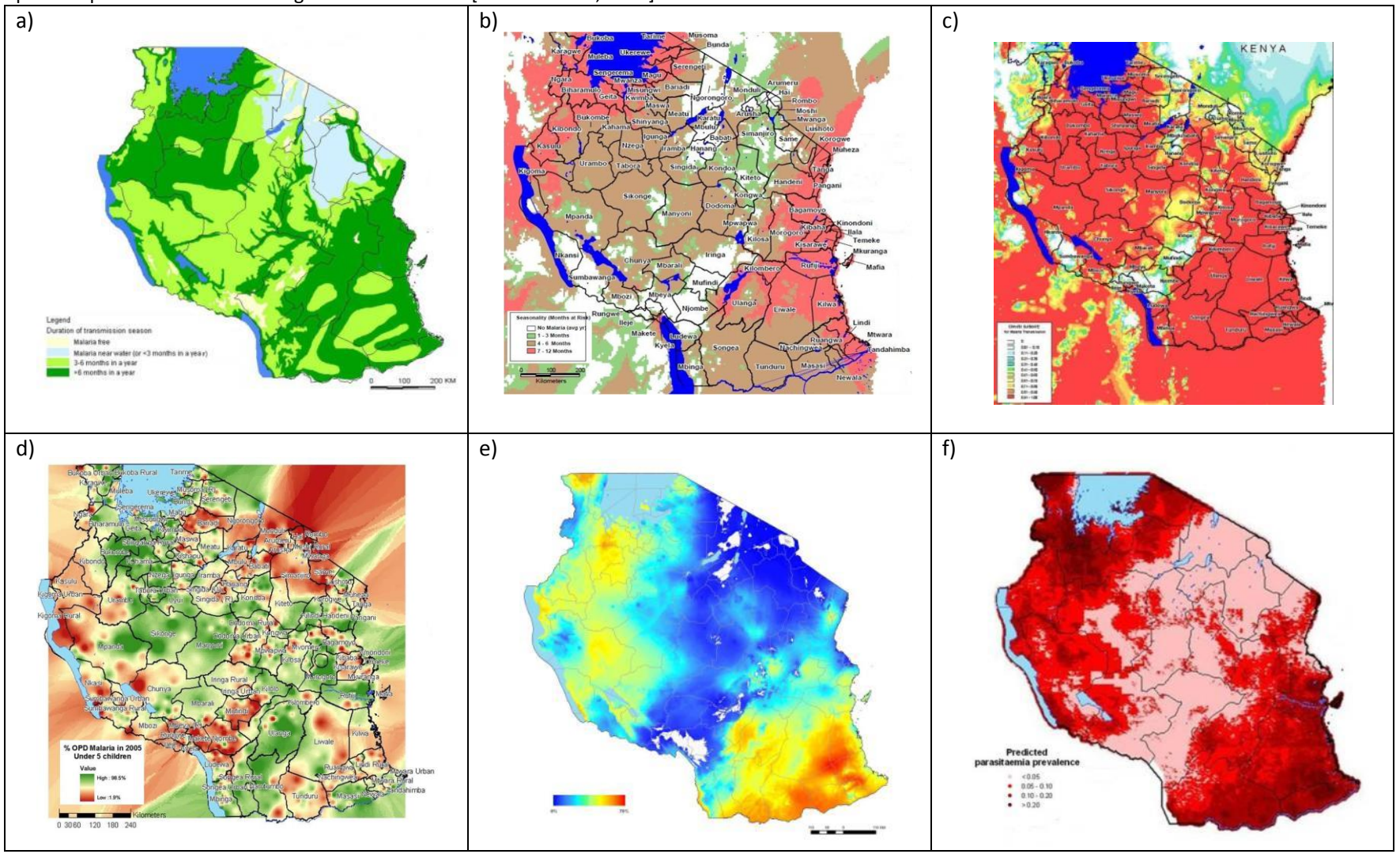
There have been two notable attempts to use MBG to predict parasite prevalence across Tanzania based on sparse, over-distributed empirical data. First, Gething et al. (2011) used empirical parasite prevalence data assembled as part of the Malaria Atlas Project [http://map.ox.ac.uk], including 1495 data points from Tanzania surveyed between 1985 and 2010. Using an assembly of environmental (including urbanisation) and climate covariates they developed a Markov Chain Monte Carlo (MCMC) Bayesian model to produce an interpolated map of *Pf*PR_{2-10} for the year 2010 (Figure 4.1e). This map is not resolved to

units of decision-making used by the NMCP to design sub-national/council control strategies and used a large set of covariates that may have over-fitted predictions [Murtaugh, 2009]. Second, Gosoniu et al. (2012) used 465 cluster-level data on parasite prevalence among children sampled during the national HIV/AIDS and malaria parasitological survey carried out in 2007–2008. The authors used an MCMC Bayesian model with climate and environmental covariates (without urbanization), to provide an interpolated map of malaria prevalence among under-fives (Figure 4.1f). The authors went further to provide population-adjusted mean estimates of prevalence in 2007-08 by administrative region, and some recommendations on where increased ITN might be beneficial. The authors claim that the mapped prevalence was lower than described previously but note that "*the magnitude of the decline is not clear in the absence of a baseline map*" [Gosoniu et al., 2012].

These two MBG approaches to providing high resolution malaria risk maps for Tanzania are important innovations in spatial epidemiology for public health. There is a congruence between the two maps and likely to be a result of a) similar covariate selection and b) the Gosinou et al. (2012) map was based on data from the 2007-08 national survey incorporated in the model by Gething et al. (2011b). It is however interesting that neither of these maps are used in national malaria planning, in part because they were not developed in partnership with the NMCP and also they provide only a snap shot of risk in 2007 or 2010; what most programme managers require is an understanding of risk before scaled intervention and how this has changed with time.

In this chapter we repeat these exercises using different, more computationally efficient MBG Bayesian methods and a larger volume of spatially curated data over a longer period of time. The model outputs are resolved as district-levels to allow for pre- and post-scaled intervention prevalence to be assessed by the NMCP at decision-making units linked to its decentralized health policy (Section 2.2).

Figure 4.1: a) Duration of malaria seasons developed from expert opinion by Government of Tanganyika (1956); b) MARA malaria seasons used in 2002-2007 National Malaria Strategy; c) MARA climate suitability model used in 2008-2013 National Malaria Strategy; d) Proportion of out-patients below five years diagnosed with malaria used in 2008-2013 National Malaria Strategy; e) Modelled prediction of *Pf*PR_{2-10} in Tanzania in 2010 [Gething et al., 2011]; f) Smoothed interpolated modelled map of parasite prevalence in children aged below 5 in 2007 [Gosinou et al., 2012]



Footnotes:

a) Tanganyika malaria seasons map developed from expert opinion [Government of Tanganyika, 1956]. Digitized from original map using ArcGIS

b) MARA modelled seasons: The MARA models of seasonality are defined using the combination of temperature and rainfall thresholds and a catalyst month. Areas where mean annual temperatures were <5^{o}C were considered not to have a malaria transmission season. A pixel was considered "seasonal" if the temperature range varied considerably or if annual rainfall was <720 mm. Seasonal zones were then classified according to the numbers of average months in which temperature was > 22^{0}C and rainfall > 60 mm within a 3-month moving window and at least one month of highly suitable conditions (> 22^{0}C, > 80 mm) occurred as a catalyst month. For areas considered "stable" the equivalent values were 19.5^{0}C and 80 mm with no requirement for a catalyst month. From these values the duration and start/end of the transmission season were predicted and the gridded surface of Africa was classified at 5x5km grids into 1-3 months of transmission (highly seasonal/epidemic), 4-6 months of transmission (representing seasonal endemic conditions) and 7-12 months reflecting perennial endemic transmission [Tanser et al., 2003; http://www.mara.org.za/].

c) MARA Climate Suitability: 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]. These theoretical maps are not trained on empirical data but reflect an approximation of local climate conditions to support stable transmission on an average year in the absence of control. The models are 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 uses monthly temperature ranges between 22-32^{o}C for optimized parasite sporogny within the mosquito and consecutive months of rainfall above 80 mm to support adequate vector abundance. The models assigns fuzzy values between 0 (unsuitable) and 1 (suitable).

d) An interpolated map of ward counts of proportions of under-five out-patient attendances documented in 2005 as "malaria" as part of HMIS. No details provided on methods of interpolation, completeness of data or spatial anomalies where no data reported.

e) Predicted malaria prevalence 2010 based on assembled data from 1495 clusters 1985 to 2010 using MCMC Bayesian methods with the inclusion of 14 covariates: urban, peri-urban, a temperature suitability index, land surface temperature (LST; six variants), precipitation (six variants) and normalized difference vegetation index (NDVI, two variants) [Gething et al., 2011b]

f) Predicted malaria prevalence 2007 based on national sample survey data from 465 clusters among children aged below five years using MCMC Bayesian methods with the inclusion of covariates: LST, precipitation, NDVI, altitude and distance to nearest permanent water body [Gosinou et al., 2012].

4.2 Malaria parasite prevalence data assembly, modelling and risk mapping

There are a variety of measures of the intensity of malaria transmission derived from field investigations of human populations or malaria vectors. The most ubiquitous measure, used for over 100 years in Africa, is the parasite rate - the proportion of individuals on a single cross-sectional survey among an entire or sampled community who have evidence of a peripheral blood stage malaria infection. 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 parasite prevalence data in Tanzania between 1980 and 2012; and therefore a reference source to the database. The following sections provide the details on how these data were modeled in time and space to provide district level estimates of malaria risk in 2000 and 2010. These data are then used to provide population-adjusted estimates of risk by district. Given the importance of seasonality to previous NMCP malaria descriptions we revisit maps of seasonal malaria transmission in Tanzania using new definitions suited for Seasonal Malaria Control (SMC).

4.2.1 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 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 "*Tanzania*" 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 March 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 anti-malarial 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 selected 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).

Unpublished archived survey reports: We undertook manual searches of archives at the World Health Organization (WHO) libraries in Geneva and Brazzaville at separate archive locations as Project, Country and Parasitology Department files. We visited the library at NMIR, Amani that housed national survey data reports from the 1960s. 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. Data from the Tanzanian HIV/AIDs and malaria national sample surveys of 2007-08 and 2011-12 were available from the MEASURE website. As a result of the generosity of the NMCP and many malaria scientists in Tanzania (all acknowledged at the beginning of the report) it was also possible to assemble a large volume of unpublished data from sub-national, wide region surveys. Finally, 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.

Search completeness: Our data searches have not used systematic, traditional evidence review strategies. These would have missed many unpublished sources of information. Rather our strategy has used a cascaded, opportunistic approach. Authors of peer-reviewed papers were often asked about additional information within their paper and directions to other possible unpublished work in their geographic area or from their institution. Importantly there are likely to be many post-graduate theses undertaken by students of the faculties of parasitology, public health and medicine at in Tanzania have not been adequately searched. Data not provided in a format usable for the current modelling exercise, despite specific requests, are those surveys undertaken by research groups working in Muleba district as part of the IRS campaigns [Mashauri et al., 2013], 26 villages at Muheza [Winskill et al., 2011] and 30 clusters examined in Lindi district in 1992 [Tatala et al., 1998]

4.2.2 Data abstraction

The minimum required data fields for each record were: description of the study area (name, administrative divisions and geographical coordinates, if available), the dates of start and end 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. 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 (>40% parasite rate) more accurately compared to microscopy [Gitonga et al., 2012].

For data derived from randomized controlled intervention trials, data 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 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. It was possible to establish the year of every survey however, the month of survey was occasionally not possible to define from the survey report. Here we used descriptions of "wet" and "dry" season, first or second school term or other information to make an approximation of the month of survey and included a record of this assumption. 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). Where additional information to provide unique time, village specific data was necessary we contacted authors to provide any missing information.

4.2.3 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 excluded 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]. 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 place names are replicated across a 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 the Food and Agriculture Organization (FAO) of the United Nations [FAO, 2008]. The spatial selection tool in ArcGIS 10.1 (ESRI, USA) was used to verify points along the coastline were within land area as defined by GAUL 2008. The Global Lakes and Wetlands (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 off the coastline, located on the river or in incorrect administrative units, every anomaly was re-checked and re-positioned using small shifts in combination with Google Earth.

4.2.4 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 entered erroneously into the data assembly where multiple reports reviewed describing similar data. These were listed, checked and duplicates removed.

Data exclusions: The search strategy identified 2,486 time-survey locations where malaria infection prevalence had been recorded between August 1980 and September 2012. This final data series was then subjected to various exclusion rules as defined below.

Location details: Despite repeated efforts and multiple on-line digital gazetteers, national resources and personal communications we were unable to identify with sufficient precision the geo-coordinates for 26 survey data points at 18 locations. Two survey data locations covered wide-areas beyond 5 km^2 and these data were excluded. In addition there were two survey locations on Mafia Island and given the difficulties in matching environmental covariates to the island we have excluded these two data points.

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 (section 4.3.2). 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 289 time-space locations and these were excluded from the final analysis. The majority of these, 182, were from the national cluster sample survey 2011-12, and these surveys are, by their design, inadequately powered to examine spatial distributions of malaria prevalence.

The final database contained 2,193 temporally unique data points at 1,447 survey locations.

4.2.5 Age standardization

There was a large diversity in the age ranges of sampled populations between studies. 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 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, $Pf\mathrm{PR}_{2\text{-}10}$ [Smith et al*.,* 2007].

4.2.6 Parasite prevalence data summaries

Of the 2193 unique time-space survey locations identified through the data search strategy described above, 1760 (80%) were identified from unpublished sources, 311 (14%) from unpublished reports from organizations working in Tanzania, 91 (4%) directly abstracted

from journals, 17 (0.7%) from post-graduate theses, 10 (0.4%) were sourced from Ministry of Health reports and 4 (0.2%) from conference abstracts.

Of all samples identified we had to presume survey month among 36 (1.6%) study locations based upon ancillary information in the report. In addition we had to estimate the minimum sample size based on information on total surveyed populations within the report at 95 (4%). Survey data were located for time-space survey data points using GPS (1053, 48%), Encarta (217, 10%), Google Earth (37, 1.6%), GeoNames (15, 0.7%), other digital place names sources (102, 4.7%), coordinates provided by individual scientists for which sources not certain (103, 4.7%) and combinations of survey maps in reports, Google Earth, repositioned GPS coordinates and other sources (666, 30%). Of the time-space survey locational data prevalence was recorded in 1114 (51%) using microscopy alone, 1039 (47%) used RDTs and 40 (2%) used RDTs with microscopic confirmation.

The 1980 to 2012 data are unevenly distributed through time and in space. To explore the temporal (not spatial) variance in the age-standardized estimates of parasite prevalence we used a LOESS regression method that fits a best fitting curve using moving temporal windows on the data using information before and after the reference year in STATA (version 12). The results suggest that from 2000 there is evidence of declining parasite prevalence, i.e. before scaled intervention (Figure 4.2). These data are however generated from different spatial locations with time and there this trend must be interpreted with extreme caution. The overall spatial distribution of *Pf*PR_{2-10} data is shown in Figure 4.3 and partitioned around 2005 in Figures 4.4a and 4.4b.

Figure 4.2: Loess regression line of 2193 survey data points assembled between 1980 and 2012

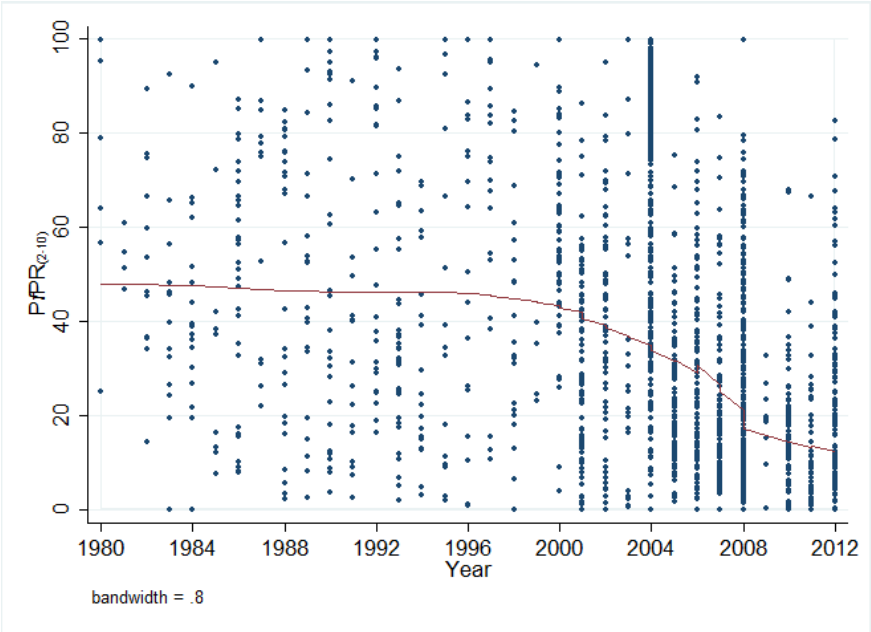


Figure 4.3 Data distribution of age-corrected *Pf*PR$_{2-10}$ estimates in six categories: <1%, 1-4%, 5-9%, 10-49%, >=50% from 2193 surveys at 1447 unique locations conducted 1980-2012. We have masked out areas of Tanzania that cannot support transmission by virtue of low temperature (dark grey) (see Section 4.4).

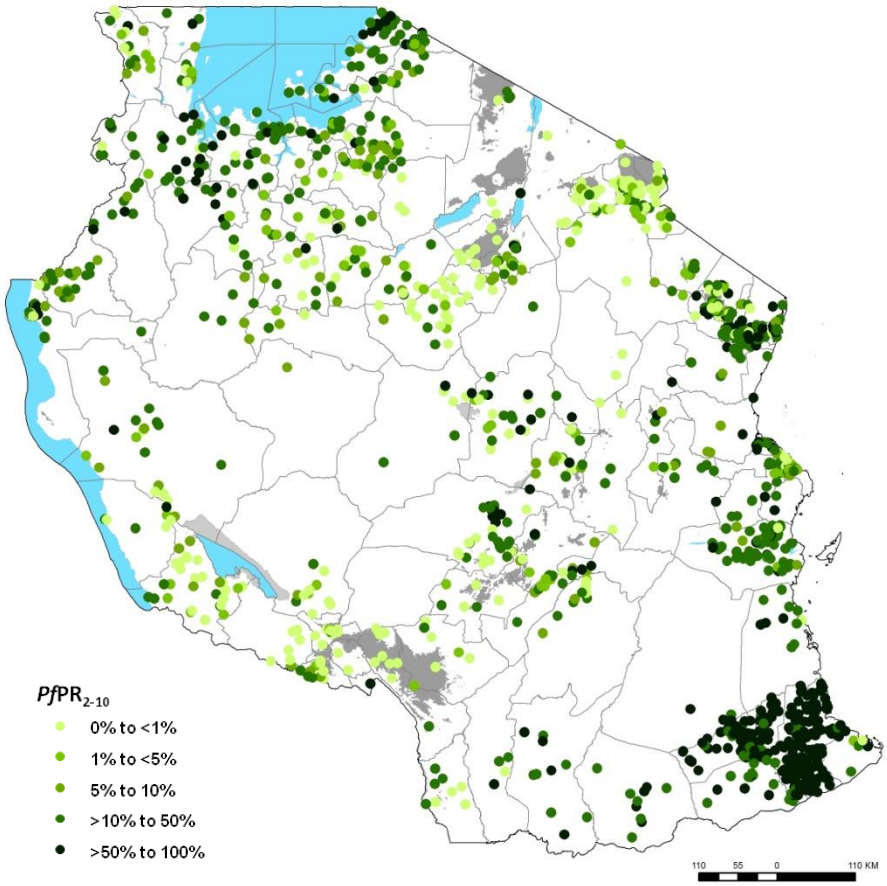
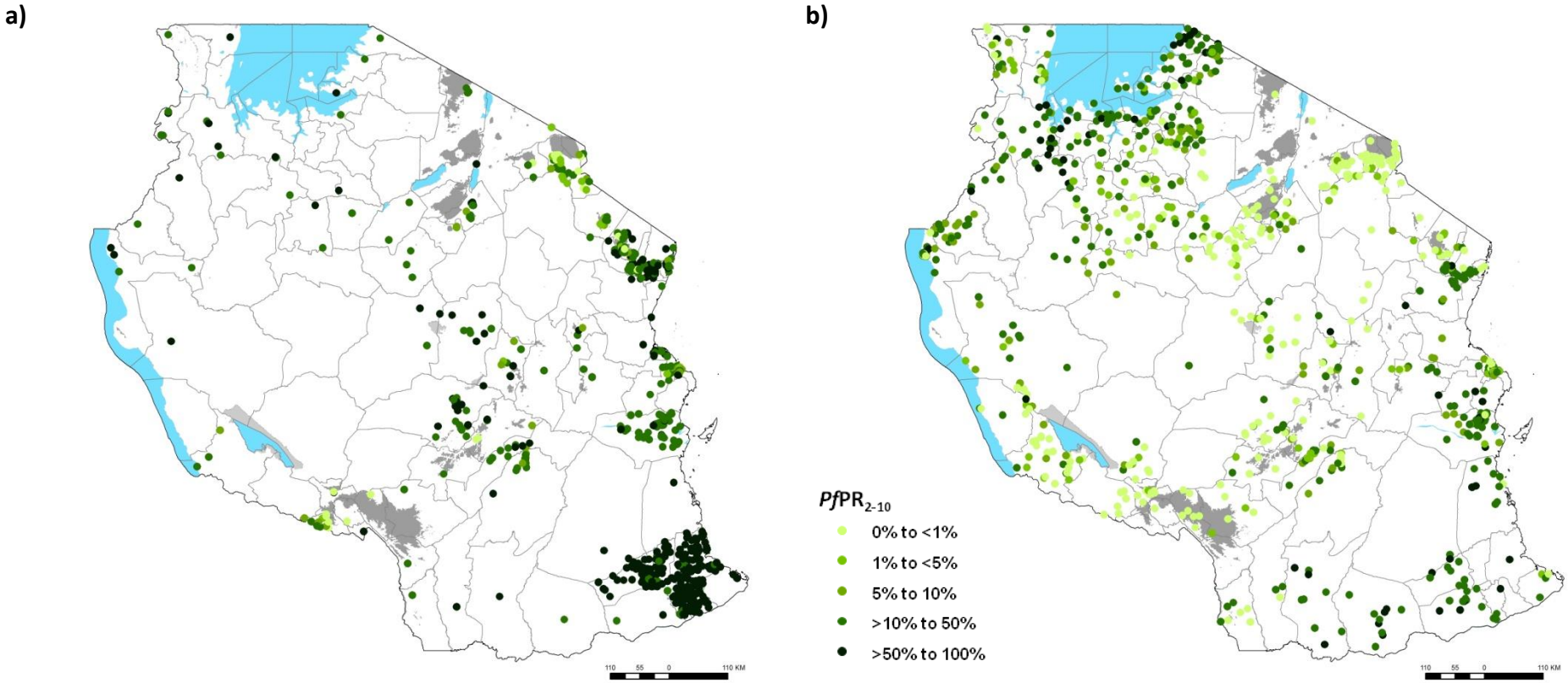


Figure 4.4 a) Data distribution of age-corrected *Pf*PR$_{2-10}$ estimates in six categories: 0%, <1%, 1-4%, 5-9%, 10-49%, >=50% from surveys conducted 1980-2005 (n=1018); b) surveys conducted 2006-2012 (n=1175). The data are shown against the 102 district councils described in Section 2.4. Areas masked dark grey malaria absent by virtue of temperature.



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

4.3.1 Model form

MBG methods interpolate from observed measure 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)[1] for inference [Rue et al., 2009; Cameletti et al., 2012] 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. 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 range and temporal the autocorrelation of the contribution data becomes almost null. Continuous predictions of *Pf*$PR_{2\text{-}10}$ at 1×1 km spatial resolutions for the year 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 A.1.

4.3.2 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

[1] 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]. Integrated Nested Laplace Approximations (INLA) are alternative algorithms with faster computational speeds and can be undertaken in open source, easily adaptable R packages [R-INLA, project].

problem can be particularly pronounced when data assembled are from observational 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 determinants of malaria transmission are climatic (rainfall and temperature), ecological (potential breeding sites and urbanisation) and control interventions (anti-vector and ant-parasitic measures) [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.

Temperature: Temperature plays a key role in determining the transmission of human malaria [Lunde 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; Bayoh & Lindsay 2004]. The mortality of the anopheles mosquitoes also increase sharply at ambient temperatures approaching 40 ^{o}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}. These were: annual mean temperatures, and a biologically modeled temperature suitability index (TSI). 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 4.5a]. TSI was developed as a quantitative value of optimal *P. falciparum* sporozoite development [Gething et al. 2011a]. 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 4.5b).

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 4.5c]. These monthly surfaces were summed to generate a synoptic annual mean precipitation surface and re-sampled 5x5 km resolutions. For vegetation, Fourier–processed enhanced vegetation index (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 4.5d). 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 URL].

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; Tatem et al., 2008]. To develop a consistently defined surface of urbanisation, information from the Global Rural Urban Mapping Project (GRUMP) [Balk et al*.,* 2006] and the Afripop project [Linard et al., 2010] was used (Section 2.5). 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 4.5e).

Pre-processing covariate grids: There were internal and 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.

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 (Table 4.1). 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. This analysis showed that four covariates contributed significantly, and independently, to the variation in *Pf*PR_{2-10}: TSI, EVI, precipitation and urbanisation (combined urban and peri-urban classes) comprised the best-fit model (Table 4.1)

Figure 4.5: Climate and environmental covariates tested for Tanzanian malaria prevalence model: a) mean ambient air temperature; b) Temperature Suitability Index; c) precipitation; d) EVI; e) urbanisation

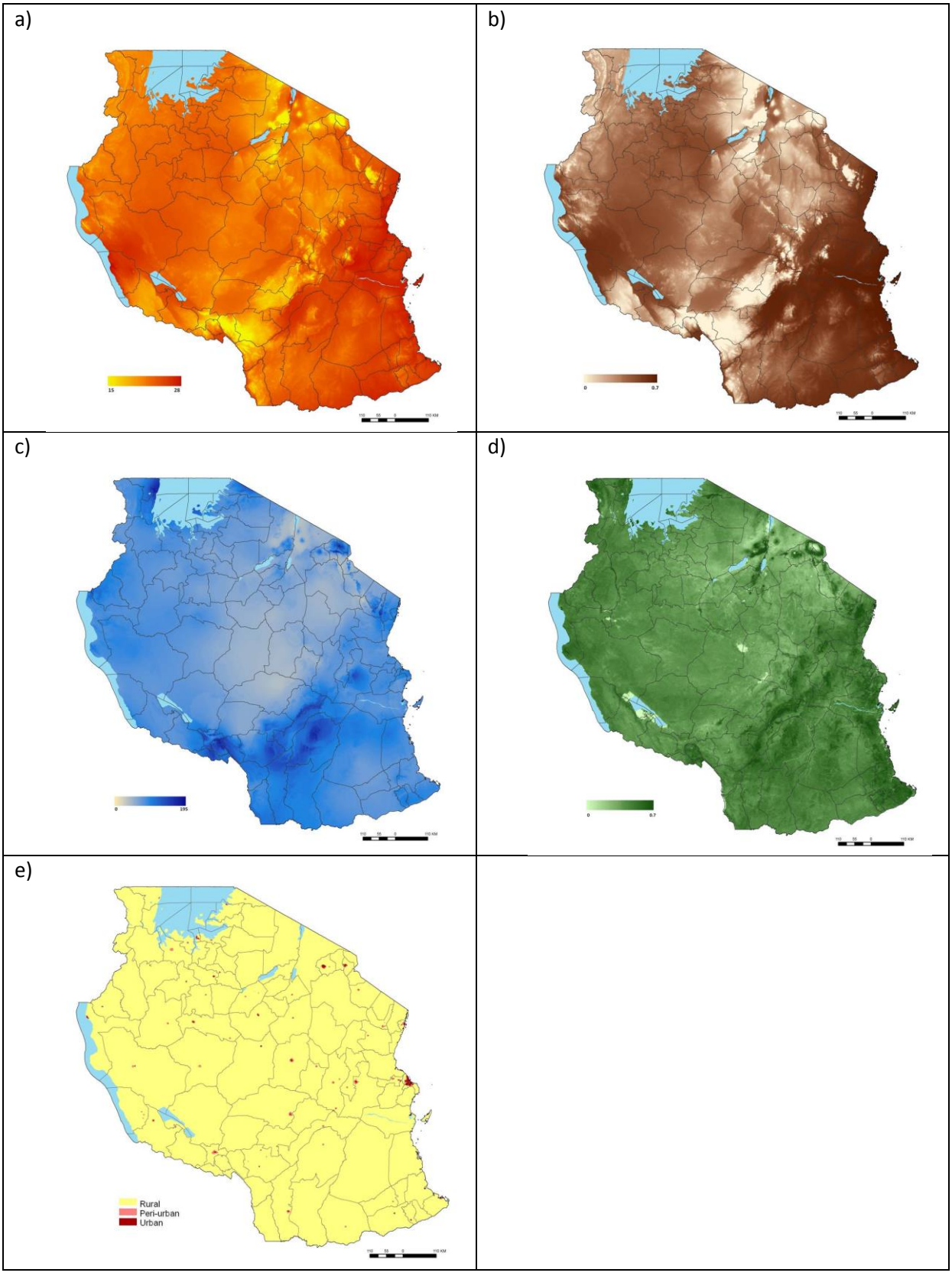


Table 4.1 The results of the bivariate generalised linear regression models of *Pf*PR_{2-10} and the climatic and ecological covariates

	Estimate	95% Confidence Interval	P value
Precipitation	0.011	0.007 – 0.014	< 0.001
EVI	0.858	0.698 - 1.019	< 0.001
TSI	0.547	0.496 - 0.597	< 0.001
Urbanization	-0.147	-0.182 - -0.112	< 0.001

4.4 Model predictions and populations at risk 2000 and 2010

We used the data from the age-corrected infection prevalence surveys (sample size, adjusted numbers positive) at known locations (longitude and latitude) and times (month and year) the minimal set of long-term climate and human settlement covariates 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 8 days to run for each prediction year 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 are shown in Figures 4.6a and 4.6b respectively.

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

- **Low stable endemic control**: areas supporting predicted *Pf*PR_{2-10} <1% which represent a pre-elimination transitional state [Cohen et al., 2010]

- **Hypoendemic 1**: areas supporting predicted *Pf*PR_{2-10} 1-<5%, separated from the below hypoendemic class to be able to distinguish finer resolution changes with time

- **Hypoendemic 2**: areas supporting predicted *Pf*PR_{2-10} 5-<10%

- **Mesoendemic**: areas supporting predicted *Pf*PR_{2-10} 10%-50%

- **Hyper-Holoendemic**: areas supporting predicted *Pf*PR_{2-10} >50%

We have included two additional classes:

Malaria free: To provide a plausible mask to eliminate the possibility of transmission, we used the temperature suitability index (TSI) [Gething et al., 2011a]. This was used to generate at each 1 x 1 km pixel, periods of an average year when a vector's lifespan would exceed the time required for sporogony, and hence when transmission was not precluded by temperature. If this time exceeded the maximum feasible vector lifespan, then the cohort was deemed unable to support transmission and the area classified as being at zero risk. These areas are notably those parts of Tanzania at exceptionally high altitude.

Unstable transmission based on aridity: Arid conditions effect anopheline development and survival [Shililu et al., 2004]. Limited surface water reduces the availability of sites suitable for oviposition and reduces the survival of vectors at all stages of their development through the process of desiccation [Gray & Bradley, 2005]. We have defined extreme aridity using monthly EVI archived over 11 years averaged to a synoptic year; we classified areas likely to support transmission by an EVI of greater than 0.1 for any two consecutive months and areas without two or more consecutive months of an EVI > 0.1 as unable to support transmission [Guerra et al., 2006, Guerra et al., 2008].

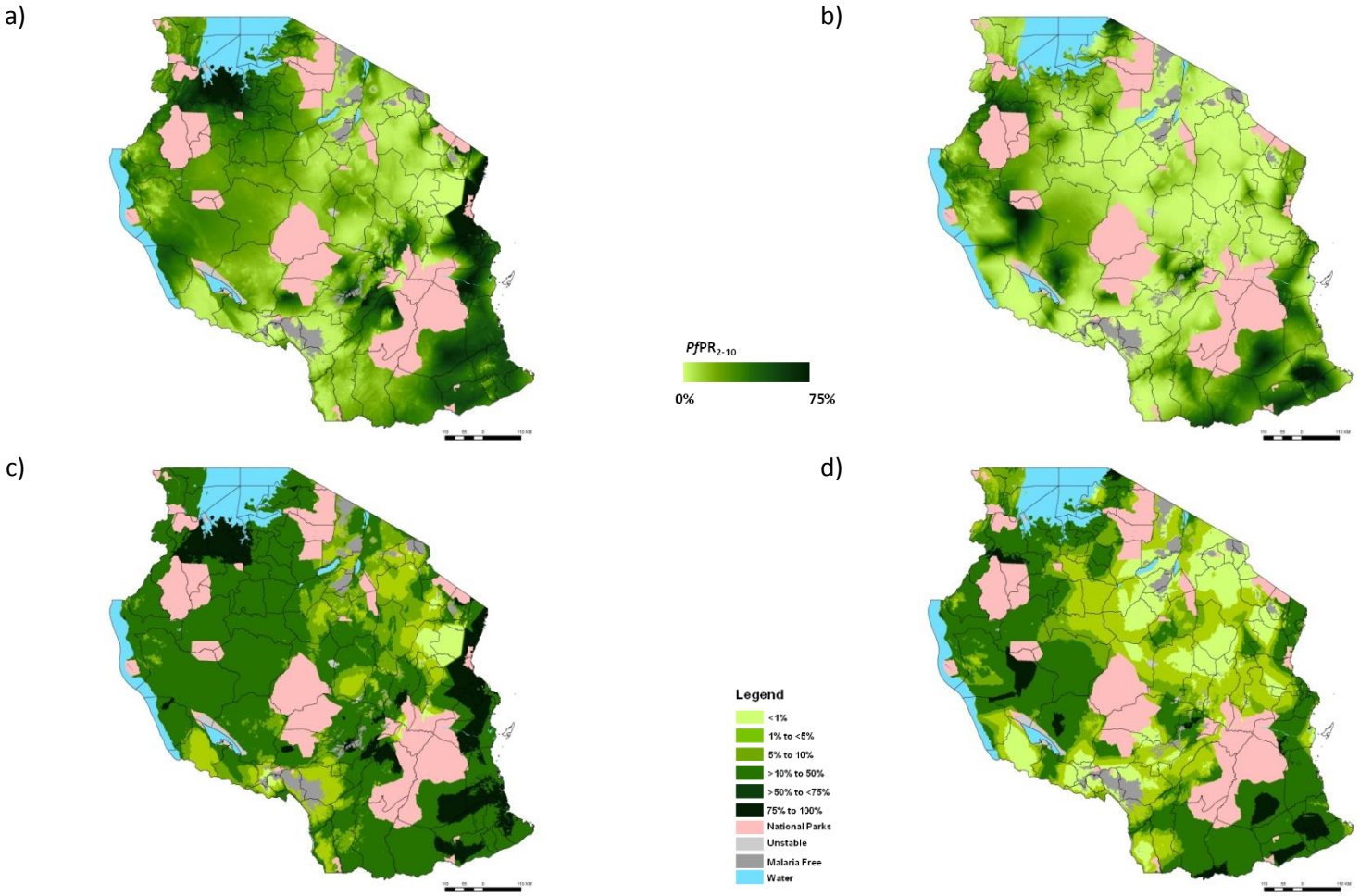
The final re-classified endemicity risks are shown for 2000 and 2010 in Figures 4.6c and 4.6d respectively.

We used the gridded population surface for Tanzania described in Section 2.5 for the years 2000 and 2010 to extract population counts at each 1 × 1 km *Pf*PR_{2-10} grid location classified by predicted malaria risk class using the *Zonal Statistics* function in ArcGIS 10.3. The population totals (%) within each risk class for 2000 and 2010 for each of the reconfigured 102 districts (Section 2.4) are shown in Tables 4.2a and 4.2b respectively.

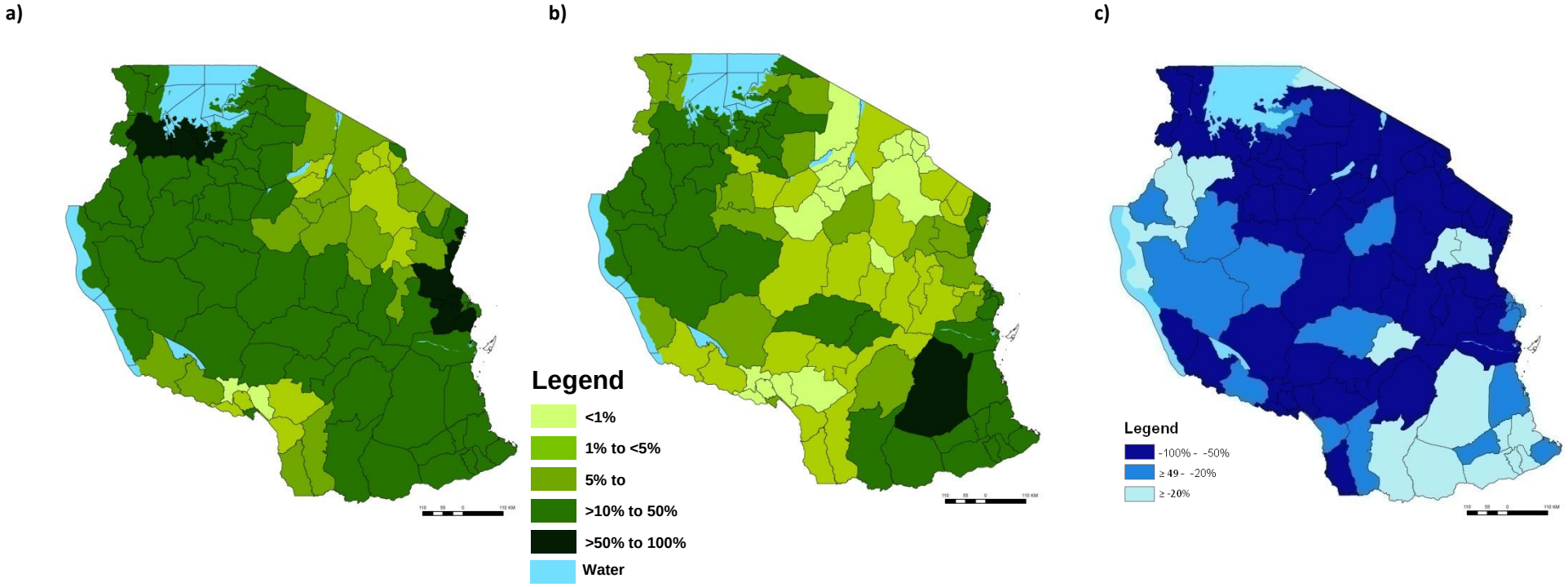
Given the over-distribution of both population density (Figure 2.5) and malaria risk (Figures 4.6a-4.6b) within each district we computed a Population Adjusted *Pf*PR_{2-10} (PA*Pf*PR_{2-10}) for each district by first multiplying the *Pf*PR_{2-10} at each 1 × 1 km with the corresponding population at 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. falcipraum* in each country which was divided by it's the total population in 2000 and 2010 to compute PA*Pf*PR_{2-10} for 2000 and 2010. The values of the mean PA*Pf*PR_{2-10} in 2000 and 2010 and the differences across the interval are shown in Annex A.2a and A.2b and Figures 4.7a-c.

Approximately 4% of Tanzania's population live in areas that are essentially free of malaria based on temperature restrictions for parasite development in the mosquito vector. For Tanzania as a whole, the mean PA*Pf*PR_{2-10} in 2000 was 25.5%; by 2010 the corresponding mean PA*Pf*PR_{2-10} was 11.6%, suggesting a greater than 50% reduction in transmission intensity over the ten year interval. In 2000, 11.6% of the Tanzanian population lived in areas predicted to support hyper-holoendemic transmission, by 2010 this had reduced to 2.3%. Conversely in 2000 3.4% of the population lived in areas supporting a predicted mean *Pf*PR_{2-10} of less than 1%, by 2010 this had increased to 21.8%. 69 districts achieved a greater than 50% reduction in mean PA*Pf*PR_{2-10} by 2010 compared to model predicted values in 2000 (Figure 4.7c). The greatest reductions (≥ 90%) were recorded in 19 districts (Figure 4.7c: Rombo, Mwanga, Mbulu, Kongwa, Karatu, Kibaha, Igunga, Arusha/Ameru, Singida, Makete, Kilosa, Tanga, Bagamoyo, Hai, Iramba, Shinyanga, Mufindi and Moshi). Conversely a small predicted rise was recorded in ten districts across the same interval (Figure 4.7c: Kigoma, Ruangwa, Liwale, Tarime, Tandahimba, Newala, Tunduru, Namtumbo, Handeni and Kilindi). Areas most resistance to changing endemicity were located in the South east, bordering Mozambique.

Figures 4.6: a) continuous 1x1 predicted mean *Pf*PR$_{2-10}$ for the year 2000; b) continuous 1x1 predicted mean *Pf*PR$_{2-10}$ for the year 2010; c) re-classified endemicity classes using the posterior distribution for the year 2000; d) re-classified endemicity classes using the posterior distribution for the year 2010; dark grey areas masked based on inability of temperature to support stable transmission; light grey areas of unstable transmission constrained by aridity; protected areas/park masked in pink **[**IUCN/UNEP 2010]



Figures 4.7: Population adjusted mean *Pf*PR_{2-10} in a) 2000, b) 2010 and c) figure showing percentage change 2000 to 2010 (light blue rise, no change or decrease within 20%; mid blue a decline of between 20% and 49% and dark blue a 50% or greater decline by 2000 compared to 2010 PA*Pf*PR_{2-10})



4.5 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 Tanzania were -0.18%, 5.4% and 0.94 respectively indicating a good model accuracy. The standard deviation of the predicted mean *Pf*PR_{2-10} are shown in Annex A.1. These indicate that the highest model uncertainties were observed in the western and central districts in 2000 and in the southern districts in 2010. However, uncertainty was much lower in 2010 due largely to the increased and spatially better-distributed data. The maximum distance of standard deviation was around 4% *Pf*PR_{2-10} indicating generally good precision of the estimates of the mean infection prevalence.

4.6 Malaria seasonality

A dominant epidemiological characteristic of malaria across much of Africa is its seasonal profile ranging from single, acute proliferation of vectors followed by a lagged short disease incidence profile, to predictable seasonal transmission with between year variability and areas that support perennial transmission due to constant rainfall or seasonal rainfall in areas adapted for permanent breeding (inland river courses or irrigated areas). Relationships between climate, seasonal parasite transmission and disease outcomes are 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) [Caniero et al., 2010; Greenwood et al., 1991].

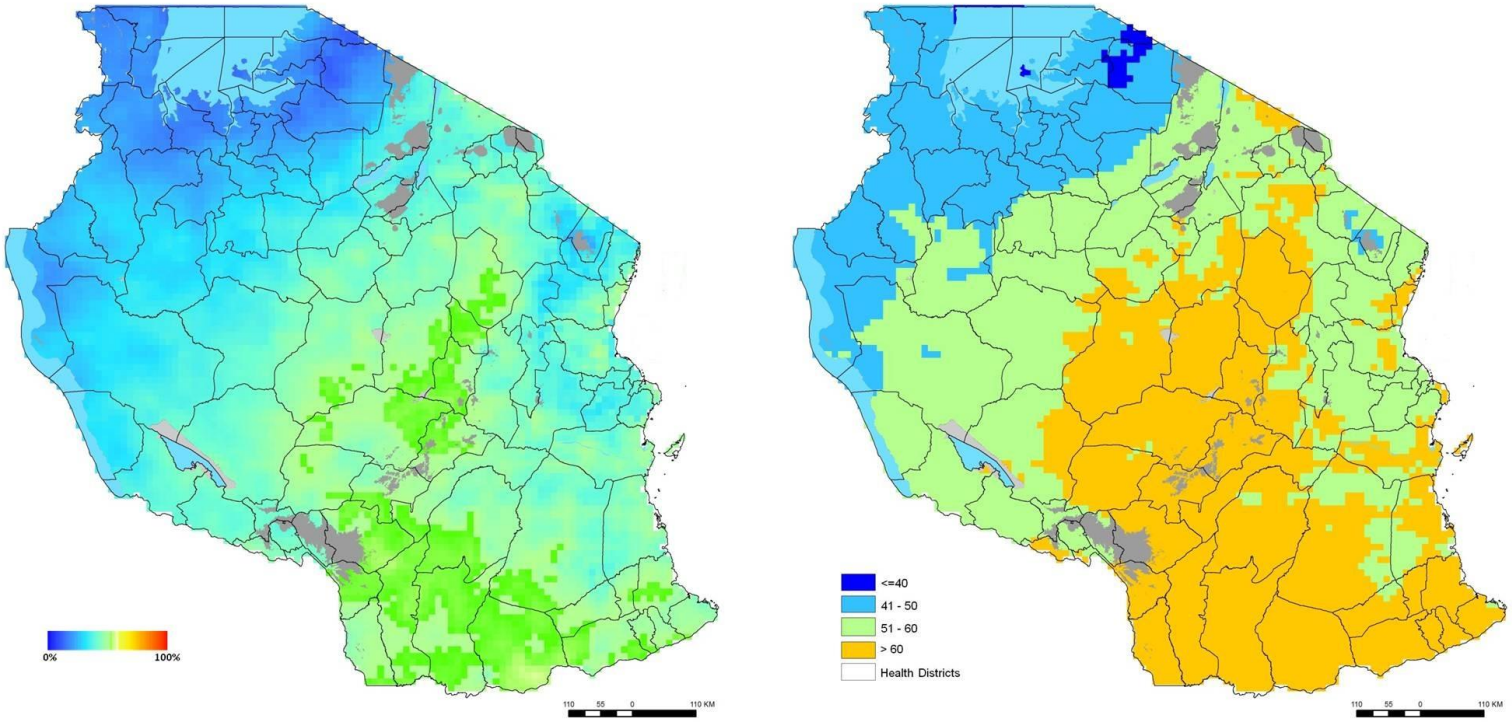
The description of seasonality represents an important operational information platform to target the timing of vector control, most notably IRS and larval control operations, and the renewed interest in pulsed mass drug administration or restricted chemoprophylaxis in the Sahel, known as Seasonal Malaria Control (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/] and used today in Tanzania (Figure 4.1b). These theoretical maps are not trained on empirical data but reflect an approximation of local climate conditions to support stable transmission on an average year in the absence of control. The MARA model was an important development over ten years ago, however its fidelity requires further validation using a wider range of time-series data on the clinical presentation of malaria to hospitals and clinics across Africa. New models of "malaria seasons" could be developed using alterative long-term climatology data [Hijmans et al., 2005; Scharleman et al., 2008], higher temporal and spatial resolution data since 1999 from SPOT imagery at 1 x 1 km resolution every 10 days [http://www.inra.fr]. An early and provisional attempt at using empirical data to define extremes of seasonality for SMC have recently 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 gauge and satellite information on a near-real time basis to provide daily rainfall estimates over the African continent and is archived from January 2000 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 (Figures 4.8a and 4.8b). These predictions are more tangibly rooted in current models of disease risk and are used here in preference to MARA models described above. These maps were used to compute the populations-at-risk of acutely seasonal malaria in 2010 using the using the *Zonal Statistics* function in ArcGIS 10.3 (Annex A 2.c).

34 districts were identified as having more than 50% of their total population in 2010 residing in areas classified as acutely seasonal transmission, covering a total population of 9.3 million people (Figure 4.8b). Of these 15 districts were classified in 2010 as harboring a mean PA*Pf*PR_{2-10} of greater than 10% (Liwale, Tandahimba, Ruangwa, Masasi, Lindi, Newala, Tunduru, Namtumbo, Nachingwea, Kilwa, Kilolo, Rufiji, Mtwara, Pangani and Iringa). Among these 15 districts eight had mean predicted PA*Pf*PR_{2-10} values in 2010 of greater than 25% and were among thjose districts most resistant to changing endemicity since 2000 (Liwale, Tandahimba, Ruangwa, Masasi, Lindi, Newala, Tunduru and Namtumbo), here one might consider attempting a programme of SMC.

Figure 4.8: a) NOAA rainfall/seasonality concentration index in Tanzania in continuous form and b) binned to show red and orange priority SMC areas where >= 60% of rainfall falls within 3 continuous months (Orange); dark grey areas represent malaria free, light grey unstable aridity defined areas



Footnotes: The gridded daily rainfall estimates at 0.1 degree resolution from the RFE 2.0 dataset between January 2002 and December 2009 was acquired from the NOAA CPC/FEWS archive [NWS, 2012; ftp://ftp.cpc.ncep.noaa.gov/fews/newalgo_est/]. The daily rainfall estimates were then aggregated to calculate total monthly and annual rainfall. For each pixel, the maximum percentage of the total annual rainfall occurring in three month-iterations was then calculated for each year using spatial analyst tool in ArcGIS 10.1 (ESRI, USA). The average pixel value between 2002 and 2009 was then calculated and the resulting image reclassified to give a binary output of areas where rainfall in three consecutive months was < 60% or > 60%

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Chapter 5

Dominant malaria vectors in Tanzania

5.1 Background

Africa is home to the most effective and efficient vectors of human malaria [Coluzzi, 1984]: *An. gambiae*, 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 (*An. quadriannulatus* A and *An. quadriannulatus* B [Coluzzi, 1984]) nature, 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 strategies 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 at 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].

The first entomologist to arrive in Tanzania was John W McHardy in August 1926, who with his staff undertook a larval survey in 1930 at multiple sites across the country including Dar es Salaam, the Tanga-Arusha railway, Tabora, Mwanza, Morogoro and Kilosa; at each location both *An. gambiae* and *An. funestus* were identified [Tanganyika Medical & Sanitary Department, 1931]. Before independence it was highlighted that *An. merus* was constrained to the coastline [Muirhead Thomson, 1951] and *An. gambiae sensu lato* (the freshwater sibling species within this complex had not been distinguished at the time) was ubiquitous across most of the Tanzanian territory.

5.2 Data assembly

Detailed inventories of species distribution began during elimination campaigns launched in the 1950s, but continued in earnest only in North Africa where elimination efforts continued through the 1970s. The notion of mapping vector species was resurrected during the mid 1990s as part of the Mapping Malaria Risk in Africa (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, 1998; Lunde et al., 2013a; Lunde et al., 2013b; Moffett et al., 2007; Sinka et al., 2010]. These model predictions have used different statistical approaches and different data sets, and are hard to systematically compare, unless their output data are shared and formally contrasted.

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]. There is also a database on insecticide resistance, the Arthropod Pesticide Resistance Database (APRD) [http://www.pesticideresistance.org/], which 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 in terms of available, geo-coded species-specific data is currently held on the MAP database [Sinka et al., 2010]. We have augmented this database for Tanzania with additional systematic on-line searches of medical literature databases including PubMed, Google Scholar and Web of Science using search terms "*Anopheles* OR *mosquito* OR *culicidae* OR malaria vector OR malaria transmission" AND "Tanzania OR Tanganyika OR German East Africa" for all study publications on malaria mosquitoes in present day mainland Tanzania. We also included data identified during searches of reports held at the WHO library in Geneva that related to vector studies in Tanzania, unpublished reports from the NIMR libraries at Amani and the Ifakara Health Institute's Digital Library (https://ihi.eprints.org/). The later was significant as it identified reports of research on *Anopheles* mosquitoes in Tanzania since 1950s, and several not captured in from other sources. We cross-referenced all data identified with a recent systematic review of vectors across Eastern Tanzania between 1950 and 2010 by Kabula and colleagues [Kabula et al., 2011]. Finally, unpublished data were included from the extensive studies undertaken over the last decade by scientists working for IHI, NIMR and Research Triangle International (RTI).

Each study site was geo-coded using methods described in Section 4.2.3. 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 (e.g. animal bait catches, bed net traps, CDC light traps, human landing catches, indoor resting searches, pyrethrum spray catches, exit traps, larval searches or tent traps), methods of species detection (PCR, Chromosome Banding Sequences, Morphology, DNA probes), estimates of numbers of vectors sampled 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, as we know it today, was not fully categorised until 1998 and *An. quadrimaculatus* species B designated a separate species after this date [Harbach & Harbach, 2004; Hunt et al., 1998]. In fact, the resolution of ambiquitoes between *An. gambiae s.s.* and *An. arabiensis*, which were formerly known as species A and B respectively, was only completed in 1970s [White, 1974; White et al., 1972; White & Rosen, 1973]. Another challenge particularly with the old datasets was that members of the *An. funestus* group were also rarely identified to species level.

In addition we developed two additional sub-databases on recorded entomological inoculation rates (EIR) and any information of insecticide susceptibility testing documented since 1970, in any of the documents obtained. This complete database is available with this report as an excel spreadsheet.

5.3 Current geographical distribution of dominant vector species

The most up-to-date description of malaria vector distribution in Tanzania was published in December 2011 [Kabula et al., 2011]. Relying primarily on published and unpublished data sources between 1950 and 2010, and the authors compiled an exemplary database of all DVS and their transmission activity. This review, however, concentrated mostly on one region of Tanzania, in primarily Eastern Tanzania. This review, however, concentrated mostly on one region of Tanzania. Here we have combined many additional sources of data to form a more contemporary, complete repository of data on DVS in Tanzania over the last four decades. These data require further work, through contacts with original report authors to disaggregate the observations in space, i.e. by village, and by time where serial observations have been made over time. This is an ongoing process which should be completed by the end of 2013. With a complete spatial and temporal database it is planned to develop a more mathematical approach to defining species distribution in Tanzania with the geo-located species data and using Boosted Trees Regression methods [Elith et al., 2008]. Meanwhile, we present a qualitative description of species distribution derived from the assembled literature in the following sections with a comment on each vectors traditional bionomics [Sinka et al., 2013].

5.3.1 Anopheles arabiensis (Patton 1905)

While *Anopheles arabiensis* is generally considered a species of dry environments, including desert, grassland, savannah and sparse woodland, evidence is growing that it is more ubiquitously distributed across Africa and Arabia. *An. arabiensis* is able to utilize a very wide variety of natural and artificial habitats including puddles, swamps, springs, stream margins, drains, ditches, trenches, borrow pits, wells, and storage containers. *Anopheles arabiensis* is described as a zoophilic, exophagic and exophilic species but exhibits a wide range of feeding and resting patterns, depending on geographical location and blood-host availability [Killeen et al., 2001]. However, it is not a generalist mosquito in the true sense, but, like most mosquitoes, rather a specialist with a specific, similar preference for two host types, humans and cattle [Killeen et al., 2001; White et al., 1972], which are usually closely associated, especially in drier habitat types where pastoralist livelihoods are common: This ability to exploit non-human blood sources renders *An. arabiensis* less vulnerable to control with

indoor residual spraying or long-lasting insecticidal nets. Blood feeding times also vary in frequency; peak evening biting times can begin in the early evening (19:00) or early morning (03:00), before people go to bed and after people come out of bed. This species also usually has a greater tendency than *An. gambiae s.s.* to rest outdoors.

Available data suggests that *An. arabiensis* has been predominant all over Tanzania, but that it currently occurs in proportionately much lower densities compared to other *Anopheles* mosquitoes in the north western regions of Kagera, Kigoma, Katavi and Geita as well as the western parts of Mwanza and Mara regions. However, because of its widespread distribution and greater resilience to control with LLINs, this species has recently replaced *An. gambiae s.s* as the most predominant vector in Tanzania. Available evidence suggests that most of this shift has been due to scale-up of indoor insecticidal interventions, particularly insecticide treated nets [Derua et al., 2012; Kitau et al., 2012; Russell et al., 2011; Russell et al., 2010]. Though most studies conducted before 1990s did not distinguish between *An. gambiae* sibling species, we now know that *An. gambiae* and *An. arabiensis* often occurred together in most locations, but that it is the former species that has been more effectively tackled by indoor insecticidal interventions than the latter [Derua et al., 2012; Kitau et al., 2012; Russell et al., 2011; Russell et al., 2010]. Indeed a significant proportion of residual malaria vectors in communities where ITNs have been used for a long time now consist of *An. arabiensis,* except in north western regions [Mng'ong'o et al., 2011; Protopopoff et al., 2013], as well as a few sites in urban settings such as Dar es Salaam [Majambere et al., 2013], where *An. gambiae s.s* still dominates, and in the south eastern parts, where overall *Anopheles* densities constituted by *An. funestus* are rising, relative to *An. arabiensis* [Lwetoijera et al., unpublished]. The increased dominance of *An. arabiensis* since 2000, and the fact that it tends to feed and rest outdoors and can feed on non-human blood sources [Takken & Verhulst, 2013], presents an important and widespread challenge to malaria control in Tanzania.

5.3.2 *Anopheles funestus* (Giles 1900)

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. It is therefore best described as being widely distributed on coarse scales but very focal at fine scales because its habitat preferences are limiting in most locations. *An. funestus* is considered to be highly anthropophilic with a late-night biting pattern, often peaking indoors after 22.00 hours [Huho et al., 2013]. 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*.

Available data suggests that *An. funestus* is found throughout mainland Tanzania, often in the same locations as *An. gambiae* complex. Following the decline in *An. gambiae*

populations and despite the rise in proportional abundance of *An. arabiensis*, *An. funestus* remains a dominant malaria vector in several parts of Tanzania. Due to its very high vectorial capacity [Kabula et al., 2011; Mboera & Magesa, 2001], this vector is increasingly associated with the persistent residual malaria, particularly in south eastern Tanzania, where its densities and sporozoite rates have risen steadily in recent years. Unpublished evidence obtained from scientists working in these regions [Kaindoa et al., unpublished, Lwetoijera et al., unpublished], suggests this vector species could be a major driver of resurging malaria transmission even in communities where universal LLIN campaigns ended only recently [Renggli et al., 2013], but further research is necessary to rigorously confirm these specific indications, before any specific policy recommendations can be made. While *An. funestus* (Giles) is the most important member of the *An. funestus* group that can sustain malaria transmission, historical evidence from north eastern Tanzania [Gillies & Smith, 1960] and recent evidence from Ulanga district in the south east [Matowo et al., 2013], suggest that other members of the group, particularly the outdoor biting *An. rivulorum* could also transmit malaria to a limited extent, particularly in areas where indoor interventions such as LLINs have already greatly reduced densities of the indoor feeding *An. funestus* Giles. Finally, because *An funestus* is so widespread, has a high vectorial capacity and is considerably more resilient against climatic variations [Lyons et al., 2012] implies that improvements on currently achievable levels of control, and the final frontiers of malaria vector control will most likely involve some efforts against rebounded populations of *An. funestus*.

5.3.3 Anopheles gambiae sensu stricto (Giles 1900)

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 (about 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 [Kiswewski et al., 2004].

Anopheles gambiae s.s occurs predominantly in the north western and in the south eastern regions of Tanzania and only rarely in the central belt regions of Mbeya, Njombe, Iringa, Singida, Dodoma, Manyara, Arusha and Kilimanjaro, which correspondingly have the lowest host parasite prevalence estimates (Chapter 4; Figures 4.7).

At least five years ago, *An. gambiae s.s.* was considered the most important malaria vector in most parts of Tanzania, particularly because of its high vectorial capacity, near-exclusive dependence on human blood and the tendency to preferentially bite sleeping humans indoors. However, recent evidence suggests that vector population densities, and contribution towards overall malaria transmission, has been dwindling, to the extent that in some parts of the country such as Lower Moshi in the north, and Ulanga and Kilombero districts in the south east, existing surveillance methods now rarely detect this vector

species. The dwindling populations of *An. gambiae s.s*. is often associated with scale up of indoor insecticidal interventions such as IRS and LLINs. However there are places such as Muleba in the Lake Victoria region [Protopopoff et al., 2013], where insecticide resistant populations of *An. gambiae s.s.* have persisted despite large-scale use of IRS, and in Dar es Salaam, where the species is still regularly caught despite in generally low densities [Govella et al., 2011].

In the eastern regions of Tanga, Pwani and Morogoro, the vector species has largely been overtaken by *An. arabiensis,* which is now the predominant vector [Derua et al., 2012; Russell et al., 2010], though there are still small pockets of colonization, such as Mbingu village in the northern fringes of Kilombero district, where *An. gambiae s.s* was still dominant by 2010 [Maia et al., 2011].

5.3.4 Anopheles merus (Donitz 1912)

Anopheles merus is a species considered as only a minor vector in many areas of East Africa, but an important vector in coastal Tanzania [Temu et al., 1998]. There is, however, limited contemporary information on the bionomics of this vector [Sinka et al., 2010]. *An. merus* was referred to as a 'salt water *An. gambiae*' variant and definitive proof of the specific status of *An. merus* was provided in the early 1960s [Paterson, 1962]. *Anopheles merus* is rarely found in the mangrove forests, unlike its sister *An. melas*, in West Africa. However, its preferred niche is in shallow brackish pools and marsh or swamp areas along the coast. The biting behaviour of *An. merus* is generally opportunistic in host selection with a tendency to bite and rest outdoors. Only one study, on the Kenyan coast, has examined the biting times of *An. merus*, which reported the number of bites gradually rising from early evening (18:00) peaking between midnight and 01:00 and then declining to 06:00 [Mutero et al., 1984].

This species is confined to the coastal regions of Tanga, Lindi, Pwani and Mtwara, though actual entomological observations in Tanzania have lately become rare. A recent study in Rufiji district, in Pwani region indicated that even though the vector species was traditionally considered to be associated with coastal regions, it can be found further inland [Kigadye et al., 2010].

5.4 Physiological insecticide resistance status of dominant vector species

Surprisingly there have been very few reports on insecticide resistance status of dominant malaria vectors in Tanzania, despite several years of ITN use. NIMR however has coordinated representative assessments of insecticide resistance status of *Anopheles gambia*e complex at national level over the past 5 years. National cross-sectional surveys of insecticide resistance began in 1999, making Tanzania one of the countries to do so other than the Republic of South Africa. The first major report was published in 2007 [Kulkarni et al., 2007] and followed by a comprehensive report in June 2012 [Kabula et al., 2012], which provided information on resistance between 2009 and 2010 from 12 sentinel districts across the country. Other than having good legacy data and being conveniently within reach of partner institutes, these sentinel sites represented areas where either IRS had been practiced for long, where LLINs had been widely used or areas where agricultural pesticides had been used

widely. As such these data represent patterns of resistance where selective pressure had been highest [Kabula et al., 2012].

Using the original WHO standard guidelines for susceptibility testing [WHO, 1998], resistance among wild caught Anophelines had been essentially absent from mainland Tanzania until and was documented at only two sites in these 2009/2010surveys [Kabula et al., 2012]: resistance to pyrethroids, lambda cyhalothrin and permethrin, at Moshi in the Kilimanjaro region and resistance to DDT at Ilala in the Dar es Salaam region. During the same period, a number of other sites showed reduced susceptibility to at least one of the tested insecticides. There was reduced susceptibility to permethrin among *An. gambiae s.l* mosquitoes collected in Arumeru, Handeni, Mvomero, Kilombero and Ilala districts; reduced susceptibility to deltamethrin in Babati, Moshi, Arumeru, Kilombero and Mvomero districts; reduced susceptibility to lambda cyhalothrin in Moshi, Babati, Arumeru, Kyela, Kilombero, Ilala, Handeni and Muheza and reduced susceptibility to DDT recorded in Kyela, Ilala and Lushoto [Kabula et al., 2012]. It should, however, be noted that according to the revised WHO guidelines on insecticide resistance monitoring [WHO, 2013], which classifies mosquito mortality of 97% or less as resistance, it is possible that by 2009/2010, physiological resistance to common insecticides for malaria prevention was already widespread in *An. gambiae* populations across of Tanzania.

Between February and September 2011, a further series of resistance surveys were undertaken [Kisinza et al., 2011]. The results from this surveillance confirmed earlier reports of continued susceptibility of malaria vectors to commonly used insecticides (based on the 1998 WHO protocol), despite isolated cases of resistance or reduced susceptibility to pyrethroid insecticides. The report did however highlight resistance or reduced susceptibility to common pyrethroids at Muheza, Handeni, Lower Moshi, Kilombero, Muleba, Arumeru, Babati, Dar es Salaam and Magu. Fortunately, no signs of resistance were recorded against Carbamates (Propoxur 0.1%) nor Organophosphates (Fenitrothion 1%), which were also assessed [Kisinza et al., 2011]. If, however, data collected in 2011 are re-interpreted based on the new WHO guidelines [WHO, 2013], there is, again, evidence of a rapid spread of resistance amongst *An. gambiae s.l* populations to pyrethroids, across the country. Further surveys were conducted between June and December 2012 [Kisinza et al., 2012], which showed that *Anopheles gambiae* s.l. were resistant to lambdacyhalothrin or permethrin in 5 out of the 14 sentinel sites i.e. Moshi, Ngara and Geita, Bariadi and Arumeru. Reduced susceptibility to DDT was recorded in Bariadi and Geita, but the mosquitoes were still highly susceptible to Fenitrothion and Bendiocab in all the sentinel sites/districts.

More recent surveys have confirmed this threat of growing insecticide resistance. Sensitivity tests in the Kagera region, one of the areas in Tanzania where *An. gambiae s.s* is still the dominant vector, in 2011 showed extremely low mortality rates to DDT, pyrethroids and even bendiocarb, which had only just been introduced for use in IRS in the region [Protopopoff et al., 2013]. Despite low densities of *An. arabiensis* in Kagera, tests revealed that this species remained susceptible to lambda cyhalothrin, deltamethrin, DDT and bendiocarb but were resistant to permethrin [Protopopoff et al., 2013]. The speed with which physiological resistance has spread in this particular region is worrisome, as tests that had been conducted only one year earlier, in May 2010, showed complete susceptibility to

DDT and pyrethroids [Malima et al., 2010]. Elsewhere studies conducted on field collected *An. arabiensis* in Ulanga district in 2011 showed that local vector populations were fully susceptible to only DDT, but had varied levels of reduced susceptibility to all the common pyrethroids (deltamethrin, permethrin and lambda cyhalothrin) [Okumu et al., 2012].

Data on vector sensitivity testing with revised WHO criteria remains limited and demands a more aggressive, routine surveillance. There is very limited information on resistance status of *An. funestus* and *An. merus.* More data is clearly required to examine the resistance status of *An. funestus,* and *An. merus* where this species occurs, to improve the planning of vector control measures in Tanzania. In addition, very little work has been done on the molecular or biochemical basis of physiological resistance in the Tanzanian dominant vector species. There is thus very little information on important aspects such as frequency of *kdr* mutation (including *kdr*-East and *kdr*-West mutations) in the vectors, or the general aetiology of the observed resistance. Fortunately, Kisinza and colleagues indicated that there is already a good strategy in place regarding these vital assessments, and the 2012 resistance monitoring surveys actually included kdr mutation assays [Kisinza et al., 2012]. Low level kdr-east frequency was detected in *An. arabiensis* in Ngara, in the North West (allelic frequency of 9.6%) and in *An. gambiae s.s.* in Geita and Ngara (allelic frequencies of 20.8% and 88.9% respectively). Fortunately, until this time, there was neither kdr-east nor west mutations in all other sentinel sites 12 sentinel sites [Kisinza et al., 2012].

The presence of insecticide resistance genes or reduced phenotypic sensitivity may not necessarily render current vector control strategies (LLIN and IRS) completely ineffective immediately and the epidemiological relevance of insecticide resistance remains poorly and at best only partially understood [WHO, 2013; Wondji et al., 2012]. However, the early indications in Tanzania of reduced sensitivity to all pyrethoid products and other classes of insecticides used for control, most notably IRS [Protopopoff et al., 2013], is a major cause for concern, and clearly highlights an urgent need for sustained, regular monitoring, as it could negatively impact on future IRS programs [Wondji et al., 2012]. Moreover, cross-resistance between classes of insecticides through the kdr mutation will mean that choices for vector control insecticides will be greatly reduced. Presently, lambda cyhalothrin has been replaced with Bendiocarb as the first line choice for IRS operations in Tanzania.

5.5 Behavioural resilience and outdoor biting habits of malaria vector species in Tanzania

The focus of attention has been mainly on detection of physiological insecticide resistance. Behavioural resilience and outdoor biting habits of malaria vectors have however had little or no emphasis in recent vector investigations, yet, such adaptations to wide-spread insecticide use on nets or indoor walls, is a feature of vector behaviour first noted in the face of insecticide use decades ago [Elliott, 1972; Gillies & Smith, 1960; Taylor, 1975]. These bionomic changes in vector populations have been rarely considered in programmatic malaria control operations, but are now receiving more attention in the global malaria research agenda [Ferguson et al., 2010; Govella & Ferguson, 2012; malERA, 2011].

The proportion of malaria transmission that occurs outdoors, has been shown to reach 50% for people are not directly protected by bed nets or mosquito proofed housing such as Dar es Salaam [Govella et al., 2010; Majambere et al., 2013]. Similar observations have been

made at high transmission intensity areas such as the Kilombero valley [Russell et al., 2010; Russell et al., 2011]. In South Eastern Tanzania, odour baited traps have recently been used to demonstrate early peak biting times, which coincides with times when people are usually outdoors [Matowo et al., 2013]. Also, in reports describing recent studies in in Dar es Salaam, *An. gambiae s.s.* has been classified as neither exophagic nor endophagic, biting 50% of the time outdoors [Majambere et al., 2013], while *An. arabiensi*s remains exophagic in these areas [Govella et al., 2010; Majambere et al., 2013].

Outdoor-biting and early-biting is, in most areas, a direct result of the changing composition on dominant vector species to *An. arabiensis*. In Tanzania, like many other countries, this shift has been associated with the observations that while common indoor ITN and IRS interventions have been extremely effective against vectors such as *An. gambiae s.s.* and *An. funestus* that mainly bite humans indoors, their protective efficacy is reduced in the face of residual vector populations that comprise behaviourally resilient *An. arabiensis* [Kitau et al., 2012], despite sensitivity to locally used insecticides [Okumu et al., 2012]. Despite these observations of differences in species specific bionomics and changing vector composition, it is probably true that substantial transmission remains indoors rather than outdoors in many areas of Tanzania [Lwetoijera et al., 2013], even though the proportion of transmission occurring outdoors, outside the direct protective spectrum of indoor insecticidal interventions like LLINs is also increasing. Evidence is still scarce in this respect but given these behavioural resilience trends, it should become a priority to monitor outdoor biting, peak feeding times and blood meal sources within current sentinel malaria surveillance systems [Govella et al., 2013] and also consider outdoor human behaviours and activities when designing complementary malaria interventions [Lindblade, 2013].

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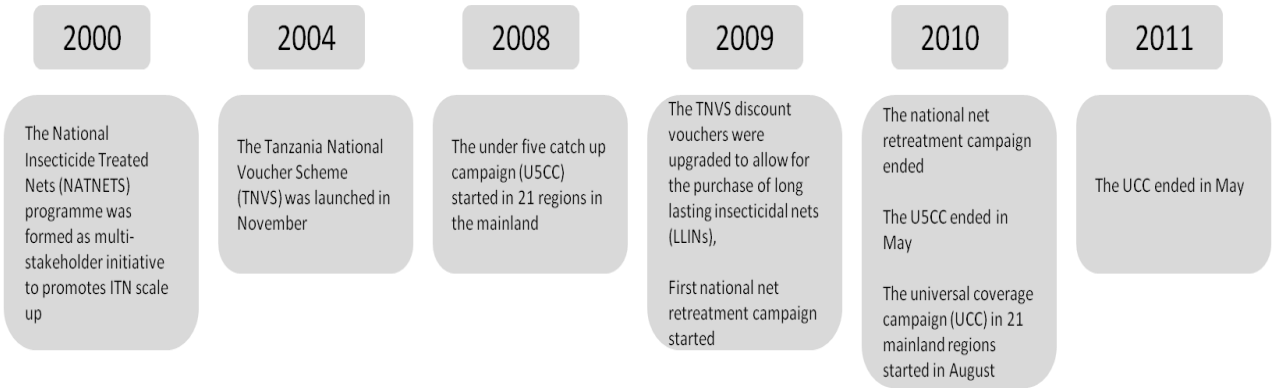
Chapter 6

Modelling the coverage of ITNs/IRS 2000, 2010 & 2012

6.1 ITN scale up in Mainland Tanzania

Tanzania was one of the first countries in Africa to establish concerted, scaled distribution of ITN nationwide following the established of the National Insecticides Treated Nets Programme (NATNETS) (Section 3.4.2). Since 2004 several multi-sectoral mechanisms have been employed to ensure maximal ITN coverage including two distinct approaches: the Tanzania National Voucher Scheme (TNVS) through which pregnant women and infants redeemed vouchers for nets in the retail sector at subsidized costs and more latterly under-five; and universal coverage campaigns designed as one-off catch up mechanisms to dramatically increase coverage within the community [Bonner et al., 2011; Koenker et al., 2013] (Figure 6.1).

Figure 6.1 Milestones in the scale up of ITNs in mainland Tanzania



ITN distribution data by district were assembled from databases provided by the NMCP and their supporting partner MEDA. Data were provided by year and were re-assembled to match each of the 102 health district/councils described in earlier chapters. Additional attributes included the mechanism of delivery, TNVS or UCC (Figures 6.2 and 6.3). These data were expressed per capita projected populations for each district for each year 2004 to 2012 (Figure 6.4). Between 2004 and 2012, about 34.5 million ITNs have been documented as distributed in Tanzania, of which 9.4 million have been distributed via the TNVS (Figures 6.2 and 6.3). Over 90% of ITN distributions happened during the period 2008-2012, with 75% of these nets distributed since 2010 and remain within the 3-year effective operational life-span of LLINs.

Figure 6.2 Annual and cummulative total distributions of ITNs from 2004 to 2012. ITN distribution per year (light green) and cummulative net distributions 2004-2012 (dark green)

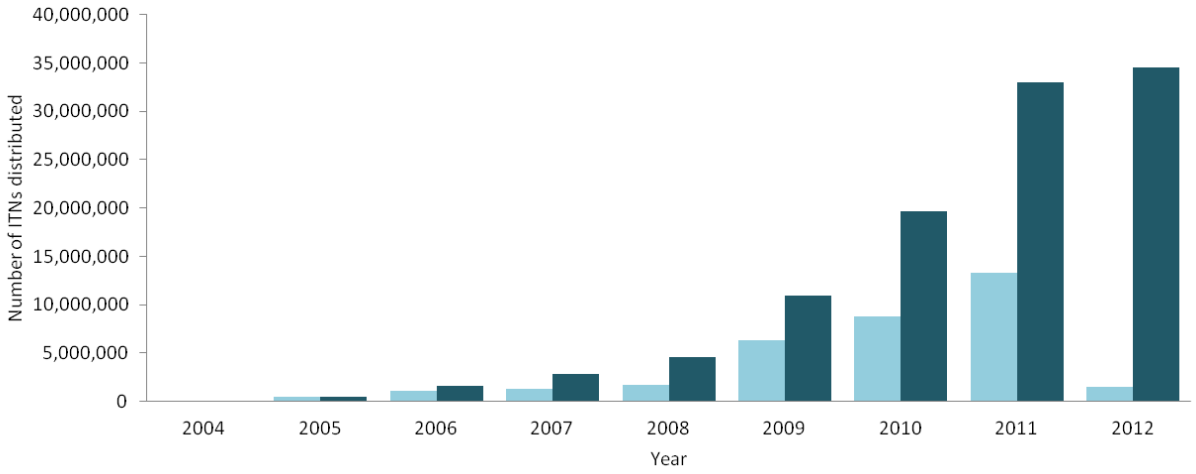


Figure 6.3 Annual total distributions of ITNs from 2004 to 2010 by main mechanisms of distribution. UCMC includes both U5 catch-up and universal coverage distributions (light blue); TNVS (dark blue)

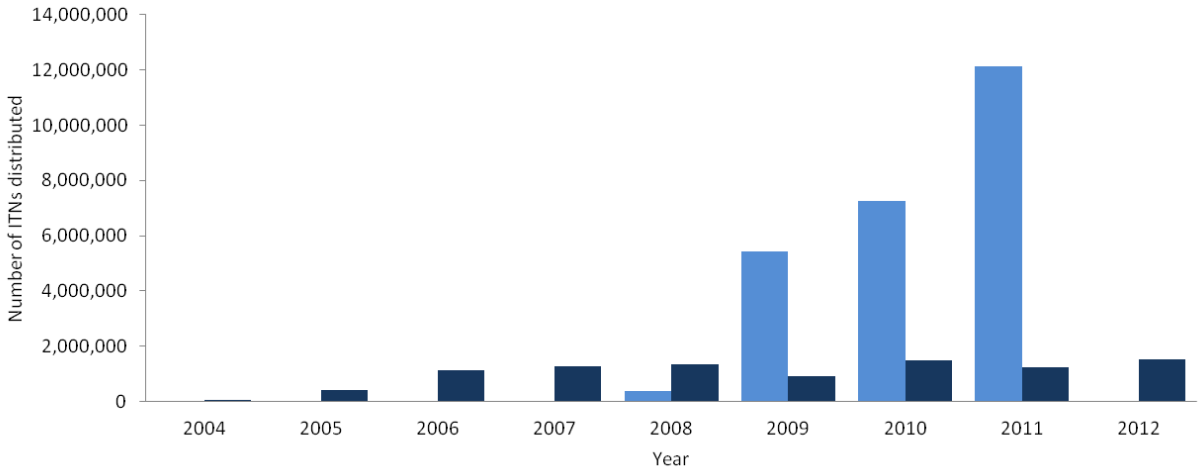
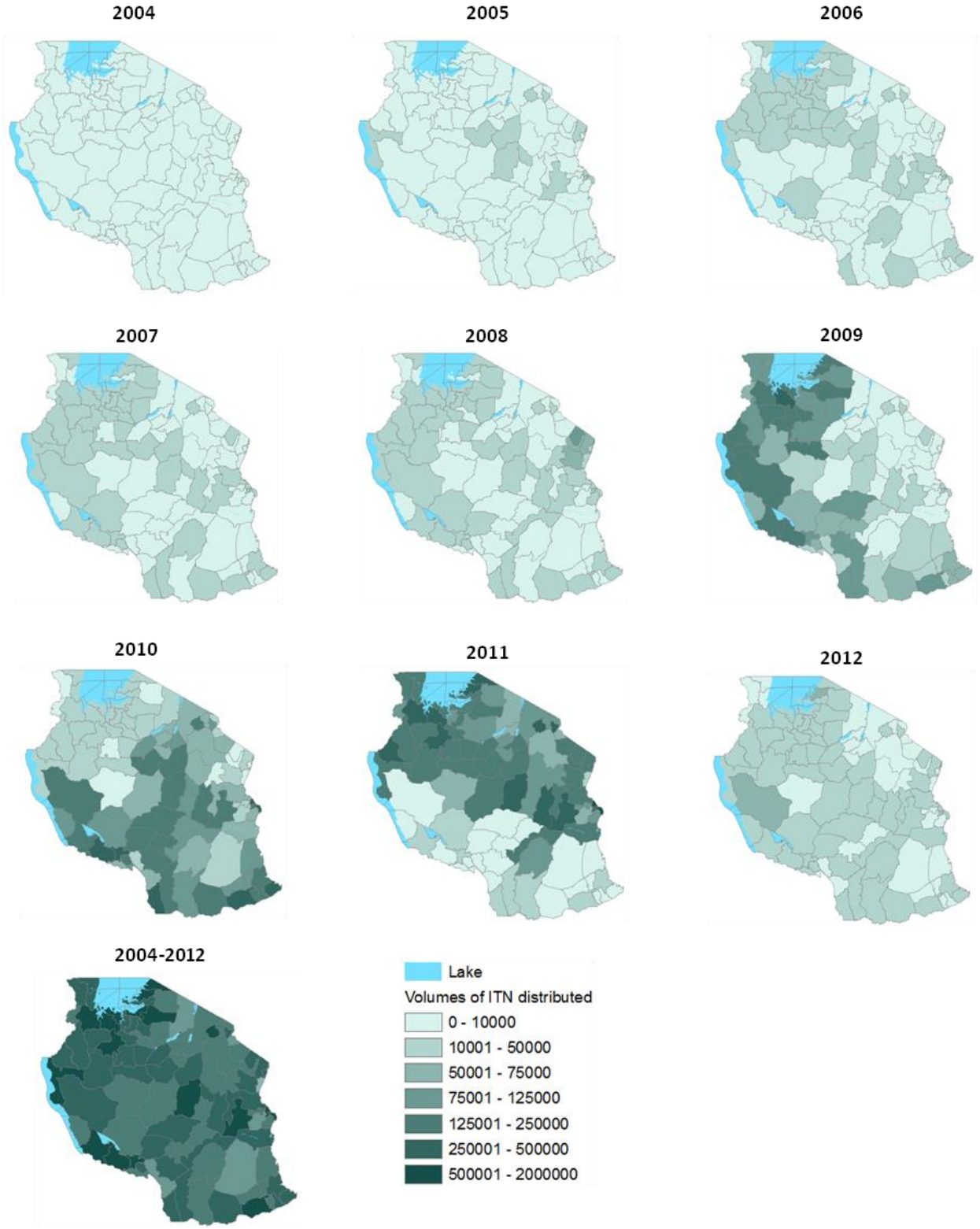


Figure 6.4 Annual total distributions (U5CC; UCC and TNVS) of ITNs from 2004 to 2012 by district



6.2 Assembling ITN coverage data

For purposes of computing progress in district level ITN coverage in Tanzania three prediction years were selected. These were 2000 and 2010 which are the RBM milestone years and 2012 which is the most recent data year. Since 1999, six large scale, sample household surveys, with information on the proportion of persons sleeping under an ITN the night before survey, have been undertaken in Tanzania. Of interest, however were surveys nearest to the selected prediction years and these were the DHS 1999, DHS 2010 and AIS 2011-12 (Table 6.1). The details of the survey sampling procedures and sample sizes are provided in Annex A3.1. National household sample surveys included data from mainland Tanzania and Zanzibar and here we have assembled only data from Mainland Tanzania. Data on ITN coverage were aggregated for each survey cluster and information on the district, year of survey, the number of persons interviewed and the number who slept under an ITN the night before survey (coverage) and the totals ITNs in the household were summarised. Each cluster and district were assigned unique identifiers.

Table 6.1 Summary of large scale household survey data with information on persons sleeping under an ITN then night before survey. DHS= Demographic and Health Survey; AIS = AIDs Indicators Survey

Survey	Clusters	Households	Persons	Age group for ITN coverage information	Source
DHS 1999	146	2,747	2,333	0-4	MEASURE DHS
DHS 2010	387	7,763	39,574	all ages	MEASURE DHS
AIS 2011-12	507	8,716	46,582	all ages	MEASURE DHS

6.3 Modelling spatial aggregates of ITN coverage using Small Area Estimation

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 et al., 2003; BIAS URL]. We have used hhierarchical Bayesian spatial and temporal SAE techniques [Banerjee et al., 2004; Best et al., 2005] to estimate the ITN coverage by district for the years 2000, 2010 and 2012. The data used were the household sample survey data assembled at cluster and district levels and the cumulative distribution per capita data to prediction years, resulting in a set of spatial and temporal neighborhood information and ancillary covariate data including per capita distribution data described above.

Here we have aimed to make a prediction of ITN coverage in all age groups, that 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]. Age correction was achieved for the DHS 1999 where only 0-4 coverage was reported using the reported age-use curves in all ages from the DHS 2004-5 by region (Table 6.2).

Table 6.2 Survey data used to predict ITN coverage among all ages in 2000, 2010 and 2012. Predictions for 2005 at the district were not possible because information on district of survey were not available

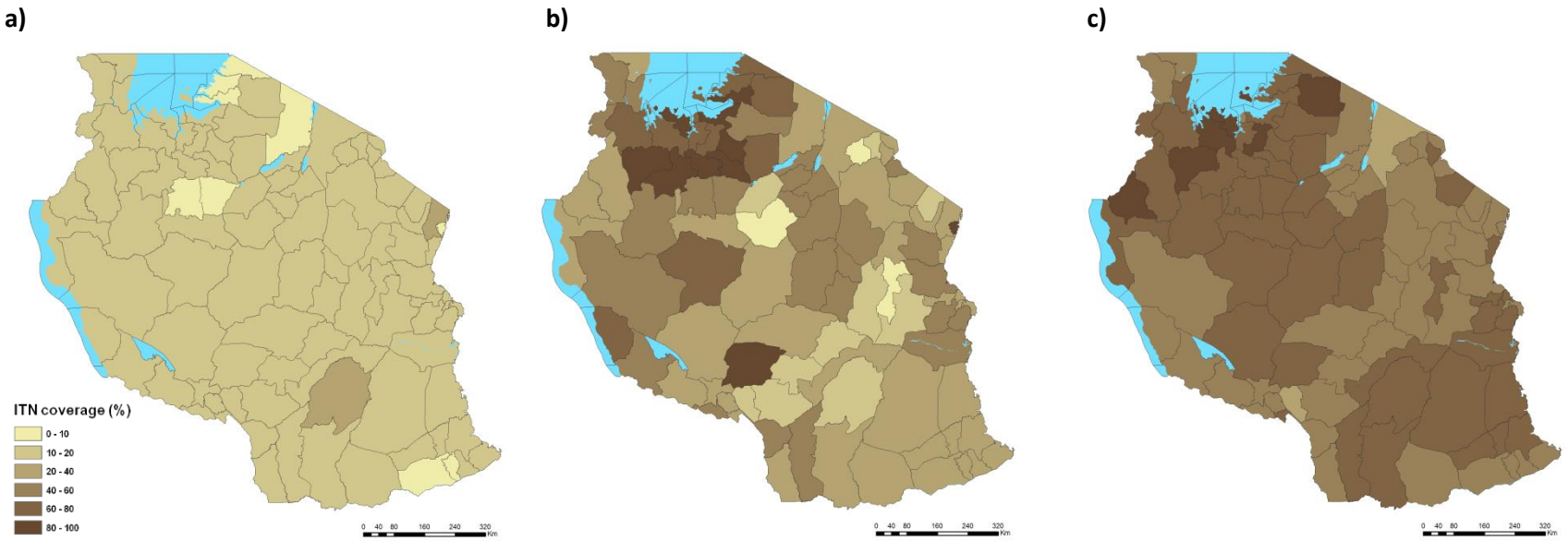
Year of prediction	Survey data used	Level of prediction	Remarks
1999	DHS 1999	District	ITN coverage for U5 corrected to all ages using the all-age ITN coverage curve from DHS 2004-5
2010	DHS 2010	District	Data on ITN coverage among all ages captured during surveys
2012	AIS 2011-12	District	Data on ITN coverage among all ages captured during surveys

To model ITN coverage a fully Bayesian geo-additive regression approach [Fahrmeir & Lang 2001; Kamman & Wand 2003] was applied. Details of model procedures are presented in Annex A3.2. In brief, the Bayesian model was based on Markov priors and used Markov Chain Monte Carlo (MCMC) techniques for inference and model checking. For model choice, the Deviance Information Criterion (DIC), a measure of fit and model complexity, was used [Spiegelhalter et al., 2002]. The analysis was carried out using version 2.0.1 of the *BayesX* software package [Lang & Brezger, 2004], which permits Bayesian inference based on MCMC simulation techniques. Multivariate analysis was used to evaluate the significance of the predicted posterior mean determined for the non-linear effects and spatial effects. A sensitivity analysis for the choice of priors was implemented. Standard choices for the hyper-parameters based on the Jeffrey's Non-informative prior were selected and the sensitivity for the spatial effects (Markov random field prior and geo-spline) were investigated. The post estimation command "predict" was used to predict mean ITN coverage for the different years by district. Two model forms were finally selected: a) for 2000 a spatial model with district as a random effect but without ITN per capita as a covariate; and b) for 2010 and 2012 a geo-spline model with ITN per capita as a covariate but weights applied as inverse proportional to the distance of the centroids of neighbouring districts (model descriptions and accuracy metrics shown in Annex A.3.3). The data-driven, modelled predictions of the proportions of all age groups sleeping under an ITN for the years 2000, 2010 and 2012 are shown in Figure 6.5. Sensitivity of district level predictions are shown in Annex Figure A.3.1 as standard deviations of predicted means.

In 2000, the overall national predicted coverage was 12.4% and almost all districts had a predicted mean ITN coverage of below 15% among all age groups. Only two districts had an ITN coverage among its population on more than 20%, Ulanga and Muheza (Figure 6.5a). Following several years of the TVNS and the launch of the catch-up campaigns, by 2010 the modelled data from household surveys and distribution data, suggested a very different pattern of coverage (Figure 6.5b). The national predicted coverage was 44.6% and 32 districts had predicted coverage estimates in excess of 50% of their populations protected. 15 districts had over 70% coverage (Bunda, Musoma, Serengeti, Kwimba, Missungwi and Ukerewe). Conversely 30 districts still had overall predicted coverage below 20% with eight districts where predicted coverage in 2010 was less than 10% (Bunda, Musoma, Serengeti, Mbarali, Magu, Missungwi, Nyamagana & Ilemela, Sengerema, Bukombe, Kahama, Kishapu, Maswa, Meatu, Shinyanga and Tanga). The patchwork of coverage in 2010 (Figure 6.5c) was improved considerably following further catch-up campaigns to provide a very different pattern of improved spatial coverage by 2012 (Figure 6.5c). By 2012 national predicted

coverage was 63.6%, 84 districts had exceeded 50% coverage of their populations; seven districts had reached 80% or more of their populations protected by an LLIN (Bukombe, Geita, Kasulu, Kwimba, Sengerema, Serengeti and Ukerewe). The highest coverage was around the high transmission areas surrounding Lake Victoria (Figure 6.5c). No districts by 2012 had predicted coverage of less than 30% and only two districts (Monduli and Makete) were predicted to have coverage of less than 40%.

Figure 6.5: The mean ITN coverage predictions in Tanzania (using neighbouring information: MRF prior) for the years: a) 2000; b) 2010; c) 2012



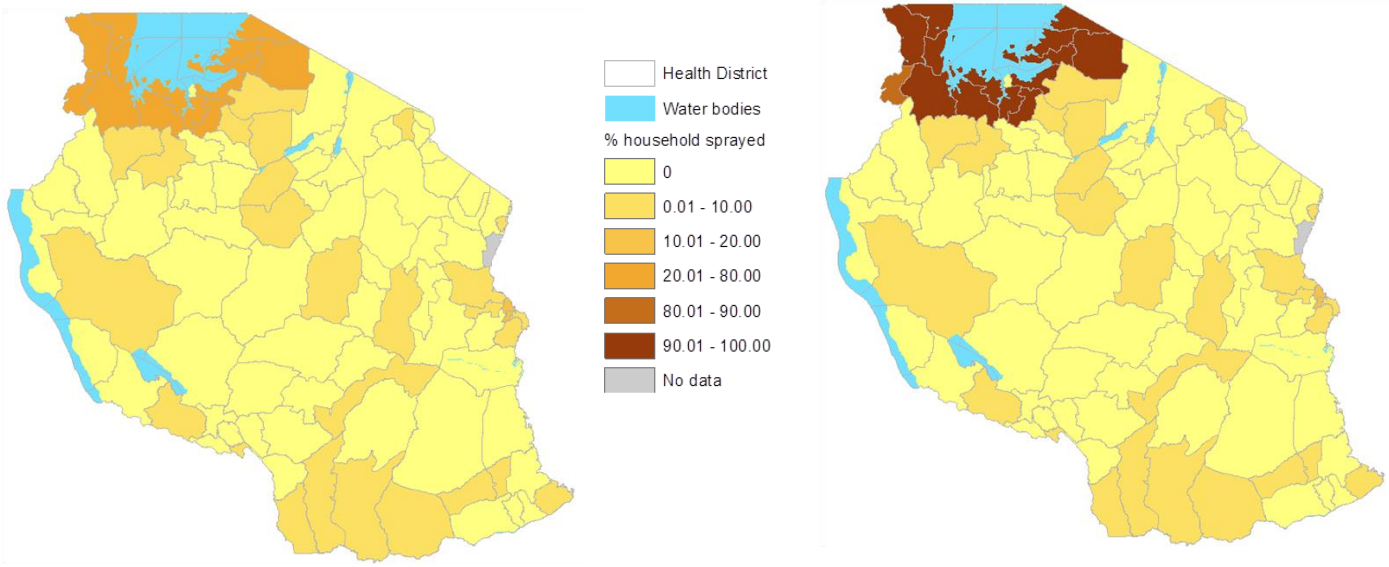
6.4 Indoor Residual House-spraying coverage

IRS was re-introduced outside of urban settings in 2007, following significant funding from PMI to RTI and the NMCP. Spray operations concentrated in the lakeside region using lambda-cyhalothrin 0.05% (ICON®) with between one and two spray rounds per year [RTI, 2012]. IRS was first mounted only in Muleba and then Karagwe districts in 2007/2008 [Mashauri et al., 2013]. Detailed inventories and coverage data were maintained by the operational teams and these have been used here to estimate the household coverage in 15 districts for the year 2011/12 (Biharamulo, Bukoba, Bunda, Geita, Karagwe, Kwimba, Magu, Missungwi, Muleba, Musoma, Ngara, Sengerema, Serengeti, Tarime and Ukerewe) [RTI, 2012]. Each of these districts had been under control since 2010 and data suggests that coverage levels in 2010 were sustained through to 2012. 2011/12 as a prediction year was selected as representing a period of sustained operations, but importantly was coincidental with other household survey data available from the national household surveys undertaken as part of the TACAIDs indicator survey in 2011/12 [TACIDS, 2013].

We have selected as the indicator the proportion of households reporting or documented as sprayed (at least once) in the last 12 months. Data from household surveys only using TACAIDs data, without SME methods described above for ITN coverage interpolation is shown in Figure 6.6a in 2011/12. Using combinations of TACAIDS and RTI survey data the estimated proportions of households sprayed in last 12 months is shown in Figure 6.6b. The differences might relate to timing of data collection between the two survey data sources, different definitions of denominators (RTI did not target municipal areas) used in the two data sources and more precise observational reports from the RTI operational data.

Figure 6.6: a) Proportion of households sprayed in last 12 months using only national household survey data (2011/12); b) combined national household survey data and RTI detailed coverage reports 2011/12.

a) b)



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Chapter 7

Summary, recommendations and action points

Understanding changes, knowing the present status and predicting the future of the malaria burden in Tanzania requires a careful examination of carefully assembled data. This report brings together detailed data that is searched, assembled and analysed within a spatial architecture necessary to understand the epidemiology of malaria within mainland Tanzania's borders.

7.1 One hundred years of malaria control (Chapter 3)

We have developed a narrative description, using archived material, on the history of malaria control in Tanzania. We feel this is necessary to provide both a recent and longer term institutional memory of what was done, when, where and how. It provides a context by which previous epidemiological strata were used to guide control and the emphasis given to particular control approaches.

Organized malaria prevention began under the German administration in the 1890s, with larval control in urban areas followed by targeted parasite control through mass "quininization". A focus on urban malaria control persisted throughout the period of British administration in Dar es Salaam, but extended before independence to other major urban settlements.

Other than a few experimental projects using Indoor Residual Spraying (IRS), there was a gradual decline in concerted malaria control efforts through the 1970s and 1980s, when malaria operations, which now focused mainly on treatment of fevers, were absorbed into a general, decentralized village-based health service provision.

During the mid-to-late 1990s the Ministry of Health & Social Welfare (MoHSW) began to grapple with an escalating malaria burden and chloroquine (CQ) resistance. Tanzania was one of the first countries in Africa to attempt scaled, operational delivery of insecticide treated nets (ITN) following consultative stakeholder meetings in 1999. The country established an enabling environment for private sector manufacture of nets, sales and subsequently social marketing of the nets. A sub-regional network of scientists and Ministry of Health staff provided a framework to assemble evidence and manage a difficult process of changing recommended first line antimalarial treatments, from CQ to sulphadoxine pyrimethamine (SP) in 2001 and finally to artemisinin-based combination therapies (ACTs) by 2004; however not implemented until 2007.

By 2007, ITN coverage and access to effective treatments remained sub-optimal. However, during the National Malaria Strategy (NMS) for 2008-2013 substantial increases in donor assistance transformed the landscape of control. Improved supplies of ACTs were supported by better information platforms, approaches to increasing access in the private sector were attempted, free mass-campaigns to fill the gaps in coverage with Long Lasting Insecticide treated Nets (LLIN) were mounted. In the same period IRS was introduced in 2007 as epidemic pre-emptive measure in selected unstable transmission areas in Kagera region and scaled up in 2010 to the remaining endemic areas of all the riparian regions in the Lake Victoria basin.

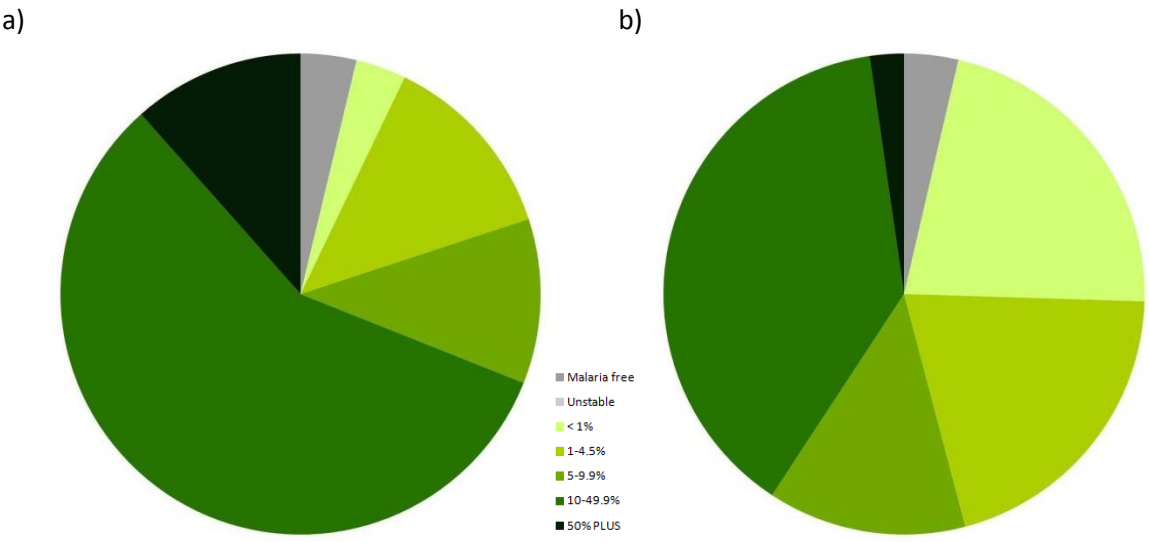
Successes in increasing coverage of available interventions and a strong political commitment mean that Tanzania is poised to make further significant gains over the next five years if adequate funding can be sustained. However, to make the business case for sustained investment requires an honest, data-driven understanding of impact and prioritization of needs that should be addressed in subsequent phases of malaria control.

7.2 Modelling/ mapping the intensity of P. falciparum transmission 2000-2010 (Chapter 4)

We have assembled the largest ever repository of community based malaria infection studies in Tanzania covering surveys undertaken from 1980 to 2012. These geo-coded data have been combined with traditional determinants of malaria transmission (temperature, rainfall, surface water and urbanization) within a Bayesian time-space model to predict malaria transmission intensity at un-sampled locations in 2000 and 2010.

There has been a greater than 50% reduction in predicted mean population-adjusted parasite prevalence in children aged 2-10 years (PA*Pf*PR_{2-10}) across Tanzania between 2000 and 2010. The mean PA*Pf*PR_{2-10} in 2000 nationwide was 25.5% declining a decade later to 11.6%. Importantly, the proportion of Tanzania's population living in areas of intense transmission (PA*Pf*$PR_{2-10} \geq 50\%$) has declined from 11.6% to only 2.3% by 2010. While only 30% of Tanzania's population lived in areas where transmission would be regarded as hypo-endemic in 2000, this had doubled by 2010 and now almost 60% of Tanzanian's live under these conditions. The proportion of the population who live under conditions of extremely low stable endemic transmission has increased from only 3.4% in 2000 to 22% in 2010 (Figure 7.1).

Figure 7.1: Percentage of Tanzania's population at various classes of *P. falciparum* endemic risk in a) 2000 and b) 2010



The rate of decline in the parasite prevalence has not been uniform across the country. Some districts in the north west and those in the south east, bordering Mozambique, have been most resistant to change, many of these districts continue to sustain moderate to high transmission conditions. At least 15 of these districts in the south also experience acute, seasonal transmission risks as defined by rainfall concentration. That is, malaria cases peak during the three months when 60% of total annual rainfall occurs. This region has a history of drug-based prevention strategies in the early 2000s and might remain suitable for seasonal malaria control based on pulsed mass drug administration.

There have been significant declines in *P. falciparum* transmission intensity among communities living in districts around Lake Victoria in Shinyanga, Mwanza, Mara and Kagera regions. These districts have witnessed the highest per-capita increases in LLIN coverage and many of them have been subject to IRS campaigns. However, despite significant epidemiological transitions many of these districts still support moderate intensity transmission.

The greatest declines in malaria transmission have been witnessed along the central belt of the country from Kilimanjaro to the border with Malawi and Zambia. Areas with the largest declines also include regions such as Morogoro, Tanga and Coast, all of which experienced extremely high transmission ten years ago. Interestingly, the predicted risks of infection in Dar es Salaam have remained the same over the last decade.

The model developed to interpolate prevalence risks across Tanzania performed with an acceptable level of precision. However, the accuracy of predictions is only as good as the amount of available data. To this end several partners have not provided information that has been collected in recent years, notably those around the IRS districts close to Lake Victoria. As available data are made accessible, the national models will be re-run to improve precision in 2010 predictions. It is anticipated that this will be done in January 2014 [***Action Point 7.1***].

The use of infection prevalence as a measure of control impact was widely used during the Global Malaria Eradication (GMEP) era 50 years ago. Current measures of impact of increased malaria financing and scaled intervention have, however, focused on modelling presumed impact on deaths averted. These models make a number of assumptions and are not anchored in empirical outcome data. We have shown here that a less ambiguous measure of impact, i.e. the proportion of children infected, can be extrapolated in time and space to provide a more reliable measure of change than might be assumed from modelled fractions of deaths presumed to be due to malaria.

Accepting the importance of parasite prevalence as a measure of impact we would recommend that this is routinely monitored with improved geographic scope and precision than is currently possible with suggested Malaria Indicator Surveys (MIS). MIS and other household survey protocols only sample very few children aged less than five years per sampled cluster. We would propose that school children serve as a more effective and efficient sample population. A strategy for surveying malaria prevalence in school children formed part of GMEP surveillance strategies in the United States and Greece during the

1950s, have been common in a number of African countries during the 1970s and 1980s as part of school health programmes and have recently been resurrected as malaria surveillance proposals in Kenya, Mozambique, Mali and Senegal. Furthermore, in 2014 schools will form part of "keep up" net distribution campaigns across Tanzania, making it logistically easier to integrate parasite prevalence surveys every two years.

It is therefore proposed that a task-force be assembled to design a school-based malaria surveillance protocol to capture circa 100 children aged 6-15 years per school and approximately four schools per district for surveys to begin in 2014. This would be repeated in 2016 and 2018 and correspond to the continued distribution of prevention and treatment commodities funded by the Global Fund's replenishment award and coincidental with the new National Malaria Strategic Plan (2013-2018) under development. Bi-lateral donors will be encouraged to support this surveillance protocol, including those more broadly interested in school health [***Action Point 7.2***].

Ensuring adequate, nationwide malaria prevalence data between 2010 and 2018 will be essential element in tracking the evolution of the malaria transition in Tanzania.

7.3 Dominant vectors (Chapter 5)

Before 2000 it was widely held that *Anopheles gambiae* s.s. was the dominant vector across mainland Tanzania. There is evidence that this is rapidly changing. *An. arabiensis* is now thought to have a more ubiquitous distribution and prominent role in *P. falciparum* transmission, with different bionomics and behavioural plasticity than *An. gambiae* s.s. In addition there are observations that the highly efficient vector species, *An. funestus*, has growing prominence in several areas of the country as well. *An. merus,* also known to transmit malaria in Tanzania remains confined to the coastal areas of the country.

Reduced sensitivity to most pyrethroids widely used as part of ITN and IRS strategies, as well as DDT has been documented among *An. gambiae* complex vectors across Tanzania. Besides, there are early signs of emerging phenotypic resistance to other classes of insecticide used for IRS, including resistance to Bendiocarb in areas around Lake Victoria

There is no uniform national profile of dominant vector species currently available to the NMCP. Neither do we have a uniform database on the role of these vectors on malaria transmission and their insecticide resistance status. In particular, very little data exists on the sensitivity of the emerging important vectors of the *An. funestus* group in Tanzania to any insecticide classes used for vector control. There is a paucity of molecular marker surveillance for resistance alleles among Tanzanian vectors and very little data on the changing behavioural responses of dominant vectors, even though evidence suggests that an increasing proportion of human-vector contacts and resulting malaria transmission now occurs outside human dwellings.

Given the significance of vector control as a means of malaria prevention in Tanzania, these gaps in vector-related data and knowledge should be urgently filled through rapid, national surveillance, perhaps tied to school-based infection prevalence monitoring as proposed above. We expect that this will vastly improve targeting of vector control interventions as

the country moves forward in the subsequent phases of malaria control starting with the 2013-2018 National Malaria Control Strategy [***Action Point 7.3***].

7.4 Intervention coverage (Chapter 6)

From the first national stakeholders meeting on scaling ITN access and use in 1999 through to 2009, private sector, social marketing and subsidized voucher schemes were the principal delivery mechanisms. In 2000, predicted ITN coverage among all age-groups across all districts in Tanzania rarely exceeded 10% and the areas where it was higher than 10% corresponded to districts where research groups had developed special initiatives, for example, the Kilombero Insecticide Nets Project (KINET). Since 2004, the Tanzanian National Voucher Scheme has increased availability and accessibility of ITNs to pregnant women and infants by subsidizing the cost of nets purchased. From 2008 to 2010, a mass distribution campaign delivered nine million LLINs free-of-charge to children under-five years of age in Tanzania mainland. In 2010 and 2011, a Universal Coverage Campaign (UCC) led by the Ministry of Health and Social Welfare (MoHSW) was implemented to cover all sleeping spaces not yet reached through previous initiatives

Using small area modelling techniques that include survey and distribution data, we predict that by 2010 45% of all Tanzanian's (i.e. all age groups) were protected by LLIN, however, predicted coverage was patchy across the country. Modelled predictions of LLIN use by 2012, following further mass catch-up campaigns had increased the proportion of all Tanzanians sleeping under an LLIN to 64%. There remain differences between districts in coverage and "universal coverage" has yet to be reached in any district.

IRS with the pyrethroid lambda-cyhalothrin was first mounted only in Muleba and then Karagwe districts in 2007/08 and gradually extended to cover 15 districts around Lake Victoria. By 2010, it was estimated that 4.9 million people were protected by IRS which reach over 90% of target households. Lambda-cyhalothrin was replaced with the carbamate Bendiocarb for IRS operations in 2012 following mounting evidence of pyrethroid resistance.

Modelling the coverage of interventions at smaller units (Districts) than used for sample precision during national household surveys (Regions) is possible with current Small Area Estimation techniques. These models require as much reported coverage data as possible using cluster level attributes and process data on distribution volumes. These data have been assembled from available sources between 2000 and 2012, however, an effort is required to maintain these data assemblies from 2013 [***Action Point 7.4***].

7.5 Mapping health service providers (Chapter 2)

As part of the present project we have used a variety of geo-coded sources to develop a spatial dimension to the MoHSWs national master health facility list. We have successfully geo-coded 5308 (85%) of the 6256 health facilities supported by the public sector; approximately 15% remain un-positioned and these will form the basis of a small survey during August and September to ensure a complete geo-coded national public health facility database necessary for improving the use of HMIS data that will include diagnostic test results from 2014 and the inclusion in platforms for the extended national SMS for life drug

management supply system [***Action Point 7.5***]. One immediate application of a complete geo-coded health facility database will be the ability to map community accessibility to service provision (out-patient care, hospital admission services, blood transfusion etc), examine spatial aspects of vulnerability and target revised community-based care provision more efficiently. This will form a body of implementation research over the next two years [***Action Point 7.6***].

7.6 Mapping human population distributions and urbanization (Chapter 2)

Vector borne diseases, including malaria are heterogeneously distributed in space. Equally over-distributed is the location of human settlement, most marked in Tanzania. We have used 2002 national census data and collateral information on night-time lights, protected areas and other land-use features to re-distribute Enumeration Area (EA) population counts to a 1 x 1 km population gridded surface and defined urban settlements using this population density and satellite data. These gridded surfaces are important to define populations at risk of malaria and target quantities for intervention delivery, defining population service access and targeted control measures, for example among urban communities.

The 2012 national census will provide more recent, reliable data at high spatial resolutions (EA) that should be re-assembled to improve population settlement mapping in Tanzania. In addition, there have been important administrative boundary changes since the 2012 national census with new regional and district divisions. These digital boundaries must be included in all future malaria attribute risk mapping. In August 2013, these data will be purchased from the TNBS and included in new population settlement and administrative boundary mapping before the 2014 repeat modelling exercise described above. An early application of this new population map will be to develop a health service accessibility map and revised urbanization assembly to consider the scope and scale of new urban control initiatives [***Action Point 7.7***]

7.7 Concluding comments

We have developed a series of important data repositories, models to handle sparse data and maps of where people live, the coverage of interventions and the changing patterns of malaria risk over the last decade. This is not a static exercise. The process of data assembly and analysis is a living, real-time exercise that demands constant updating with new information and new predictions. The NMCP is investing in data management to serve as the custodians of national data. The work presented in this report serves as a catalyst for a new repository of national malaria data. The report provides the description of these data, and the associated *metadata* that should accompany the databases. It should be a priority to ensure that the national data repository is adequately funded and resourced with technical staff able to manage, update and disseminate information between partners [***Action point 7.8***]

All data assembly exercises identify as much about what we do know as what we do not know. There are two important observations to make with respect to what we do not know: a) vector data (species distribution, species behaviour and insecticide resistance status of

different species) are not as spatially ubiquitous as they need to be to provide a reliable information platform to decide on vector control across Tanzania; and b) ensuring that parasite prevalence data are continually collected, curated and modelled is necessary to track the changing epidemiology of transmission over the next 5-10 years. Both require increased investment and should become entrenched in future Monitoring and Evaluation strategies of the NMCP.

We have presented data on changing malaria transmission intensity and changing intervention coverage. We have not constructed a detailed analysis of why transmission intensity has declined over the last decade. Reasons for the epidemiological transition are likely to be complex, different in different parts of the country and not uniquely attributable to scaled intervention coverage. Understanding the transition is important and should form the basis of detailed enquiry by the NMCP and research partners [***Action point 7.9***]. What the current exercise does provide is the basis and outputs necessary to conduct this enquiry.

Annexes

Annex A.1: Parasite prevalence model development

A.1.1 *Pf*PR$_{2\text{-}10}$ Model specification

A Bayesian hierarchical spatial-temporal model was implemented through SPDE approach using R-INLA library [R-INLA] to produce continuous maps of *PfPR*$_{2\text{-}10}$ at 1 × 1 km spatial resolution using data ranging from 1960-2011. The continuous indexed 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 Gaussian Field (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

$$(k^2-\Delta)^{\alpha/2}(\tau x(u)=W(u),\quad u\in\mathbb{R}^d,\ \alpha=v+d/2,\quad \sigma^2-\Gamma(\mathrm{v})(\Gamma(\alpha)(4\pi)^{d/2}k^{2v}\tau^2)^{-1}$$
$$k>0,\ v>0, \qquad \text{(Equation A.1.1)}$$

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

$$\pi(\mathrm{u})=(2\pi)^{-n/2}|Q|^{1/2}\exp(-\frac{1}{2}(\mathrm{u}-\mu)'\,\mathrm{Q}(\mathrm{u}-\mu)) \qquad \text{(Equation A.1.2)}$$

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

$$x(u)=\sum_{i=1}^{n}\psi_i(u)w_i \quad , \qquad \text{(Equation A.1.3)}$$

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

$$C(u,v) = \frac{\sigma^2}{2^{\nu-1}\Gamma(\nu)}(k\|v-u\|)^{\nu} K_{\nu}(k\|v-u\|) \ , \qquad \text{(Equation A.1.4)}$$

Where K_V is the modified Bessel function of the second kind, $\|\cdot\|$ denotes the Euclidean distance and order $v > 0$. $k > 0$ is a scaling parameter and σ^2 is the marginal variance. For the stationary model, k and v 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

$$(k(u)^2 - D)(t(u)x(u)) = W(u) \ , \ u \in \mathbb{R}^2 \ , \qquad \text{(Equation A.1.5)}$$

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 $\left\{\mathrm{B}_i^{(\cdot)}(\cdot)\right\}$ are smooth over the domain of interest.

$$\log(k^2(u)) = \sum b_i^{(k^2)}\mathrm{B}_i^{(k^2)}(u) \ \text{ and } \ \log(\tau(\mathrm{u})) = \sum \beta_i^{(\tau)}\mathrm{B}_i^{(\tau)}(\mathrm{u}), \qquad \text{(Equation A.1.6)}$$

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

$$y(s,t) = z(s,t)\beta + \xi(s,t) + \varepsilon(s,t) \ , \qquad \text{(Equation A.1.7)}$$

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, $\varepsilon(s_i,t)\square N(0,\sigma_\varepsilon^2)$ 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.1.2 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.

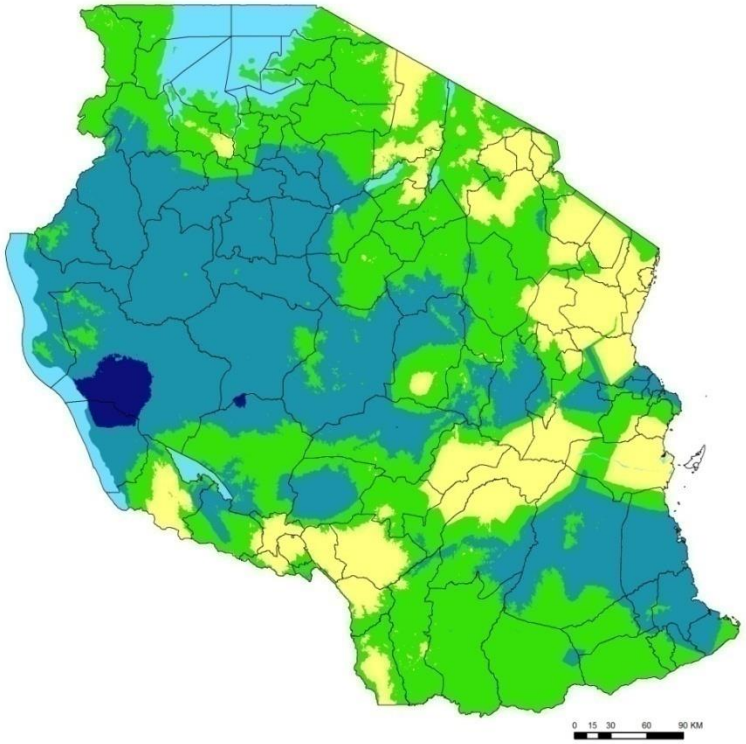
A matrix was then constructed to link the $PfPR_{2\text{-}10}$ input locations to the triangles on the mesh defined by ŋ* as $\eta^* = A(x + 1\beta_0)$ and in the inla code in the following *inla.spde.make.A* function. This makes each row in the matrix to have three non-zero elements since every data 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.1.3 Prediction accuracy

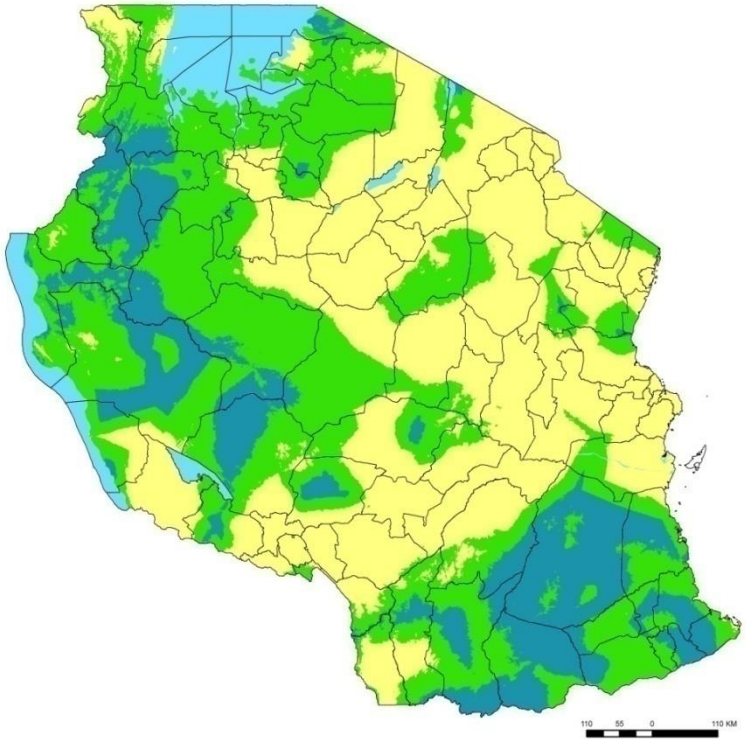
The standard deviation is a measure of the variability or dispersion of an expected value of a variable from its mean. High/low standard deviations indicate that data points are far/close to the mean. In scientific measurements it can be used as a measure of uncertainty. Of particular importance is the distance of the standard deviation 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 $Pf\text{PR}_{2\text{-}10}$ were computed for the years 2000 and 2010 (Figures A.1.1a-b). In 2000 the western districts and parts of central and south-eastern districts of Tanzania had posterior predictions that were generally outside of two standard deviations from the posterior mean $Pf\text{PR}_{2\text{-}10}$. Uncertainty around predicted mean $Pf\text{PR}_{2\text{-}10}$, however, was much lower in 2010 due largely to larger and spatially better distributed data with most parts of the country within two standard deviations of mean $Pf\text{PR}_{2\text{-}10}$ prediction.

Figure A.1.1: Maps of the number of standard deviation maps from posterior mean *Pf*PR $_{2-10}$ for a) 2000; and b) 2010. darker blue the more imprecise the predictions.

a)



b)



Number of standard deviations to mean *Pf*PR$_{2-10}$

- 0 to 1
- >1 to 2
- >2 to 3
- >3 to 4

A.1.4 References

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Annex A2. a: Population (%) in 2000 exposed to various classes of malaria and population-adjusted *Pf*PR_{2-10} for the year 2000 by reconfigured 102 health district/councils

Region/District	Total Pop 2000	Malaria Free	Unstable Transmission	*Pf*PR_{2-10} <1%	*Pf*PR_{2-10} 1-4.5%	*Pf*PR_{2-10} 5-9.9%	*Pf*PR_{2-10} 10-49.9%	*Pf*PR_{2-10} 50% +	Population-weighted mean *Pf*PR_{2-10}
Arusha									
Arusha & Arumeru	731,632	56,167 (7.7%)	0 (0%)	0 (0%)	644,899 (88.1%)	30,566 (4.2%)	0 (0%)	0 (0%)	2.41
Karatu	367,038	148,786 (40.5%)	0 (0%)	0 (0%)	169,654 (46.2%)	26,365 (7.2%)	22,233 (6.1%)	0 (0%)	2.77
Monduli	199,465	16,295 (8.2%)	39 (0%)	0 (0%)	38,765 (19.4%)	79,090 (39.7%)	65,224 (32.7%)	0 (0%)	8.87
Ngorongoro	133,168	65,962 (49.5%)	15 (0%)	0 (0%)	14,435 (10.8%)	25,800 (19.4%)	26,899 (20.2%)	28 (0%)	6.05
Dar es Salaam									
Ilala	466,646	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	423,465 (90.7%)	43,181 (9.3%)	37.19
Kinondoni	826,151	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	779,917 (94.4%)	46,233 (5.6%)	37.09
Temeke	629,823	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	616,926 (98%)	12,898 (2%)	34.43
Dodoma									
Dodoma	763,421	0 (0%)	0 (0%)	0 (0%)	103,839 (13.6%)	324,495 (42.5%)	335,087 (43.9%)	0 (0%)	11.07
Kondoa	391,541	527 (0.1%)	0 (0%)	0 (0%)	59,930 (15.3%)	179,779 (45.9%)	151,509 (38.7%)	0 (0%)	9.61
Kongwa	236,812	0 (0%)	0 (0%)	0 (0%)	6,030 (2.5%)	175,432 (74.1%)	54,823 (23.2%)	0 (0%)	8.64
Mpwapwa	241,428	5,520 (2.3%)	0 (0%)	0 (0%)	25,624 (10.6%)	50,854 (21.1%)	159,367 (66%)	63 (0%)	12.91
Iringa									
Iringa	310,884	3,569 (1.1%)	0 (0%)	0 (0%)	242 (0.1%)	5,624 (1.8%)	295,695 (95.1%)	5,754 (1.9%)	24.04
Kilolo	168,660	1 (0%)	0 (0%)	107 (0.1%)	420 (0.2%)	4,256 (2.5%)	121,337 (71.9%)	17,194 (10.2%)	23.79
Ludewa	116,349	40,518 (34.8%)	0 (0%)	0 (0%)	44,884 (38.6%)	13,020 (11.2%)	17,927 (15.4%)	0 (0%)	4.64
Makete	96,375	75,837 (78.7%)	0 (0%)	1 (0%)	15,897 (16.5%)	3,873 (4%)	767 (0.8%)	0 (0%)	0.74
Mufindi	252,095	59,612 (23.6%)	6 (0%)	0 (0%)	36,024 (14.3%)	59,109 (23.4%)	85,549 (33.9%)	11,795 (4.7%)	13.19
Njombe	390,203	131,601 (33.7%)	0 (0%)	0 (0%)	225,327 (57.7%)	29,616 (7.6%)	3,659 (0.9%)	0 (0%)	2.28
Kagera									
Biharamulo	438,044	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	83,277 (19%)	354,766 (81%)	61.53
Bukoba	512,890	0 (0%)	0 (0%)	0 (0%)	0 (0%)	571 (0.1%)	512,280 (99.9%)	0 (0%)	23.64
Karagwe	430,482	18,709 (4.3%)	0 (0%)	0 (0%)	0 (0%)	613 (0.1%)	410,305 (95.3%)	86,971 (20.2%)	20.91
Muleba	392,054	1,580 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	387,873 (98.9%)	2,601 (0.7%)	26.17
Ngara	338,056	370 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	330,021 (97.6%)	0 (0%)	23.56
Kigoma									
Kasulu	519,171	0 (0%)	0 (0%)	0 (0%)	0 (0%)	88,027 (17%)	428,038 (82.4%)	4 (0%)	18.84
Kibondo	345,263	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	306,707 (88.8%)	36,033 (10.4%)	39.56
Kigoma	594,935	207 (0%)	0 (0%)	0 (0%)	552 (0.1%)	48,068 (8.1%)	543,287 (91.3%)	2,774 (0.5%)	28.75

Region/District	Total Pop 2000	Malaria Free	Unstable Transmission	*Pf*PR$_{2-10}$ <1%	*Pf*PR$_{2-10}$ 1-4.5%	*Pf*PR$_{2-10}$ 5-9.9%	*Pf*PR$_{2-10}$ 10-49.9%	*Pf*PR$_{2-10}$ 50% +	Population-weighted mean *Pf*PR$_{2-10}$
Kilimanjaro									
Hai	242,042	12,741 (5.3%)	0 (0%)	48,640 (20.1%)	179,929 (74.3%)	724 (0.3%)	7 (0%)	0 (0%)	1.41
Moshi	485,023	8,904 (1.8%)	0 (0%)	36,595 (7.5%)	395,739 (81.6%)	43,335 (8.9%)	451 (0.1%)	0 (0%)	2.27
Mwanga	111,102	563 (0.5%)	0 (0%)	0 (0%)	29,888 (26.9%)	49,221 (44.3%)	31,033 (27.9%)	1 (0%)	9.38
Rombo	219,769	22,105 (10.1%)	0 (0%)	0 (0%)	11,495 (5.2%)	68,663 (31.2%)	117,506 (53.5%)	0 (0%)	10.17
Same	200,028	15,150 (7.6%)	136 (0.1%)	33,511 (16.8%)	61,426 (30.7%)	34,389 (17.2%)	52,405 (26.2%)	3,012 (1.5%)	8.30
Lindi									
Kilwa	141,616	104 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	99,688 (70.4%)	39,770 (28.1%)	43.51
Lindi	237,336	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	119,925 (50.5%)	117,410 (49.5%)	47.10
Liwale	71,195	0 (0%)	0 (0%)	110 (0.2%)	102 (0.1%)	42 (0.1%)	29,121 (40.9%)	41,819 (58.7%)	49.76
Nachingwea	150,261	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	134,218 (89.3%)	16,043 (10.7%)	41.19
Ruangwa	116,738	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	92,483 (79.2%)	24,255 (20.8%)	43.97
Manyara									
Babati	341,144	45,830 (13.4%)	348 (0.1%)	0 (0%)	48,951 (14.3%)	190,119 (55.7%)	55,895 (16.4%)	0 (0%)	6.56
Hanang	228,972	8,073 (3.5%)	112 (0%)	0 (0%)	28,576 (12.5%)	191,942 (83.8%)	268 (0.1%)	0 (0%)	5.94
Kiteto	168,618	323 (0.2%)	0 (0%)	154 (0.1%)	17,333 (10.3%)	124,071 (73.6%)	26,957 (16%)	0 (0%)	7.89
Mbulu	266,630	183,386 (68.8%)	0 (0%)	0 (0%)	24,526 (9.2%)	57,535 (21.6%)	1,183 (0.4%)	0 (0%)	1.76
Simanjiro	313,480	0 (0%)	0 (0%)	1,376 (0.4%)	263,996 (84.2%)	36,610 (11.7%)	11,498 (3.7%)	0 (0%)	3.81
Mara									
Bunda	289,376	0 (0%)	0 (0%)	0 (0%)	0 (0%)	26 (0%)	289,350 (100%)	0 (0%)	26.67
Musoma	467,545	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	464,749 (99.4%)	2,795 (0.6%)	29.60
Serengeti	188,133	75 (0%)	0 (0%)	0 (0%)	1 (0%)	24,645 (13.1%)	163,412 (86.9%)	0 (0%)	19.05
Tarime	522,598	0 (0%)	0 (0%)	0 (0%)	0 (0%)	50,458 (9.7%)	471,189 (90.2%)	457 (0.1%)	25.71
Mbeya									
Chunya	215,516	7 (0%)	0 (0%)	0 (0%)	5,425 (2.5%)	31,708 (14.7%)	178,375 (82.8%)	0 (0%)	15.96
Ileje	112,241	12,298 (11%)	0 (0%)	25,841 (23%)	40,261 (35.9%)	27,951 (24.9%)	5,678 (5.1%)	0 (0%)	3.61
Kyela	177,284	0 (0%)	0 (0%)	0 (0%)	1,395 (0.8%)	2,330 (1.3%)	173,559 (97.9%)	0 (0%)	23.33
Mbarali	243,930	0 (0%)	0 (0%)	0 (0%)	5,904 (2.4%)	51,650 (21.2%)	182,785 (74.9%)	3,591 (1.5%)	17.75
Mbeya	507,929	101,581 (20%)	0 (0%)	285,701 (56.2%)	111,435 (21.9%)	5,078 (1%)	4,133 (0.8%)	0 (0%)	0.86
Mbozi	533,012	465 (0.1%)	0 (0%)	0 (0%)	139,580 (26.2%)	256,376 (48.1%)	136,516 (25.6%)	0 (0%)	9.48
Rungwe	315,160	19,842 (6.3%)	0 (0%)	148,654 (47.2%)	99,172 (31.5%)	31,333 (9.9%)	16,160 (5.1%)	0 (0%)	2.29

Region/District	Total Pop 2000l	Malaria Free	Unstable Transmission	*Pf*PR$_{2-10}$ <1%	*Pf*PR$_{2-10}$ 1-4.5%	*Pf*PR$_{2-10}$ 5-9.9%	*Pf*PR$_{2-10}$ 10-49.9%	*Pf*PR$_{2-10}$ 50% +	Population-weighted mean *Pf*PR$_{2-10}$
Morogoro									
Kilombero	298,991	4,661 (1.6%)	0 (0%)	71,708 (24%)	30,714 (10.3%)	17,590 (5.9%)	121,780 (40.7%)	57,199 (19.1%)	24.18
Kilosa	474,126	0 (0%)	0 (0%)	36,314 (7.7%)	29,925 (6.3%)	85,274 (18%)	271,455 (57.3%)	46,499 (9.8%)	22.83
Morogoro	441,179	3,628 (0.8%)	0 (0%)	33,382 (7.6%)	43,317 (9.8%)	208,387 (47.2%)	142,637 (32.3%)	9,828 (2.2%)	11.72
Mvomero	241,623	5,898 (2.4%)	0 (0%)	11,440 (4.7%)	104,974 (43.4%)	43,814 (18.1%)	75,496 (31.2%)	0 (0%)	8.73
Ulanga	183,150	0 (0%)	0 (0%)	0 (0%)	701 (0.4%)	3,405 (1.9%)	118,552 (64.7%)	60,493 (33%)	43.98
Mtwara									
Masasi	421,187	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	287,739 (68.3%)	133,448 (31.7%)	46.79
Mtwara	258,203	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	234,889 (91%)	23,314 (9%)	33.64
Newala	153,082	0 (0%)	0 (0%)	0 (0%)	0 (0%)	366 (0.2%)	152,638 (99.7%)	79 (0.1%)	32.82
Tandahimba	191,552	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	189,821 (99.1%)	1,731 (0.9%)	42.76
Mwanza									
Geita	693,718	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	162 (0%)	693,556 (100%)	79.70
Kwimba	303,350	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	289,056 (95.3%)	14,294 (4.7%)	41.55
Magu	408,862	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	407,665 (99.7%)	1,198 (0.3%)	34.56
Missungwi	247,337	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	113,626 (45.9%)	133,711 (54.1%)	51.64
Nyamagana & Ilemela	404,123	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	342,750 (84.8%)	61,373 (15.2%)	37.82
Sengerema	484,522	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	14,487 (3%)	470,035 (97%)	73.16
Ukerewe	259,226	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	233,562 (90.1%)	25,664 (9.9%)	42.23
Pwani									
Bagamoyo	213,646	0 (0%)	0 (0%)	7,679 (3.6%)	2,788 (1.3%)	1,975 (0.9%)	28,996 (13.6%)	172,208 (80.6%)	72.44
Kibaha	121,460	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	24,517 (20.2%)	96,943 (79.8%)	61.20
Kisarawe	88,901	0 (0%)	0 (0%)	0 (0%)	0 (0%)	26 (0%)	15,673 (17.6%)	73,202 (82.3%)	58.59
Mafia	34,906	Not able to predict using current model							
Mkuranga	174,232	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	26,823 (15.4%)	146,939 (84.3%)	57.40
Rufiji	188,182	0 (0%)	111 (0.1%)	217 (0.1%)	303 (0.2%)	290 (0.2%)	82,497 (43.8%)	104,723 (55.6%)	48.41
Rukwa									
Mpanda	429,183	0 (0%)	0 (0%)	0 (0%)	404 (0.1%)	5,244 (1.2%)	423,221 (98.6%)	315 (0.1%)	28.07
Nkasi	232,813	0 (0%)	0 (0%)	0 (0%)	32 (0%)	7,220 (3.1%)	223,152 (95.9%)	2,410 (1%)	33.66
Sumbawanga	551,606	0 (0%)	0 (0%)	0 (0%)	381,537 (69.2%)	45,788 (8.3%)	124,043 (22.5%)	0 (0%)	7.43

Region/District	Total Pop 2000	Malaria Free	Unstable Transmission	*Pf*PR$_{2-10}$ <1%	*Pf*PR$_{2-10}$ 1-4.5%	*Pf*PR$_{2-10}$ 5-9.9%	*Pf*PR$_{2-10}$ 10-49.9%	*Pf*PR$_{2-10}$ 50% +	Population-weighted mean *Pf*PR$_{2-10}$
Ruvuma									
Mbinga	397,682	4,527 (1.1%)	0 (0%)	0 (0%)	223,950 (56.3%)	63,627 (16%)	105,577 (26.5%)	0 (0%)	7.78
Namtumbo	171,492	0 (0%)	0 (0%)	0 (0%)	168 (0.1%)	18,142 (10.6%)	153,169 (89.3%)	0 (0%)	14.97
Songea	275,673	0 (0%)	0 (0%)	0 (0%)	102,976 (37.4%)	105,109 (38.1%)	67,583 (24.5%)	0 (0%)	7.83
Tunduru	239,656	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (0%)	233,081 (97.3%)	6,569 (2.7%)	30.82
Shinyanga									
Bariadi	688,174	234 (0%)	0 (0%)	0 (0%)	157 (0%)	18,146 (2.6%)	669,638 (97.3%)	0 (0%)	23.15
Bukombe	450,123	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	265,300 (58.9%)	184,823 (41.1%)	48.19
Kahama	668,926	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	581,955 (87%)	0 (0%)	37.61
Kishapu	268,878	0 (0%)	91 (0%)	0 (0%)	0 (0%)	0 (0%)	268,787 (100%)	0 (0%)	35.10
Maswa	347,794	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	347,794 (100%)	0 (0%)	32.97
Meatu	285,387	0 (0%)	0 (0%)	0 (0%)	1,108 (0.4%)	10,832 (3.8%)	273,447 (95.8%)	0 (0%)	22.35
Shinyanga	455,758	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	409,019 (89.7%)	46,739 (10.3%)	39.01
Singida									
Iramba	359,678	0 (0%)	0 (0%)	0 (0%)	8,804 (2.4%)	201,087 (55.9%)	149,787 (41.6%)	0 (0%)	11.74
Manyoni	206,325	0 (0%)	0 (0%)	0 (0%)	0 (0%)	47,557 (23%)	158,768 (77%)	0 (0%)	13.93
Singida	508,257	0 (0%)	7,199 (1.4%)	0 (0%)	250,546 (49.3%)	201,209 (39.6%)	49,304 (9.7%)	0 (0%)	5.82
Tabora									
Igunga	350,928	0 (0%)	9 (0%)	0 (0%)	0 (0%)	0 (0%)	350,920 (100%)	0 (0%)	26.33
Nzega	437,279	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	437,279 (100%)	0 (0%)	29.89
Sikonge	143,257	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4,755 (3.3%)	138,501 (96.7%)	0 (0%)	21.20
Urambo	397,191	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2,480 (0.6%)	394,712 (99.4%)	0 (0%)	21.98
Uyui & Tabora Urban	555,918	0 (0%)	94 (0%)	0 (0%)	0 (0%)	671 (0.1%)	555,153 (99.9%)	0 (0%)	20.21
Tanga									
Handeni	232,119	0 (0%)	0 (0%)	208,968 (90%)	3,540 (1.5%)	1,672 (0.7%)	4,275 (1.8%)	13,664 (5.9%)	6.06
Kilindi	140,330	25,346 (18.1%)	0 (0%)	84,571 (60.3%)	41,595 (29.6%)	11,079 (7.9%)	3,086 (2.2%)	0 (0%)	1.77
Korogwe	244,098	2 (0%)	0 (0%)	72,081 (29.5%)	46,389 (19%)	21,038 (8.6%)	104,204 (42.7%)	383 (0.2%)	10.72
Lushoto	398,722	134,483 (33.7%)	0 (0%)	0 (0%)	73,273 (18.4%)	88,593 (22.2%)	86,242 (21.6%)	16,131 (4%)	9.21
Muheza	267,777	0 (0%)	0 (0%)	3,134 (1.2%)	18,785 (7%)	7,718 (2.9%)	134,637 (50.3%)	103,496 (38.7%)	44.25
Pangani	40,469	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	58 (0.1%)	40,412 (99.9%)	89.04
Tanga	196,809	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	196,809 (100%)	93.19

Annex A2 b: Population (%) in 2010 exposed to various classes of malaria and population-adjusted *Pf*PR_{2-10} for the year 2010 by reconfigured 102 health district/councils

Region/District	Total Pop 2010	Malaria Free	Unstable Transmission	*Pf*PR_{2-10} <1%	*Pf*PR_{2-10} 1-4.5%	*Pf*PR_{2-10} 5-9.9%	*Pf*PR_{2-10} 10-49.9%	*Pf*PR_{2-10} 50% +	Population-weighted mean *Pf*PR_{2-10}
Arusha									
Arusha & Arumeru	1,029,480	72,327 (7%)	0 (0%)	957,134 (93%)	19 (0%)	0 (0%)	0 (0%)	0 (0%)	0.19
Karatu	467,043	189,325 (40.5%)	0 (0%)	273,107 (58.5%)	4,611 (1%)	0 (0%)	0 (0%)	0 (0%)	0.17
Monduli	253,803	20,727 (8.2%)	50 (0%)	116,176 (45.8%)	97,091 (38.3%)	17,411 (6.9%)	2,284 (0.9%)	0 (0%)	1.67
Ngorongoro	169,451	83,935 (49.5%)	19 (0%)	28,158 (16.6%)	51,810 (30.6%)	4,764 (2.8%)	728 (0.4%)	0 (0%)	0.99
Dar es Salaam									
Ilala	721,782	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	721,782 (100%)	0 (0%)	18.61
Kinondoni	1,288,390	0 (0%)	0 (0%)	0 (0%)	0 (0%)	772 (0.1%)	1,287,620 (99.9%)	0 (0%)	19.40
Temeke	986,105	0 (0%)	0 (0%)	0 (0%)	912 (0.1%)	2,657 (0.3%)	981,859 (99.6%)	677 (0.1%)	23.24
Dodoma									
Dodoma	1,024,650	0 (0%)	0 (0%)	537,969 (52.5%)	411,366 (40.1%)	68,108 (6.6%)	7,206 (0.7%)	0 (0%)	1.79
Kondoa	503,744	411 (0.1%)	0 (0%)	63 (0%)	198,058 (39.3%)	258,280 (51.3%)	46,932 (9.3%)	0 (0%)	6.36
Kongwa	301,336	671 (0.2%)	0 (0%)	293,197 (97.3%)	7,468 (2.5%)	0 (0%)	0 (0%)	0 (0%)	0.47
Mpwapwa	313,500	7,024 (2.2%)	0 (0%)	103,811 (33.1%)	139,566 (44.5%)	60,215 (19.2%)	2,884 (0.9%)	0 (0%)	2.64
Iringa									
Iringa	424,568	4,541 (1.1%)	0 (0%)	31,202 (7.3%)	39,422 (9.3%)	58,107 (13.7%)	291,296 (68.6%)	0 (0%)	12.93
Kilolo	214,614	32,252 (15%)	0 (0%)	2,529 (1.2%)	22,427 (10.4%)	20,232 (9.4%)	103,931 (48.4%)	33,243 (15.5%)	22.92
Ludewa	148,050	51,558 (34.8%)	0 (0%)	13,533 (9.1%)	51,979 (35.1%)	13,352 (9%)	17,629 (11.9%)	0 (0%)	3.45
Makete	122,633	96,500 (78.7%)	0 (0%)	25,383 (20.7%)	751 (0.6%)	0 (0%)	0 (0%)	0 (0%)	0.06
Mufindi	321,803	75,855 (23.6%)	8 (0%)	84,110 (26.1%)	153,974 (47.8%)	7,676 (2.4%)	180 (0.1%)	0 (0%)	1.29
Njombe	497,418	168,035 (33.8%)	0 (0%)	161,355 (32.4%)	165,414 (33.3%)	1,816 (0.4%)	798 (0.2%)	0 (0%)	0.73
Kagera									
Biharamulo	559,818	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1,006 (0.2%)	542,599 (96.9%)	16,214 (2.9%)	29.94
Bukoba	664,296	0 (0%)	0 (0%)	0 (0%)	176,620 (26.6%)	469,611 (70.7%)	18,014 (2.7%)	0 (0%)	6.20
Karagwe	547,278	23,806 (4.3%)	0 (0%)	0 (0%)	216,258 (39.5%)	279,185 (51%)	27,437 (5%)	0 (0%)	5.60
Muleba	498,876	2,010 (0.4%)	0 (0%)	0 (0%)	171,698 (34.4%)	238,485 (47.8%)	86,682 (17.4%)	0 (0%)	7.06
Ngara	430,154	470 (0.1%)	0 (0%)	0 (0%)	117,710 (27.4%)	117,465 (27.3%)	184,767 (43%)	0 (0%)	9.79
Kigoma									
Kasulu	668,754	0 (0%)	0 (0%)	0 (0%)	57,425 (8.6%)	172,045 (25.7%)	435,290 (65.1%)	0 (0%)	13.12
Kibondo	439,373	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	361,154 (82.2%)	74,971 (17.1%)	39.43
Kigoma	810,033	263 (0%)	0 (0%)	0 (0%)	1,913 (0.2%)	61,659 (7.6%)	708,398 (87.5%)	37,740 (4.7%)	29.95

Region/District	Total Pop 2010	Malaria Free	Unstable Transmission	*Pf*PR$_{2-10}$ <1%	*Pf*PR$_{2-10}$ 1-4.5%	*Pf*PR$_{2-10}$ 5-9.9%	*Pf*PR$_{2-10}$ 10-49.9%	*Pf*PR$_{2-10}$ 50% +	Population-weighted mean *Pf*PR$_{2-10}$
Kilimanjaro									
Hai	307,990	16,213 (5.3%)	0 (0%)	291,777 (94.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.12
Moshi	664,971	11,330 (1.7%)	0 (0%)	653,603 (98.3%)	38 (0%)	0 (0%)	0 (0%)	0 (0%)	0.22
Mwanga	141,362	716 (0.5%)	0 (0%)	140,132 (99.1%)	21 (0%)	0 (0%)	0 (0%)	0 (0%)	0.31
Rombo	279,649	28,128 (10.1%)	0 (0%)	251,522 (89.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.22
Same	258,290	19,278 (7.5%)	173 (0.1%)	106,369 (41.2%)	116,275 (45%)	16,195 (6.3%)	0 (0%)	0 (0%)	1.77
Lindi									
Kilwa	180,202	0 (0%)	0 (0%)	0 (0%)	3,291 (1.8%)	18,421 (10.2%)	154,523 (85.7%)	1,220 (0.7%)	22.93
Lindi	309,418	0 (0%)	0 (0%)	0 (0%)	0 (0%)	21,334 (6.9%)	171,269 (55.4%)	116,815 (37.8%)	41.67
Liwale	90,593	0 (0%)	0 (0%)	0 (0%)	112 (0.1%)	98 (0.1%)	35,113 (38.8%)	55,269 (61%)	51.92
Nachingwea	194,276	0 (0%)	0 (0%)	0 (0%)	0 (0%)	327 (0.2%)	190,497 (98.1%)	3,452 (1.8%)	24.64
Ruangwa	148,545	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	90,453 (60.9%)	58,092 (39.1%)	45.15
Manyara									
Babati	440,300	58,317 (13.2%)	443 (0.1%)	201,407 (45.7%)	180,133 (40.9%)	0 (0%)	0 (0%)	0 (0%)	0.93
Hanang	291,360	10,273 (3.5%)	143 (0%)	229,386 (78.7%)	51,558 (17.7%)	0 (0%)	0 (0%)	0 (0%)	0.61
Kiteto	214,561	132 (0.1%)	0 (0%)	97,845 (45.6%)	97,837 (45.6%)	18,633 (8.7%)	114 (0.1%)	0 (0%)	1.70
Mbulu	339,278	233,352 (68.8%)	0 (0%)	105,926 (31.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.08
Simanjiro	398,893	0 (0%)	0 (0%)	377,050 (94.5%)	19,929 (5%)	1,912 (0.5%)	1 (0%)	0 (0%)	0.57
Mara									
Bunda	368,222	0 (0%)	0 (0%)	0 (0%)	12,040 (3.3%)	25,389 (6.9%)	330,794 (89.8%)	0 (0%)	17.05
Musoma	625,275	0 (0%)	0 (0%)	91,358 (14.6%)	343,386 (54.9%)	78,698 (12.6%)	111,833 (17.9%)	0 (0%)	5.74
Serengeti	239,393	95 (0%)	0 (0%)	0 (0%)	72,015 (30.1%)	80,088 (33.5%)	87,195 (36.4%)	0 (0%)	9.46
Tarime	677,222	0 (0%)	0 (0%)	0 (0%)	544 (0.1%)	68,021 (10%)	450,903 (66.6%)	157,140 (23.2%)	33.62
Mbeya									
Chunya	274,670	9 (0%)	0 (0%)	54,160 (19.7%)	99,068 (36.1%)	72,284 (26.3%)	46,859 (17.1%)	2,290 (0.8%)	7.42
Ileje	142,907	15,648 (10.9%)	0 (0%)	65,699 (46%)	59,875 (41.9%)	1,292 (0.9%)	40 (0%)	0 (0%)	0.98
Kyela	225,588	0 (0%)	0 (0%)	2,329 (1%)	62,148 (27.5%)	160,148 (71%)	964 (0.4%)	0 (0%)	6.16
Mbarali	310,393	0 (0%)	0 (0%)	90,874 (29.3%)	146,710 (47.3%)	0 (0%)	33,627 (10.8%)	0 (0%)	4.40
Mbeya	700,256	129,300 (18.5%)	0 (0%)	567,118 (81%)	3,837 (0.5%)	0 (0%)	0 (0%)	0 (0%)	0.10
Mbozi	683,074	592 (0.1%)	0 (0%)	313,893 (46%)	183,448 (26.9%)	69,225 (10.1%)	115,826 (17%)	0 (0%)	4.91
Rungwe	401,476	25,263 (6.3%)	0 (0%)	292,431 (72.8%)	83,347 (20.8%)	435 (0.1%)	0 (0%)	0 (0%)	0.76

Region/District	Total Pop 2010	Malaria Free	Unstable Transmission	*Pf*PR$_{2-10}$ <1%	*Pf*PR$_{2-10}$ 1-4.5%	*Pf*PR$_{2-10}$ 5-9.9%	*Pf*PR$_{2-10}$ 10-49.9%	*Pf*PR$_{2-10}$ 50% +	Population-weighted mean *Pf*PR$_{2-10}$
Morogoro									
Kilombero	393,419	1 (0%)	0 (0%)	68,471 (17.4%)	260,805 (66.3%)	49,978 (12.7%)	14,164 (3.6%)	0 (0%)	3.08
Kilosa	615,119	5,931 (1%)	0 (0%)	276,387 (44.9%)	296,069 (48.1%)	30,716 (5%)	6,016 (1%)	0 (0%)	1.92
Morogoro	610,049	4,617 (0.8%)	0 (0%)	25,331 (4.2%)	502,674 (82.4%)	76,322 (12.5%)	1,106 (0.2%)	0 (0%)	2.81
Mvomero	307,565	7,505 (2.4%)	0 (0%)	34,959 (11.4%)	232,793 (75.7%)	29,915 (9.7%)	2,393 (0.8%)	0 (0%)	3.02
Ulanga	233,605	0 (0%)	0 (0%)	18,719 (8%)	139,777 (59.8%)	30,550 (13.1%)	44,558 (19.1%)	0 (0%)	5.45
Mtwara									
Masasi	540,926	0 (0%)	0 (0%)	0 (0%)	0 (0%)	95,983 (17.7%)	400,340 (74%)	140,586 (26%)	42.24
Mtwara	347,496	0 (0%)	0 (0%)	0 (0%)	114,716 (33%)	40,635 (11.7%)	178,392 (51.3%)	13,753 (4%)	18.82
Newala	195,873	0 (0%)	0 (0%)	0 (0%)	0 (0%)	527 (0.3%)	140,996 (72%)	54,351 (27.7%)	41.08
Tandahimba	243,743	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	199,137 (81.7%)	44,607 (18.3%)	46.36
Mwanza									
Geita	883,755	0 (0%)	0 (0%)	0 (0%)	1,641 (0.2%)	134,107 (15.2%)	748,008 (84.6%)	0 (0%)	16.73
Kwimba	386,003	0 (0%)	0 (0%)	0 (0%)	40,131 (10.4%)	129,813 (33.6%)	216,059 (56%)	0 (0%)	11.52
Magu	521,116	0 (0%)	0 (0%)	0 (0%)	0 (0%)	251 (0%)	520,865 (100%)	0 (0%)	20.66
Missungwi	314,728	0 (0%)	0 (0%)	0 (0%)	461 (0.1%)	80,441 (25.6%)	233,826 (74.3%)	0 (0%)	15.55
Nyamagana & Ilemela	600,228	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	600,228 (100%)	0 (0%)	17.03
Sengerema	626,184	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4,335 (0.7%)	621,849 (99.3%)	0 (0%)	21.79
Ukerewe	329,857	0 (0%)	0 (0%)	324 (0.1%)	0 (0%)	151 (0%)	329,382 (99.9%)	0 (0%)	17.67
Pwani									
Bagamoyo	277,624	0 (0%)	0 (0%)	65,715 (23.7%)	78,634 (28.3%)	82,526 (29.7%)	50,633 (18.2%)	116 (0%)	6.13
Kibaha	169,597	0 (0%)	0 (0%)	18,848 (11.1%)	100,450 (59.2%)	44,722 (26.4%)	5,577 (3.3%)	0 (0%)	3.92
Kisarawe	113,227	0 (0%)	0 (0%)	481 (0.4%)	32,370 (28.6%)	33,408 (29.5%)	46,968 (41.5%)	0 (0%)	9.05
Mafia	44,417	Not able to predict using current model							
Mkuranga	221,771	0 (0%)	0 (0%)	0 (0%)	363 (0.2%)	8,528 (3.8%)	209,909 (94.7%)	2,373 (1.1%)	31.55
Rufiji	239,455	0 (0%)	141 (0.1%)	19,323 (8.1%)	35,519 (14.8%)	20,692 (8.6%)	162,116 (67.7%)	1,612 (0.7%)	19.77
Rukwa									
Mpanda	557,338	0 (0%)	0 (0%)	21 (0%)	51,693 (9.3%)	114,123 (20.5%)	373,235 (67%)	18,267 (3.3%)	18.30
Nkasi	296,446	0 (0%)	0 (0%)	20,509 (6.9%)	119,847 (40.4%)	87,156 (29.4%)	68,704 (23.2%)	231 (0.1%)	7.08
Sumbawanga	715,894	0 (0%)	0 (0%)	530,554 (74.1%)	137,451 (19.2%)	34,918 (4.9%)	12,682 (1.8%)	0 (0%)	1.37

Region/District	Total Pop 2010	Malaria Free	Unstable Transmission	*Pf*PR$_{2-10}$ <1%	*Pf*PR$_{2-10}$ 1-4.5%	*Pf*PR$_{2-10}$ 5-9.9%	*Pf*PR$_{2-10}$ 10-49.9%	*Pf*PR$_{2-10}$ 50% +	Population-weighted mean *Pf*PR$_{2-10}$
Ruvuma									
Mbinga	506,037	5,761 (1.1%)	0 (0%)	300,128 (59.3%)	127,139 (25.1%)	48,211 (9.5%)	24,798 (4.9%)	0 (0%)	2.27
Namtumbo	218,218	0 (0%)	0 (0%)	22 (0%)	4,340 (2%)	14,620 (6.7%)	196,155 (89.9%)	3,064 (1.4%)	25.05
Songea	377,184	0 (0%)	0 (0%)	888 (0.2%)	285,083 (75.6%)	46,210 (12.3%)	44,996 (11.9%)	0 (0%)	4.82
Tunduru	305,281	0 (0%)	0 (0%)	0 (0%)	0 (0%)	48 (0%)	271,473 (88.9%)	33,760 (11.1%)	36.22
Shinyanga									
Bariadi	875,679	298 (0%)	0 (0%)	0 (0%)	475 (0.1%)	517,814 (59.1%)	357,092 (40.8%)	0 (0%)	10.37
Bukombe	575,456	0 (0%)	0 (0%)	0 (0%)	0 (0%)	11,237 (2%)	440,663 (76.6%)	123,556 (21.5%)	38.66
Kahama	860,648	0 (0%)	0 (0%)	0 (0%)	78,720 (9.1%)	276,303 (32.1%)	505,625 (58.7%)	0 (0%)	12.73
Kishapu	342,952	0 (0%)	116 (0%)	0 (0%)	84,255 (24.6%)	75,253 (21.9%)	183,328 (53.5%)	0 (0%)	12.48
Maswa	442,556	0 (0%)	0 (0%)	0 (0%)	729 (0.2%)	39,181 (8.9%)	345,844 (78.1%)	0 (0%)	15.39
Meatu	363,146	0 (0%)	0 (0%)	44,284 (12.2%)	133,653 (36.8%)	124,379 (34.3%)	60,830 (16.8%)	0 (0%)	5.61
Shinyanga	604,260	0 (0%)	0 (0%)	55 (0%)	507,810 (84%)	72,581 (12%)	23,815 (3.9%)	0 (0%)	3.75
Singida									
Iramba	458,481	0 (0%)	0 (0%)	260,880 (56.9%)	197,601 (43.1%)	0 (0%)	0 (0%)	0 (0%)	1.12
Manyoni	267,744	0 (0%)	0 (0%)	81,202 (30.3%)	135,069 (50.4%)	40,170 (15%)	11,304 (4.2%)	0 (0%)	2.93
Singida	668,218	0 (0%)	10,938 (1.6%)	582,072 (87.1%)	74,977 (11.2%)	230 (0%)	0 (0%)	0 (0%)	0.46
Tabora									
Igunga	446,545	0 (0%)	11 (0%)	0 (0%)	435,999 (97.6%)	10,496 (2.4%)	38 (0%)	0 (0%)	1.93
Nzega	563,437	0 (0%)	0 (0%)	0 (0%)	275,504 (48.9%)	119,519 (21.2%)	168,415 (29.9%)	0 (0%)	8.00
Sikonge	182,289	0 (0%)	0 (0%)	0 (0%)	168 (0.1%)	73,738 (40.5%)	108,383 (59.5%)	0 (0%)	12.22
Urambo	510,373	0 (0%)	0 (0%)	0 (0%)	0 (0%)	58,799 (11.5%)	451,344 (88.4%)	231 (0%)	16.84
Uyui & Tabora Urban	761,090	0 (0%)	119 (0%)	0 (0%)	442,905 (58.2%)	247,668 (32.5%)	70,397 (9.2%)	0 (0%)	5.90
Tanga									
Handeni	297,823	0 (0%)	0 (0%)	95,404 (32%)	60,660 (20.4%)	51,792 (17.4%)	89,955 (30.2%)	11 (0%)	7.57
Kilindi	178,566	0 (0%)	0 (0%)	72,661 (40.7%)	48,510 (27.2%)	16,515 (9.2%)	40,880 (22.9%)	0 (0%)	5.29
Korogwe	319,073	3 (0%)	0 (0%)	160,378 (50.3%)	89,434 (28%)	21,183 (6.6%)	48,076 (15.1%)	0 (0%)	3.35
Lushoto	507,360	171,125 (33.7%)	0 (0%)	224,578 (44.3%)	68,850 (13.6%)	25,564 (5%)	17,243 (3.4%)	0 (0%)	1.22
Muheza	340,737	0 (0%)	0 (0%)	0 (0%)	27,671 (8.1%)	14,684 (4.3%)	298,373 (87.6%)	0 (0%)	15.61
Pangani	51,496	0 (0%)	0 (0%)	0 (0%)	44 (0.1%)	22,941 (44.5%)	28,511 (55.4%)	0 (0%)	15.35
Tanga	295,727	0 (0%)	0 (0%)	0 (0%)	2,910 (1%)	241,348 (81.6%)	51,469 (17.4%)	0 (0%)	7.86

Annex A2c : Number and percentage of total 2010 population living in areas suitable for seasonal malaria control

Region	District	Seasonality (>60% rainfall in 3 consecutive months)
Arusha	Arusha & Arumeru	25,945 (2.5%)
	Karatu	0 (0%)
	Monduli	49,536 (19.5%)
	Ngorongoro	0 (0%)
Dar es Salaam	Ilala	0 (0%)
	Kinondoni	0 (0%)
	Temeke	28,043 (2.8%)
Dodoma	Dodoma	1,008,570 (98.4%)
	Kondoa	244,785 (48.6%)
	Kongwa	281,001 (93.3%)
	Mpwapwa	312,517 (99.7%)
Iringa	Iringa	424,259 (99.9%)
	Kilolo	214,614 (100%)
	Ludewa	145,793 (98.5%)
	Makete	5,281 (4.3%)
	Mufindi	321,803 (100%)
	Njombe	488,048 (98.1%)
Kagera	Biharamulo	0 (0%)
	Bukoba	0 (0%)
	Karagwe	0 (0%)
	Muleba	0 (0%)
	Ngara	0 (0%)
Kigoma	Kasulu	0 (0%)
	Kibondo	0 (0%)
	Kigoma	0 (0%)
Kilimanjaro	Hai	14,721 (4.8%)
	Moshi	0 (0%)
	Mwanga	24,002 (17%)
	Rombo	0 (0%)
	Same	1,061 (0.4%)
Lindi	Kilwa	138,982 (77.1%)
	Lindi	308,573 (99.7%)
	Liwale	81,425 (89.9%)
	Nachingwea	166,324 (85.6%)
	Ruangwa	144,419 (97.2%)
Manyara	Babati	24,926 (5.7%)
	Hanang	67,027 (23%)
	Kiteto	212,175 (98.9%)
	Mbulu	0 (0%)
	Simanjiro	51,370 (12.9%)

Region	District	Seasonality (>60% rainfall in 3 consecutive months)
Mara	Bunda	0 (0%)
	Musoma	0 (0%)
	Serengeti	0 (0%)
	Tarime	0 (0%)
Mbeya	Chunya	61,558 (22.4%)
	Ileje	99,212 (69.4%)
	Kyela	127,762 (56.6%)
	Mbarali	249,533 (80.4%)
	Mbeya	2,862 (0.4%)
	Mbozi	3,537 (0.5%)
	Rungwe	734 (0.2%)
Morogoro	Kilombero	388,775 (98.8%)
	Kilosa	390,737 (63.5%)
	Morogoro	50,905 (8.3%)
	Mvomero	9,158 (3%)
	Ulanga	211,351 (90.5%)
Mtwara	Masasi	540,926 (100%)
	Mtwara	232,796 (67%)
	Newala	195,873 (100%)
	Tandahimba	243,743 (100%)
Mwanza	Geita	0 (0%)
	Kwimba	0 (0%)
	Magu	0 (0%)
	Missungwi	0 (0%)
	Nyamagana & Ilemela	0 (0%)
	Sengerema	0 (0%)
	Ukerewe	0 (0%)
Pwani	Bagamoyo	60,113 (21.7%)
	Kibaha	0 (0%)
	Kisarawe	0 (0%)
	Mafia	
	Mkuranga	49,318 (22.2%)
	Rufiji	157,682 (65.9%)
Rukwa	Mpanda	0 (0%)
	Nkasi	0 (0%)
	Sumbawanga	1,870 (0.3%)
Ruvuma	Mbinga	506,037 (100%)
	Namtumbo	218,218 (100%)
	Songea	377,184 (100%)
	Tunduru	305,281 (100%)

Region	District	Seasonality (>60% rainfall in 3 consecutive months)
Shinyanga	Bariadi	0 (0%)
	Bukombe	0 (0%)
	Kahama	0 (0%)
	Kishapu	0 (0%)
	Maswa	0 (0%)
	Meatu	0 (0%)
	Shinyanga	0 (0%)
Singida	Iramba	0 (0%)
	Manyoni	243,959 (91.1%)
	Singida	178,951 (26.8%)
Tabora	Igunga	0 (0%)
	Nzega	0 (0%)
	Sikonge	14,953 (8.2%)
	Urambo	0 (0%)
	Uyui & Tabora Urban	3,000 (0.4%)
Tanga	Handeni	37,962 (12.7%)
	Kilindi	64,424 (36.1%)
	Korogwe	0 (0%)
	Lushoto	0 (0%)
	Muheza	9,752 (2.9%)
	Pangani	46,362 (90%)
	Tanga	255,531 (86.4%)

Annex A3: Survey data with information on ITN utilisation and Bayesian mapping procedures

A.3.1 ITN coverage data for Tanzania

The national household sample surveys where data are available on household and individual net ownership and use and were used for purposes of age correction (DHS 2004-05) and for modelling ITN coverage (DHS 1999, DHS 2010 and AIS 2011-12) are described here. We have selected only data that were collected on mainland Tanzania and have excluded data from the islands of Zanzibar and Pemba.

Demographic and Health Survey (DHS) 1999: The survey was undertaken by the National Bureau of Statistics (NBS) in collaboration with the Reproductive and Child Health Section of the Ministry of Health. The data collection was carried out within the period September to November 1999. A three-stage sample design was used and overall, 146 census enumeration areas were selected on the Mainland with probability proportional to size on an approximately self-weighting basis. The enumeration areas were selected from the sample locations used during the 1996 DHS. Before the data collection, fieldwork teams visited the selected enumeration areas to list all the households. From these lists, households were selected to be interviewed. A total of 2,747 households were interviewed. ITN usage information was recorded only for children under the age of five years [NBS & MACRO, 2000].

DHS 2004-05: The 2004-05 DHS was implemented by the NBS in collaboration with the Reproductive and Child Health Section and the Policy and Planning Department of the Ministry of Health. Data collection began on October 7, 2004 and was completed in mid-February 2005. A representative probability sample of 10,312 households was selected to provide an expected sample of 10,000 eligible women. The sample was selected in two stages. In the first stage, 385 clusters were selected from a list of enumeration areas from the 2002 Population and Housing Census. Eighteen clusters were selected in each region except Dar es Salaam, where 25 clusters were selected. In the second stage, a complete household listing exercise was carried out between June and August 2004 within all the selected clusters. Households were then systematically selected for participation in the survey. Twenty-two households were selected from each of the clusters in all regions except for Dar es Salaam where 16 households were selected. A total of 8,221 households were successfully interviewed [NBS & MACRO, 2005]. Information on usage of ITNs were collected for persons of all ages. Information on the survey district were not available in the public domain and nor were coordinates of the enumeration areas provided.

DHS 2010: The 2010 DHS was implemented by the NBS in collaboration with the MoHSW. Data collection was conducted between 19th December 2009 and 23rd May 2010. The sample was selected in two stages. 385 clusters were selected from a list of enumeration areas in the 2002 Population and Housing Census. Twenty-five sample points were selected in Dar es Salaam, and 18 were selected in each of the other twenty regions in mainland Tanzania. A total 7,763 households were successfully interviewed and net usage among all resident members was recorded [NBS & MACRO, 2011]

AIS 2011-12: Data collection in the Mainland took place over a five-month period from 16th December 2011 to 24th May 2012. The sampling frame used for the 2011-12 AIS was developed by the NBS after the 2002 Population and Housing Census (PHC) and is the same as that used for the 2010 and 2007-8 AIS-MIS. The first stage involved selecting sample points (clusters) consisting of EAs delineated for the 2002 Population and Housing Census. A total of 510 clusters were selected. On the Mainland, 30 sample points were selected in Dar es Salaam and 20 were selected in each of the other 24 regions. Approximately 18 households were selected from each sample point for a total sample size of 9,180 households. A total of 8,716 households were successfully interviewed and ITN usage among all members recorded [TACAIDS, 2013].

A 3.2 Bayesian geo-additive regression models

The presentation of ITN coverage data is often limited only to the lowest sampling precision estimates of national surveys, regions in the case of Tanzania. Here, we use the properties of intervention coverage at geo-coded cluster levels with additional data on process delivery at district levels using combined data within a simultaneous, coherent regression framework using a geo-additive semi-parametric mixed model. Because the predictor contains nonlinear effects of metrical covariate (ITN per capita) and geographic effects in additive form, such models are also called geo-additive models and best constructed within a Bayesian framework [Kammann & Wand, 2003]. Here, we use a fully Bayesian approach based on Markov priors that uses MCMC techniques for inference and model checking [Fahrmeir & Lang, 2001; Lang & Brezger, 2004] where the cclassical linear regression model forms are as follows

$$y_i = w_i'\gamma + \varepsilon_i, \qquad \varepsilon_i \sim N(0,\sigma^2), \qquad \text{(Equation A.3.1)}$$

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 and in many other regression situations, we are facing the following problems: First, for the *continuous covariates* in the data set, the assumption of a strictly linear effect on the response *y* may not be appropriate. In our study, such covariates is the ITN per capita. Generally, it will be difficult to model the possibly nonlinear effect of such covariates through a parametric functional form, which has to be *linear* in the parameters, prior to any data analysis.

Second, in addition to usual covariates, geographical small-area information was given in form of a location variable *s*, indicating the region, district or community where ITN was distributed to individuals or units in the sample size live or come from. In our study, this geographical information is given by the districts of Tanzania. 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 cannot also 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*

$$y_i = f_1(x_{i1}) + ... + f_p(x_{ip}) + f_{spat}(s_i) + w'_i\,\gamma + \varepsilon_i \quad . \qquad \text{(Equation A.3.2)}$$

here, $f_1,...,f_p$ are non-linear smooth effects of the metrical covariates, and f_{spat} is the effect of the spatial covariate $s_i \in \{1,...,S\}$ labelling the districts in Tanzania. Regression models with predictors as in (2) are sometimes referred to as geo-additive models. The observation model (2) may be extended by including interaction $f(x)w$ between a continuous covariate x and a binary component of w, say, leading to so called varying coefficient models, or by adding a nonlinear interaction $f_{1,2}(x_1, x_2)$ of two continuous covariates.

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 P(enalized) – 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 $B_m(x)$,

$$f(x) = \sum_{m=1}^{l} \beta_m B_m(x) \qquad \text{(Equation A.3.3)}$$

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

$$\beta_m = 2\beta_{m-1} - \beta_{m-2} + u_m, \qquad \text{(Equation A.3.4)}$$

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

$$f_{str}(s) \mid f_{str}(r), r \neq s \sim N(\sum_{r \in \partial_s} f_{str}(r) / N_s, \tau^2 / N_s) \qquad \text{(Equation A.3.5)}$$

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

$$f_{unstr}(s) \mid \tau^2_{unstr} \sim N(0, \tau^2_{unstr}) \qquad \text{(Equation A.3.6)}$$

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.3.3 Model selection

The spatial effects were modelled through the Markov random field prior (MRF) and the nonlinear effect of ITN per capita 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. Three model forms were explored: spatial model with district as a random effect but without ITN per capita as a covariate (Model A); a spatial model with district as random effect and with ITN per capita as a covariate and with MRF priors (Model B); and geo-spline model with ITN per capita as a covariate but weights applied as inverse proportional to the distance of the centroids of neighbouring districts (Model C). For the 2000 estimates of ITN coverage these models were compared without ITN per capita as covariate. Table A.2.1. summarises the comparison of the DIC and prior sensitivities for the three models.

Table A.3.1 Summary of the DIC & sensitivity analysis of the choice of spatial priors for model selection

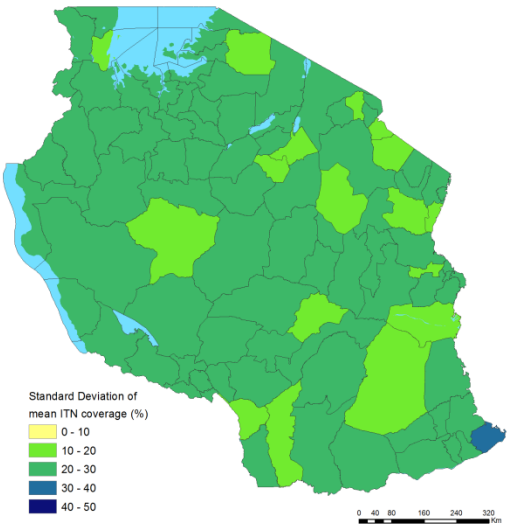
Hyper-parameters	Year	Diagnostics	Spatial (A)	Nonlinear (B) With MRF	Nonlinear (C) With geo-spline
a=1, b=0.005	2000	Deviance	129.60	0.85*	0.86
		pD	17.43	73.15	73.22
		DIC	164.47	147.16*	147.31
a=1, b=0.005	2010	Deviance	1477.23	1470.05	1468.60
		pD	38.10	54.11	48.23
		DIC	1553.44	1578.28	1565.05*
a=1, b=0.005	2012	Deviance	813.05	785.42	797.75
		pD	37.45	65.28	53.88
		DIC	887.95	915.97	905.51*

Models with asterisks (*) is the best.

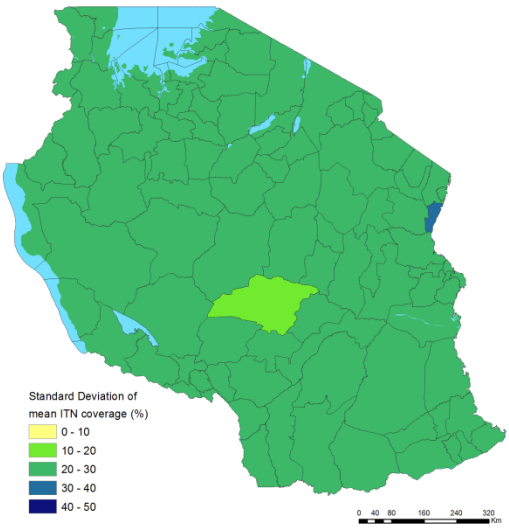
The results indicate for the year 2000 Model B (albeit without ITN per capita) was most accurate and for 2010 and 2012 the geo-spline provided the best fit (Model C). In addition to the sensitivity analysis (Table A.2.1), the standard deviations (SD) of the mean ITN coverage predictions per district were computed for each year with higher values of the SD indicating greater uncertainty (Figure A.2.1).

Figure A.3.1: standards deviations of mean ITN coverage predictions in Tanzania for the years: a) 2000; b) 2010; and c) 2012

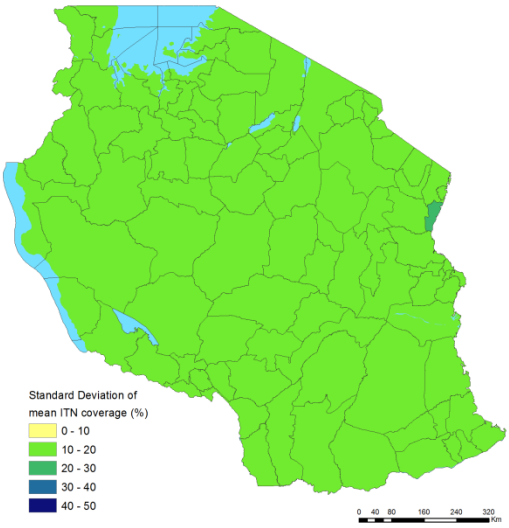
a) 2000



b) 2010



c) 2012



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