Identifying, characterizing, and targeting the reservoir of malaria transmission in Southern Tanzania

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Dekan der

Philosophisch-Naturwissenschaftlichen Fakultät

To my family and friends

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List of abbreviations

1,7-mRCTR	-	1,7- malaria Reactive Community-based Testing and Response
ACT	-	Artemisinin-based combination therapy
aOR	-	Adjusted Odds Ratio
CHCWs	-	Community-based Health Care Workers
CHMT	-	Council Health Management Team
CI	-	Confidence interval
cMTS	-	Community-based mobile test stations
DDT	-	Dichlorodiphenyltrichloroethane
DFID	-	Department for International Development
DHIS	-	District Health Information System
GEE	-	Generalized Estimating Equations
GLMM	-	Generalized linear mixed effect model
GMEP	-	Global Malaria Eradication Program
GTS	-	Global Technical Strategy
HFs	-	Health facilities
HMIS	-	Health Management Information System
IDSR	-	Integrated Disease Surveillance and Response Strategy
IQR	-	Interquartile range
IRS	-	Indoor residual spray
ITN	-	Insecticide-treated net
ITT	-	Ifakara Tent Trap (C type)
LLINs	-	Long-lasting insecticides treated nets
mRDT	-	malaria Rapid Diagnostic Test
NIMR	-	National Institute for Medical Research
NMCP	-	National Malaria Control Programme
OR	-	Odds ratio
PCR	-	Polymerase chain reaction
RBM	-	Roll Back Malaria
SDGs	-	Sustainable Development Goals
SES	-	Socio-economic status
SMMSP	-	Supplementary Malaria Midtem Strategic Plan (2018-2020)
SSA	-	sub-Saharan Africa
UCC	-	Universal Coverage Campaign
UK	-	United Kingdom
WHO	-	World Health Organization
WHO-T3	-	World Health Organization, Test, Treat and Track

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Summary

Malaria continues to be a leading cause of morbidity and mortality in countries where it is endemic. While dramatic progress has been achieved globally, recent global malaria reports suggested that overall global progress has stalled since 2014. The plateau in improvement, particularly in high transmission settings of Africa, is associated with several factors, including inadequate coverage and use of the interventions, poor health service coverage, changes in vectors bionomics and insecticides resistance to malaria vectors. In addition, many high transmission countries have insufficient community based interventions to reduce malaria morbidity and mortality. Barriers to progress are associated with uncoordinated surveillance systems, low socioeconomic and living standards as well as inadequate adherence of the affected population to interventions. This hinders the efforts to achieve the overall goal of malaria elimination in many malaria endemic settings, highlighting the need for overall health system improvement to allow for innovative control and surveillance techniques. Furthermore, it necessitates a better understanding of malaria transmission dynamics. In order to meet this challenge, we must delve deeper into the underlying malaria transmission dynamics.

The proposed PhD project was embedded within a tripartite pilot project between China-United Kingdom-Tanzania. The project was about Malaria control in Rufiji district, Tanzania, that started in September 2015. The overarching goal of the PhD project was to study the dynamics of malaria transmission and evaluate the impact of community-based malaria reactive case detection strategy in strengthening the transmission-reduction of human malaria infections in areas with high coverage of LLINs. To achieve the project's goal, four specific objectives were specified. This matches to the project chapters' conclusions in this thesis.

In Chapter three of this thesis, the effectiveness of implementing a community-based testing and treatment plan to reduce the malaria burden in moderate to high transmission areas is analyzed. The "1-3-7" surveillance and response model developed in China, which prompted the development of this initiative and subsequent adoption of the 1,7-malaria Reactive Community-based Testing and Response (1,7mRCTR) approach, is a novel method for implementing the WHO-T3 and surveillance intervention to eliminate malaria. However, the 1-3-7 model is more effective in China, where the goal is to eradicate the disease, than in Tanzania, where the bulk of the population still has moderate to high transmission.

The 1,7-mRCTR is locally-tailored for reporting malaria cases on day one and intervention on day seven, with community-based testing and treatment in high-burden areas stratified based on weekly data from health facilities. In the same district, control areas with comparable epidemiology (no 1,7-mRCTR) were selected and monitored for the duration of the project. After two years of implementing the 1.7 mRCTR, the prevalence of parasites in the target areas was reduced by 66 percent above and above the benefit provided by national measures already in place. Despite the fact that new technology and techniques may be required to eradicate malaria in stable transmission areas of Sub-Saharan Africa, this experiment proved that a locally tailored approach could help to expedite malaria control and elimination efforts. In addition, it highlight the opportunities of validating the results and possibilities of scaling up 1,7-mRCTR approach in other settings within Tanzania, and other African countries for accelerating malaria control and elimination across Africa.

In chapter four of this dissertation, the household cross-sectional survey data gathered prior to 1,7-mRCTR intervention were used to describe and characterize the malaria prevalence and the associated exposures risk . In the context of the Tanzania Demographic and Health Survey and Malaria Indicator

Survey (TDHS-MIS) 2015-16, this study's findings are discussed. The findings highlight the importance of national malaria monitoring, and its ramifications for present malaria management strategies. The prevalence of malaria varied by ward, ranging from 5.6 percent to 18 percent, with the average prevalence reported by this study (13 percent) being higher than the reported by the RDHS-MIS national (7.3 percent). Based on the findings of this chapter, t is important for the new malaria control plans to be effective in sustaining gains and accelerating progress towards the end goals in the fight against malaria will depend on clearing parasitaemia and ensuring that poverty is eleviated Importantly, programs intended to improve malaria interventions for the currently recognized vulnerable groups should be modified to include other groups observed with highest parasitaemia.

Chapter five investigated and assessed one of the extremely sensitive epidemiological study of malaria transmission (host preference by malaria vectors). In addition to being a significant predictor of malaria transmission patterns, this indicator is essential for determining the appropriateness and efficacy of vector control interventions and for predicting malaria transmission patterns. Using the direct host-preference experiment, the host preference of the primary malaria vector species, *Anopheles arabiensis* and *Anopheles gambiae sensu stricto*, was examined in two distinct ecological contexts in Tanzania. In contrast to historical accounts, the data indicate that urban *An. arabiensis* showed a stronger preference for cattle than rural *An. arabiensis*, but *An. gambiae* showed no preference for either people or animals under the same conditions. To achieve malaria eradication, we must have a deeper understanding of the prevalent vectors, their feeding behavior in varied ecological situations, and their feeding preferences. This will allow us to more effectively design and implement locally-tailored, high-impact, integrated interventions.

Anopheles mosquito species composition, abundance, and spatial-temporal variability must be thoroughly understood in order to optimally exploit high-resolution malaria vector control strategies. Community-based mapping of residual malaria vector densities to support malaria elimination efforts in southeastern Tanzania is discussed in Chapter six. The findings highligth the changing composition of vector species through time, as well as the presence of many malaria vector species at the village scale, which is characterized by a wide spectrum of ecological variation. Human biting rates (HBR) in the study wards ranged from 1.5 to 73 bites per person every night. Characterization of Anopheles vectors indicated disparities between villages and wards in the distribution of *Anopheles gambiae s.l.*, *Anopheles funestus*, and *Anopheles coustani*. This study's findings give evidence-based information that is essential for planning and implementing vector control actions in a local setting, complementing the results of Chapter four. In addition, the findings highlight the significance of comprehending and incorporating vector bionomics data into surveillance and response systems in order to successfully implement the ongoing micro-stratification of malaria strata.

Surveillance is acknowledged as an intervention and considered instrumental in accelerating global malaria elimination efforts. However, all available evidence to date supports the incorporation of surveillance as in intervention in low endemicity areas, with no evidence comes from moderate to high endemicity areas. Therefore, this PhD project is the first attempt to develop a surveillance and response strategy in moderate to high transmission setting. The findings aline the current Tanzania mid-term review of the national malaria control as well as with the goals Global Technical Strategy 2015-2030 (GTS) and the High Burden to High Impact (HBHI) initiative, which both reiterated the importance of tailoring intervention approaches to the sub-national local context in order to accelerate progress toward malaria reduction and elimination. Behaviour ecology matters and so does evolutionary biology in human-modified environment, the spatial-temporal variation findings in

vector composition at a fine scale level of village and the reduced human-biting preference of the primary malaria vectors collected from two distinct characterized with different ecological features is an example illustrating why regular surveys of mosquito compositions and behaviour need to be incorporated in malaria surveillance. Furthermore, support that, in regions with a high malaria incidence, the convention interventions should be maintained, while prioritizing taiolored approach based on the local contex.

Chapter 1: Introduction

1.1 Global malaria burden

Malaria is an infectious disease carried by mosquitoes and transmitted to humans through the bite of infected female Anopheles mosquitoes (Gilles and Warrell 2002). Malaria is most prevalent in the poorest nations of the world. Approximately fifty percent of the world's population lives in a malaria-risk area (Murray et al. 2012, WHO 2019), with a greater burden concentrated in tropical and subtropical countries where environmental circumstances favour the survival of both malaria vectors and parasites (Figure 1.1) (Bhatt et al. 2015, Murray et al. 2012, Sachs and Malaney 2002).

Malaria still ranks amongst the most prevalent tropical infectious diseases by causing high morbidity and mortality worldwide (Bhatt et al. 2015, Murray et al. 2012, WHO 2019). Globally, malaria affected 228 million people and killed 405,000 in 2019. ~ 93% of all malaria cases and deaths are reported in the sub-Saharan Africa (SSA) region. In particular, children under five years contributed 67% of all malaria deaths (WHO 2019). The consequences of malaria impose a direct economic and social negative impact on families and communities, thereby strongly contributing to the vicious cycle of poverty and inequity (Breman et al. 2004, Sachs and Malaney 2002, WHO and UNICEF 2017). In most African countries, preventing and treating malaria is estimated to cost up to one-third of the families' total annual income (Sachs and Malaney 2002, Shretta et al. 2016). Therefore, unless this disease is effectively controlled, attaining most of the world's Sustainable Development Goals (SDGs) remains questionable (Kruk et al. 2018, WHO 2016a).

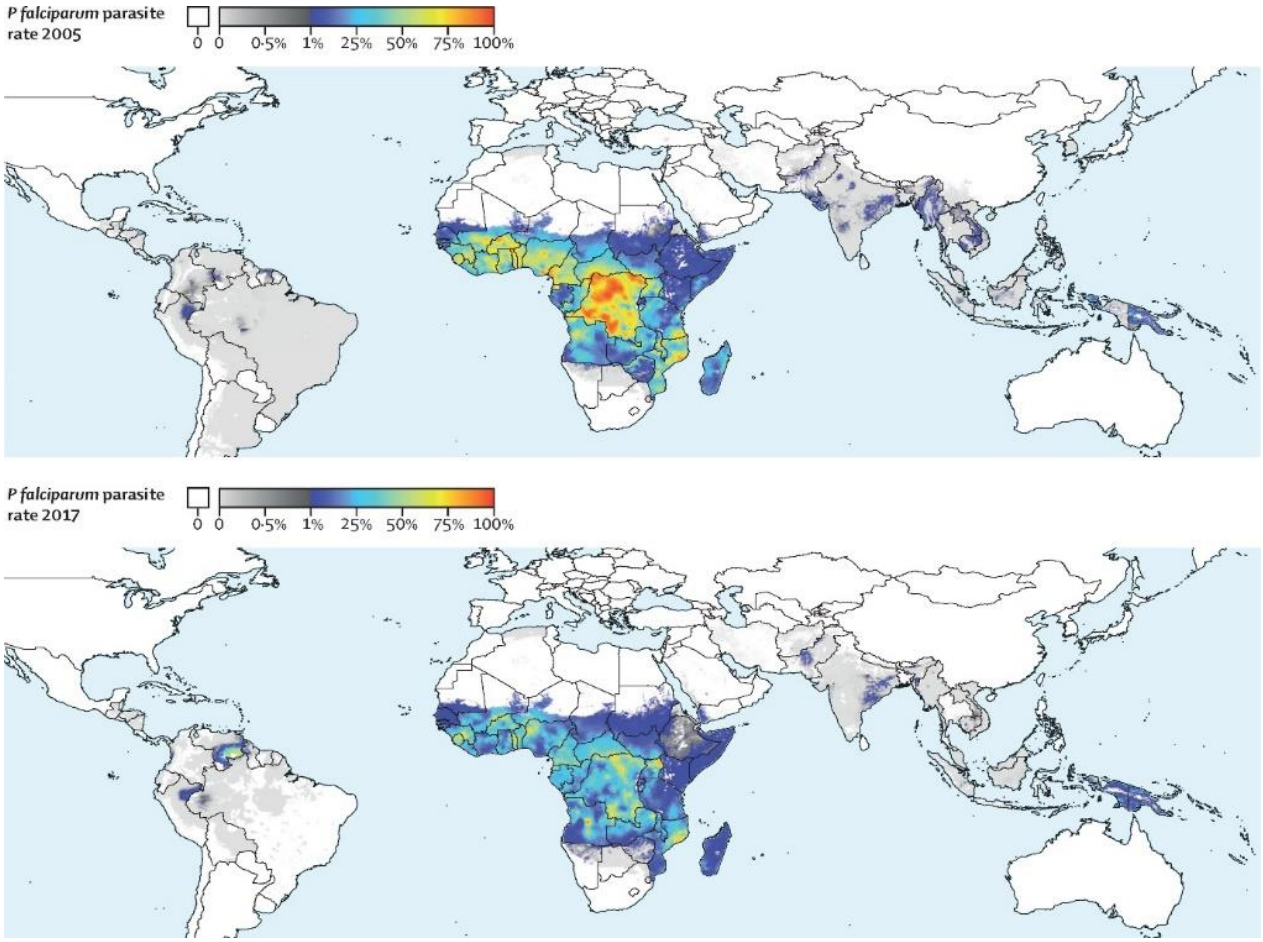


Figure 1.1. The global distribution of the *P. falciparum* parasite. Top and down layers present the disease burden in 2005 and 2017, respectively. Figure adapted from (Weiss et al. 2019).

1.2 Malaria control strategies

Malaria control extends back to the 1930s, when pyrethrum produced from flowers and dichloro-diphenyl-trichloroethane (DDT) discovered in the early 1940s were utilized to target indoor-resting mosquitoes (Livadas 1953, Najera et al. 2011). The extensive use of DDT was highly effective in eradicating malaria by reducing the prevalence of *Plasmodium falciparum* and *Plasmodium vivax*, particularly in the Americas, Europe, and a few Asian regions (Pampana 1969).

1.2.1 Global malaria eradication era

Since the discovery of DDT and chloroquine, malaria control has passed several initiatives that have helped control and eliminate malaria in many countries. In 1955 a Global Malaria Eradication Program (GMEP), a globally coordinated program, was initiated to control malaria. GMEP contributed to a considerable reduction of the malaria burden and permanent elimination in many countries (Livadas 1953, Najera et al. 2011). The indoor residual spray IRS was the primary approach for vector control strategies, targeting the house dwelling mosquitoes and case treatment campaigns. Unfortunately, the program was terminated after 14 years and malaria eradication was not realized in many tropical regions, particularly the SSA (Carter and Mendis 2002). The program ending was much related to insecticides resistance reported in Greece and the financial crisis (Livadas and Georgopoulos 1953). Therefore impeding the ability of the indoor residual spray (IRS) programs to accomplish the GEMP objective, notwithstanding their continued validity (Bruce-Chwatt 1984, Dobson et al. 2000, Najera et al. 2011).

1.2.2 From 2000 to future

As a result of the IRS's inability to stop the transmission, numerous African countries decided to cease the intervention; consequently, the malaria research fund was impacted by the decline in international interest. In response to the increased burden in the Africa content, in 1987, a new initiative strategical focusing on Africa was initiated (Malaria Control Strategy for Africa). Despite implementation and sustainability challenges, the plan was accepted in 1992 as part of the Global Malaria Control Strategy targeting a portion of tropical countries (WHO 1993). The operational strategy focused on case management through a primary health care approach (early detection and treatment). Importantly, advocating the needs of adapting local conditions and decentralizing programs based on disease status instead of parasite control (Bruce-Chwatt 1984, Trigg and Kondrachine 1998).

Following the launch of the Roll Back Malaria (RBM) campaign in 1998, the world of malaria garnered increased attention on both a local and worldwide level. As a result, a new targeted goal of halving the malaria burden by 2010 was established (WHO 1998). Because of this movement, 53 African head of state pledged to make preventions are available and accessible to everyone (WHO 1998). Lessons learned from other campaigns helped RBM to come up with four evidence-based approaches that could aid global malaria control programs. These include (i) vector control strategy (primarily with the recommended insecticide), (ii) prompt treatment with effective antimalarial drugs, (iii) intermittent preventive treatment for the high-risk groups (pregnant mothers, infants, and children), and (iv) the emergence and epidemic preparedness and response (Roll Back Malaria 2005, WHO 1998).

Between 2000 and 2015, malaria control has been possible due to the increased political commitment and funds internationally and by countries. For instance, between 2000 and 2016, the world has witnessed an unprecedented increase in funds from US$ 1.5 to nearly US$ 4.3 billion in malaria control's global resources (Feachem et al. 2019, Tanner et al. 2015a). The renewed efforts to control malaria globally and move towards elimination in some countries are based on the most advanced technologies and effective preventive and therapeutic measures (Feachem et al. 2019, Killeen et al. 2017c, Roll Back Malaria 2005). This has made possible of scaling up of life serving intervention. The core malaria prevention has been long-lasting insecticide nets (LLINs), indoor residual spray (IRS), effective treatment artemisinin-based combination therapy (ACT), and technological advancement of diagnostic tools, especially the rapid diagnostic tests (mRDT) (Bhatt et al. 2015, Choi et al. 2019, Lengeler 2004). Since 2000, we have witnessed 17 countries attaining zero local transmission, and 21 countries are in line to eliminate malaria by 2020 (WHO 2018, WHO 2019).

1.2.3 Challenges with malaria control

While some countries have progressively reduced the malaria burden, a recent global malaria report suggested that the overall global progress has stalled from 2014 onwards (WHO 2015c, WHO 2019). The stall of the progress particularly in the high transmission setting of Africa is associated with several factors, such as inadequate coverage and use of the interventions, poor health service coverage, and vectors bionomics and insecticides resistance to malaria vectors (Govella et al. 2013, Killeen 2020, Sherrard-Smith et al. 2022). In addition, many high transmission countries have inadequate less community-based interventions to reduce malaria morbidity and mortality. The slow progress is also associated with the poor socio-economic, and living standards, and inadequate adherence of the affected population to the interventions (Cohen and Saran 2018). This situation hinders the possibility of achieving malaria elimination's overall goal in many malaria-endemic settings, highlighting the need for innovative control and surveillance techniques.

The ecological and epidemiological transitions in malaria transmission bring us to the critical question of whether the available malaria control strategies will eliminate malaria. There is mounting evidence that existing malaria control tools will not eliminate malaria (Durnez and Coosemans 2013, Tanner et al. 2015a). Historical transitions in malaria control provide a valuable lesson for the future plan to attain the worldwide objective of malaria elimination (Feachem et al. 2019, Roll Back Malaria 2015, WHO 2015a, WHO 2020b). Taking on this problem necessitates a deeper investigation of the underlying malaria transmission dynamics, given the variable intensity and dynamics of malaria transmission.

1.3 The Plasmodium life-cycle

Human malaria is caused by five protozoan parasites of the genus *Plasmodium*: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, *Plasmodium ovale*, and *the Plasmodium knowlesi* (Singh et al. 2004, White et al. 2014). *P. falciparum* causes severe malaria, often fatal, and accounts for 97% of the global burden. *P. falciparum* is the most widespread in Africa (WHO 2019). *P. vivax* causes mild to severe illness with few deaths. In Asia and South America, *P. vivax* is more frequent than in Africa (Schmidt and Robert 2000). The underlying reasons for the rare occurrence of *P. vivax* malaria in Africa are attributable to the low prevalence of Duffy glycoprotein (an inherited trait) in the most African population, which is an essentials agent on the surface of the red blood cells allowing the invasion of the merozoites (Mueller et al. 2009). Figure 1.2 (A, B, C, and D) shows the *Plasmodium* species transmission cycle in humans and mosquitoes (White et al. 2014).

1.3.1 Life cycle in the human host

When an Anopheles mosquito bites a person, sporozoites (an immature *Plasmodium* form) are delivered into the bloodstream (A). The sporozoites pass into the liver (B). Inside the liver, sporozoites become schizonts, which then become merozoites. After entering the bloodstream, merozoites infect red blood cells (RBC). Merozoites undergo asexual reproduction and mature into trophozoites and schizonts. RBCs become infected with Schizont and break, releasing merozoites into the bloodstream (C). The constant discharge of merozoites, re-infecting and killing RBC, as well as rising parasitemia levels, cause chills, fever, and sweating. If left untreated, this cycle in the circulation can lead to a severe form of the disease and death.

1.3.2 Life cycle in the vector

Some merozoites develop into sexual erythrocytic stages, producing male and female gametocytes, which can be ingested by a feeding mosquito (D). The zygote migrates, penetrates the mosquito's midgut wall, and develops into oocysts. The oocytes mature into sporozoites, which travel into the salivary grand to be injected into another individual (Figure 2). It should be note that in *P. vivax* (Gilles and Warrell 2002, Mueller et al. 2009) and *P. ovale* (Gilles and Warrell 2002, Marquardt et al. 2000, Schmidt and Robert 2000), sporozoites infecting the liver might mature into schizonts or dormant hypnozoites, which may remain inactive for long period. No known factor influences whether sporozoites evolve into active bloodstage or hypnozoites liver stage. However, genetic differences in the original injected sporozoites (Coatney 1976, Miller et al. 1994) may cause some schizonts to mature more slowly (Coatney 1976). Reactivation of hypnozoites might take weeks, months, or even years if not eliminated by antimalarial drugs that target this cryptic liver stage (Coatney 1976, Marquardt et al. 2000, Miller et al. 1994). Although female Anopheles mosquito bites are the primary way that malaria transmitted to human (Gilles and Warrell 2002, Greenwood et al. 2005), it can also be transmitted through blood transfusions (Diop et al. 2009, Kitchen and Chiodini 2006) or from a pregnant woman to her unborn child (Ouedraogo et al. 2012, Schwetz and Peel 1934).

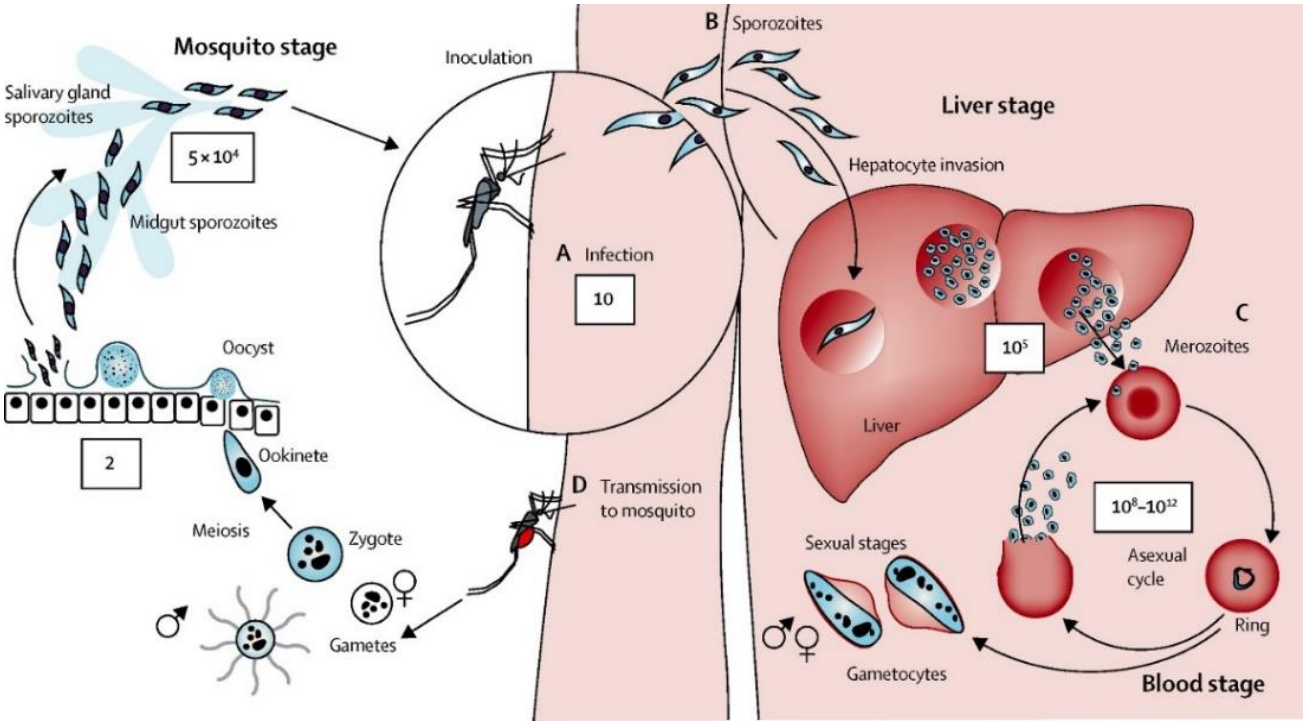


Figure 1.2. *P. falciparu*m life cycle in humans and the mosquito. Figure adapted from (White et al. 2014).

1.4 Malaria burden and transmission in Africa

Malaria is still a major health problem in Africa, and enormous sums of money are being spent on research, prevention, treatment, and control (WHO 2020a). The WHO's African Region continues to bear an excessively large share of the burden associated with malaria in the world. 96% of all malaria deaths and 95% of all malaria cases in 2020 occurred in the Region (WHO 2020b). Approximately 80% of all malaria-related deaths in the Region were attributable to children under the age of five. According to the WHO Malaria Report, slightly more than half of all malaria deaths worldwide were caused by Nigeria (31,9%), the Democratic Republic of the Congo (13,2%), Tanzania (4,1%), and Mozambique (3,8%)(WHO 2020b). With COVID-19 and other humanitarian crises in the background, certain countries with moderate or high transmission had worsening rate stagnation (from 2015), with over 95% of the rise in cases and deaths from 2019 to 2020 being attributed to the WHO African Region.

The ability of the environment to sustain the development of Anopheles mosquitoes and Plasmodium parasites is a significant barrier to malaria transmission control, particularly in Africa. Approximately 50 recognized mosquito species of the Anopheles genus transmit malaria parasites (Gilles 1988). *Anopheles gambiae* complex and *Anopheles funestus* group are the primary vectors responsible for the majority of transmission in most parts of Africa (Gilles 1989, Gillies and De Mellion 1968). *An. gambiae s.s*, member of the *An. gambiae* complex and *An. funestus s.s*, a species are widespread across SSA. These two highly notorious malaria vector species survive relatively longer than other malaria vector species on other continents. They also prefer feeding predominantly on humans, even when other alternative hosts are equally available. These two biological factors are the most sensitive and robust determinants of malaria transmission dynamics (Macdonald 1957, malERA Consultative Group on Modeling 2011, Smith et al. 2012). The prosperity of these vector surviving long and strong affinity feeding on humans represent underlying biological factors that explain why malaria transmission is more in Africa than other continents (Macdonald 1957, Smith et al. 2012, Smith et al. 2014).

In the past 15 years, the population of *An. gambiae* has been drastically reduced to near extinction in various contexts, notably countries in east Africa (Bayoh et al. 2010a, Derua et al. 2012, Killeen 2014) due to the widespread use of LLINs throughout SSA. The *An. gambiae* was highly vulnerable to LLINs, because of their behaviors of feeding mostly on humans and resting indoors, which increased lethal contact with insecticidal treated nets. *An. arabiensis*, its sibling species, has surpassed it in terms of population dominance. Another highly widespread and numerically dominant malaria vector species in various regions of SSA (Bayoh et al. 2014, Derua et al. 2012, Govella and Ferguson 2012a, Killeen et al. 2006, Kitau et al. 2012, Lobo et al. 2015). This species, unlike *An. gambiae*, has versatile host feeding patterns; it can feed equally on people and non-humans, depending on the

availability of hosts (Killeen Gerry F 2014, Killeen et al. 2001, Torr et al. 2008). In contrast to *An. gambiae*, this species has been observed eating early in the evening and outdoors, before most inhabitants are outside (Govella et al. 2013, Killeen et al. 2016, Nkumama et al. 2017, Russell et al. 2011). These present significant challenges in eliminating this species because they avoid fatal contact from indoor-targeted interventions such as LLIN and IRS, the primary malaria vector control.

On the other hand, *An. funestus* feeds on human blood; usually, they tend to rest indoor (endophilic), and hence they have a preference for biting indoor (endophagy) (Gillies and De Mellion 1968). The *An. funestus* possesses a high degree of susceptibility to *P. falciparum* and a high survival rate that allows the parasite to complete its sexual reproduction and development to the infectious stage (Gillies and Coetzee 1987, Gillies and Wilkes 1965, Kaindoa et al. 2017, Mendis et al. 2000, Sougoufara et al. 2014). This behavior (high degree of susceptibility and high survival rate) accounts for the increased capacity of *An. funestus* in malaria transmission in Africa.

1.5 Malaria surveillance and response

The underlying principle of malaria surveillance is to predict malaria trends and bring health information that can put together malaria control interventions based on evidence (Lourenço et al. 2019, WHO 2006, WHO 2012b, WHO 2015a). The surveillance system should always include the timely response package, such as targeted community screening and treatment, reducing the disease burden and mortality or vector control measures to suppress the transmission across settings. As such, surveillance becomes an essential elimination intervention in itself (Kelly et al. 2012, WHO 2012b, WHO 2015a). The success of malaria control has inspired many countries to revise their strategic plans by strengthening malaria surveillance and control to accelerate malaria elimination efforts (Simon et al. 2013, Tanner et al. 2015b, Zhou et al. 2013).

Like other sub-Saharan African countries that have made progress in malaria reduction, the nature of transmission in Tanzania appears to be highly spatially heterogeneous at the sub-national level (Chacky et al. 2018, Runge et al. 2020, Thawer et al. 2020). When considering the presence of heterogenous transmission, the goal of malaria elimination, and limited operational resources, interventions would ideally and preferentially target higher burden areas to further reduce transmission towards optimizing allocation of resources (Carter et al. 2000, Raman et al. 2016). Spatial heterogeneity of malaria incidence requires more focused, locally tailored strategies (Loha et al. 2012). Complementing a targeted approach, community-based malaria reactive approaches using reactive case detection (RCD) with MSAT (Kern et al. 2011, Silumbe et al. 2020, Silumbe et al. 2015) or targeted MSAT (t-MDA) (Conner et al. 2020, Landier et al. 2018) strategies also enable the tailoring of response to local requirements thereby offering the opportunity to complement current interventions to both treat malaria cases, reduce the parasite reservoir and suppress onward transmission. Seasonal malaria chemoprevention (SMC), a form of t-MDA aims to prevent malaria in children (usually under the age of 5) during the high malaria transmission season (Baba et al. 2020). However, supporting research on the effectiveness and operational feasibility of the various forms of community-based reactive focal strategies is required.

In response to the current situation and fast-tracking malaria elimination goal, in 2015, WHO released the Global Technical Strategy (GTS) as operational guidance on how effective strategies and activities be implemented to accelerate malaria elimination efforts (WHO 2015a). The strategy outlines the operational guidance for transforming malaria surveillance into a core intervention. The GTS strategy of taking surveillance as a core intervention strengthens the WHO's Test-Treat-Track (WHO-T3) initiative for malaria surveillance and the response (WHO 2012c). The GTS urges countries to stratify areas according to the disease transmissions' burden and conduct epidemiological

characterization of the risk, a shift from a one-size-fits-all approach to a data driven, surveillance based, targeted response. The malaria burden micro-stratification allows for local tailoring of interventions to respective strata to the lowest possible level closer to the community. This reflects the goals and strategy of the High Burden to High Impact (HBHI) initiative (WHO 2018) to reignite the pace of progress in the global malaria fight.

1.6 Tanzania malaria epidemiology and its diversity

Tanzania is the largest country in East Africa, covering 885,800 square kilometers. Tanzania is one of the eleven countries responsible for 70% globally malaria burden (WHO 2018, WHO 2019). *P. falciparum* is responsible for 96% of malaria infections in Tanzania, with *P. malariae* and *P. ovale* accounting for the remaining 4% (Yman et al. 2019). The malaria parasites prevalence has decreased by 50 percent over the past decade as a result of a combination of preventative and therapeutic strategies (Chacky et al. 2018). Malaria prevalence decreased from an average of 18.1% in 2008 to 6.3% in 2017, according to the most recent malaria indicator surveys (Chacky et al. 2018, National Bureau of Statistics (NBS) 2018). In addition, the proportion of Tanzania's population residing in areas of intense transmission decreased from 11.6% in 2000 to 2.3% in 2010(Ministry of Health and Social Welfare 2014). Despite overall reductions observed, malaria remains the major cause of death and morbidity across all age groups in Tanzania.

1.6.1 Malaria control strategies

Malaria control in Tanzania (formely Tanganyika) dates back to the 1870s, with infected persons receiving quinine and non-immune populations receiving prophylaxis(Gilles and Warrell 2002). The control of adult mosquitoes with insecticides such as DDT and/or dieldrin for indoor spraying was combined with the distribution of quinine for mass therapy. The initiatives were ultimately followed

by the removal of all larval habitats by means of larviciding, riverbank cutting, puddle oiling, streambed straightening, and other control measures.

After the World War I, the British government adopted Tanganyika as one of its colonies and and directed the Royal Army Medical Corps to continue the German government's malaria control efforts. It enhanced surveillance and enacted a rule requiring animals to be kept away from streams and marshes to prevent the creation of hoof prints that could serve as breeding grounds for more mosquitoes (De Castro et al. 2004). After independence in 1961, the program was maintained, but it was terminated in 1972 due to the terrible economic condition and poorly planned decentralizations, which resulted in inadequate or nonexistent drain maintenance (Kilama 1994). Efforts to improve environmental management and community health education throughout the 1960s led to considerable reductions in Anopheles and Culex mosquito larvae and malaria transmission (Kilama 1994). Prior to the RBM era in 2000, the ITN was promoted through social marketing in several locations throughout Tanzania. Other methods included rapid treatment with chloroquine and malaria detection using a blood slide stained with Giemsa.

In 2001 the Ministry of Health and Social Welfare (MoHSW) chose to re-formulate its malaria control strategies (National Malaria Medium Term Strategic Plan, (2002–2007) with the goal of using the integrated malaria intervention. These include vector control using ITN, case management using sulfadoxine-pyrimethamine (SP), drug resistance monitoring, and intermittent malaria treatment in pregnant women. The overarching goal was to reduce malaria morbidity by 25% by 2007 and by 50% by 2010 (Ministry of Health 2002). The goal, however, could not be achieved. Deaths caused by malaria-related increased from 34.3 percent in 2003 to 37.3 percent in 2004. Less efficacious antimalarial drugs, insufficient diagnostic tools, reliance on clinical judgment, and delayed health-

seeking were all contributors to the failure (Mboera et al. 2007). Malaria control has evolved since 2007, as depicted in Figure 1.3, into a variety of intervention approaches and additional malaria control strategies. Tanzania's malaria control achievement has been mostly related to the intense scale-up of vector control measures, particularly ITNs (National Malaria Control Programme (NMCP) 2012) among all the interventions in place. Typically, mass LLIN distribution efforts occur every four years.

In 2017, at least 78% of Tanzanian households possessed a single-bed net, and 52% utilized ITNs every night (National Bureau of Statistics (NBS) 2018). The under-five keep up campaign (U5CC) incorporated in the antenatal clinic program. Recent implementation of the School Net Program (SNP) in a few highly endemic districts of southern Tanzania has also increased the availability of LLINs throughout the country (Lalji et al. 2016, Yukich et al. 2020). In addition, the IRS protects over five million people who reside in highly endemic regions of the northwestern (Tanzania Commission for AIDS 2013). The use of larviciding to control mosquitoes while they are in their larvae stage is proposed to be implemented at the district level as a supplementary vector control tool . The NMCP’s current strategic plan is to reduce parasite prevalence to one percent by 2020, which is currently unattainable.

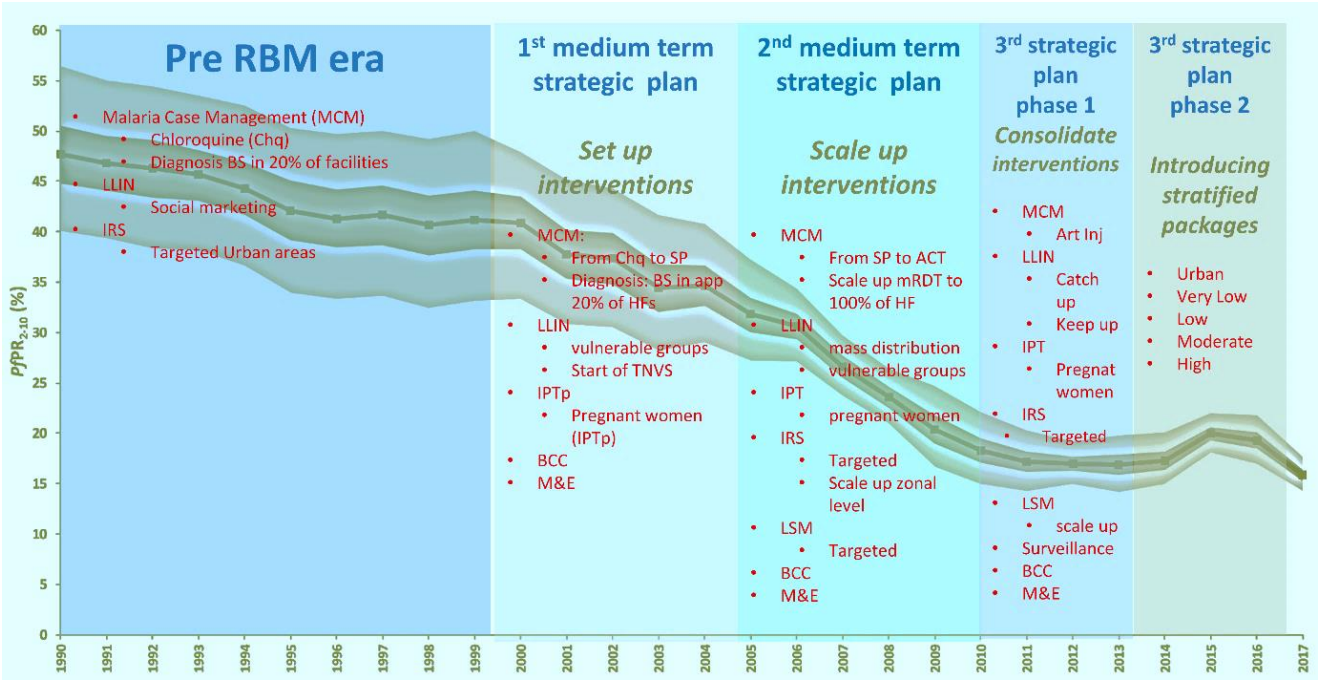


Figure 1.3. Timeline depicting malaria and control strategies in Tanzania (1990-2017) (Source: NMCP 2020).

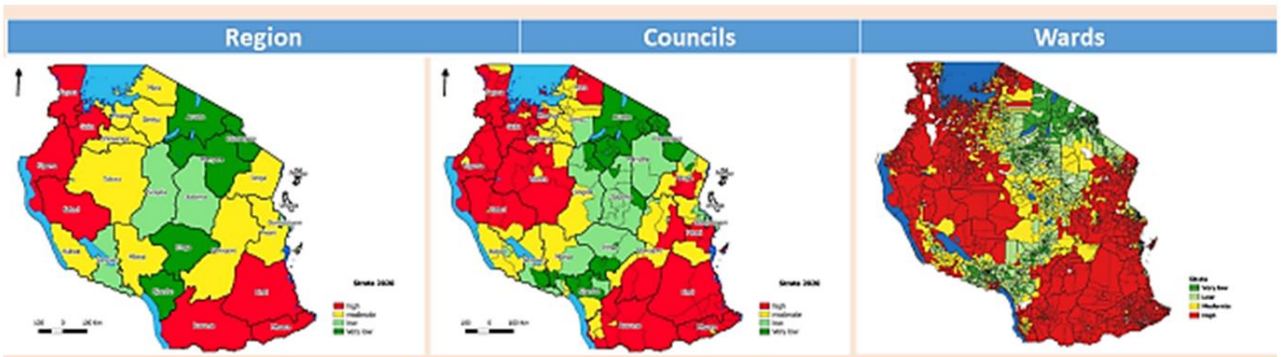
1.6.2 Malaria heterogeneity

Malaria transmission declines in Tanzania have not been observed everywhere and resulting in an interesting malaria epidemiological diversity. Malaria transmission is persistently intense in the Lake Zone (upper northwest) and coastal belt (east and south), with prevalence ranging from 20 to more than 40 percent. The Central Plateau of the country experiences seasonal malaria transmission, with prevalence between 5% and 20%. The Southern and Northern Highlands have a pattern of low or seasonal transmission (less than three months per year) and a prevalence of less than 5 percent (National Malaria Control Programme 2018, National Malaria Control Programme et al. 2013). The underlying drivers for these regional variations remain unclear.

Due to the diversity that has been reported to exist at the level of the household and the individual, it is necessary to expand beyond the sub-national level stratification by investigating the underlying dynamics of malaria risk factors at a high resolution in order to enhance evidence-based decision making and resource allocation for more effective malaria control strategies based on the established

guidelines. Ideally, adjusting local settings' intervention choices would directly benefit malarious communities by prioritizing locally targeted active case detection and treatment, mass drug administration, or additional vector control management and control measures to enhance malaria control programs (Bejon et al. 2010, Bousema et al. 2012).

In response to this, the NMCP has implemented the stratification control strategic plan outlined in the Supplementary Malaria Strategic Plan (SMSP) 2018-2020 (National Malaria Control Programme 2018). This plan aims to establish a concept of malaria risk stratification which will enable allocating interventions package tailored to the local context in order to accelerate elimination efforts by 2020. The SMSP has been fully embraced by the National Malaria Strategic Plan (NMSP) 2021-2025, which provides the road map for the national malaria technical guideline. The NMCP has divided the country into four transmission strata, the fifth one as urban for operation purposely. As indicated in Figure 1, the four strata are as follows: very low (parasite prevalence less than 1 percent), low (parasite prevalence between 1 and 5 percent), moderate (5 to 30 percent), and high (more than 30 percent). With this approach, a potentially highly cost-effective and high impact strategy could be selected and implemented. These plan aligh with the GTS (WHO 2015a), the Sustainable Development Goal (SDG) (WHO 2015b), and the HBHI (WHO 2018) with regard to the global goal of fighting against malaria.



Stratum	Region		Councils	
	Epi strata	Epi + non epi strata	Epi strata	Epi + non epi strata
Very Low	5	5	36	31
Low	4	3	32	22
Moderate	10	10	52	45
High	7	7	64	61
Urban	NA	1	NA	25

Figure 1.4. Stratification of Tanzania malaria burden at the regional, council, and ward level, Figure adopted from SMMSP.

1.6.3 Malaria vector surveillance

Due to the high scale-up of vector control, the historically dominant and highly efficient malaria vector *An. gambiae s.s.* has been virtually eliminated across many countries (Derua et al. 2012, Lwetoijera et al. 2014), leaving its sibling species *An. arabiensis* currently as numerically dominant vectors (Derua et al. 2012, Lwetoijera et al. 2014). The widespread use of LLINs, have strongly impacted the population of *An gambiae s.s.*, because this vector species feed preferentially indoor and late part of a night, behaviors that have made them highly vulnerable to contact with insecticides treated nets or surfaces. Unlike *An. gambiae s.s*, *An. arabiensis* exhibits flexible feeding behavior by feeding early in the evening, outdoors, and non-human hosts when they are available (Govella et al. 2010, Kreppel et al. 2020, Mayagaya et al. 2015). These behaviors allow them to evade fatal contact from LLINs and therefore contribute to sustaining their populations.

An. funestus, although it exists in a very low number across settings in the country, it remains the primary vector species driving most of the human malaria infection in the country. It is estimated to account for about 80% of all ongoing malaria transmission (Kaindoa et al. 2017, Kaindoa et al. 2019, Mboera et al. 2015). Despite commonly known to prefer feeding indoors and on humans, recent evidence from southern Tanzania, these species suggest reduced feeding preference on humans (Meza et al. 2019) relative to historical records (Kitau et al. 2012). Together with their high resistance to the most widely used insecticides (Hemingway 2018, Killeen and Ranson 2018, Kisinza et al. 2017, Namountougou et al. 2019), this behavior might have enabled *An. funestus* to remain prevalent, unlike *An. gambiae s.s*.

As a result, investigations are needed to highlight the variability of vector populations, their feeding and biting preferences, and the possible impact of species composition on malaria transmission (Govella et al. 2013, Killeen et al. 2018, Killeen et al. 2017b). Furthermore, due to existing variety in host preference within and between species, it is vital to evaluate and understand the host preference demonstrated by vector species across diverse ecosystem situations for practical decision and assessment of the efficacy of interventions. These measurements should be incorporated into entomological monitoring in order to enable spatial tailoring of complementing intervention in response to the local context in order to accelerate malaria elimination efforts (Bridges et al. 2012, Govella and Ferguson 2012b, Tanner et al. 2015b).

1.6.4 Facility-based systems for measuring and mapping malaria transmission

Most of the standard measures for monitoring and mapping malaria transmission that have been used by, not only research projects, but also national monitoring and evaluation program, have relied on well-defined demographic and spatial samples of relevant human populations (Bousema et al. 2010,

Hay et al. 2008, Tusting et al. 2014). A common practice in most malaria endemic countries is the aggregation of individual malaria positive cases by geography during routine passive testing and treatment. This blurs the actual burden of malaria cases at sub-national and sub-district levels eliminating the opportunity to tailor and target responses, and allocate resources optimally. While the uncontrolled, passive population samples obtained through centralized facility-based case reporting is a great strength in terms of absolute sensitivity, it also represents the greatest challenge to their wide-scale use for mapping malaria transmission so that residual foci of persistent transmission can be identified and targeted with supplementary interventions. While temporal variations in transmission are captured and seasonality patterns clearly differ from one location to another, the most important feature of such systems which needs development and validation is the ability to map malaria transmission back to source from a central reporting location. In its current form, each case or prevalence estimate is only attributable to a single central reporting point within a much larger and poorly defined catchment area (Rumisha et al. 2007). The underlying challenge to tracking malaria transmission back to where it occurred is that the catchment areas of health facilities are distributed unpredictably across fine-scale geographic subunits with undefined reporting rates which are difficult to characterize or predict (Alegana et al. 2012, Sturrock et al. 2014). However, prevalence rates among attendees of such facilities are relatively robust to such reporting rate variations because they are captured in both the nominator and the denominator. It is therefore possible to map such facility-reported prevalence rates across the surrounding catchment area if the geographic point of origin of the patients can be determined at the contact point in the facility (Mlacha et al. 2017, Stresman et al. 2014).

Chapter 2: Rationale of the study and General Objective

2.1 Rationale of the study

Within the overall aim of the collaborative malaria control project between China-UK and Tanzania. The present PhD project analyzed the data collected from the pilot project to assess the effectiveness of the collaboration between China, the United Kingdom, and Tanzania (Wang et al. 2019).

The main objectives of the China-UK-Tanzania tripartite pilot project were (i) to reduce the malaria burden by 30% in 2018 compared to that of 2015; (ii) to strengthen the capacity of malaria control at the local level; and (iii) to explore the appropriate model and mechanism to develop scalable antimalarial programs for Tanzania by the implementation of Chinese experiences in combination with WHO-T3 strategy in the pilot areas. The pilot project was conducted in Rufiji district, Coast region (famous as Pwani, in Swahili), in southern Tanzania Figure 2.1. The critical issue to be solved was developing a stratified prevention and control strategy adapted to local malaria prevalence features; and (ii) adjusting the strategy by integrating locally available resources. The local resources included a platform of health system infrastructures, human resources, funds, and supplies that existed to provide the intervention base. The 'project's intervention package involved applying a modified Chinese "1-3-7" (Cao et al. 2014b, Zhou et al. 2015c) model for malaria surveillance and response combined with the WHO-T3 Initiative and the local resources.

This PhD project was designed to answer important research questions related to the surveillance and response strategy, the impact of community-based targeted intervention, and the malaria vector composition variation to guide targeted intervention. Furthermore, we utilized the previously collected data on assessing the host preference of malaria vectors to highlight how feeding preference affects the ongoing vector control interventions. In the meantime, combination of such data collection

has not been used to guide malaria control efforts in the country. The PhD project's finding contributes to the understanding of malaria epidemiology in Tanzania to the ongoing malaria control strategies, as highlighted in the SMMSP plan (2018-2020). Importantly, improving our understanding of malaria transmission dynamics at a fine-scale of village settings.

2.2 Main objective

The PhD overall objective was to assess the dynamics of malaria transmission and evaluate the impact of community-based malaria reactive case detection strategy in strengthening the transmission-reduction of human malaria infections in areas with high coverage of LLINs.

2.3 Specific Objectives

1. Determine the malaria parasite prevalence and associated risk of exposures to inform targeted malaria control strategies.
2. Determine the impact of a community-based malaria reactive case detection (1,7-mRCTR) strategy in reducing human malaria infections.
3. Assess the host preferences of An. arabiensis and An. gambiae sensu stricto, using direct host-preference assays in two distinct ecological settings in Tanzania
4. Assess the association between malaria vector densities and human malaria infection prevalence across various district epidemiological clusters to identify high-risk areas.

Chapter 3: Effectiveness of the innovative 1,7-malaria reactive community-based testing and response (1, 7-mRCTR) approach on malaria burden reduction in Southeastern Tanzania

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3.1 Abstract

Background: In 2015, a China-UK-Tanzania tripartite pilot project was implemented in southeastern Tanzania to explore a new model for reducing malaria burden and possibly scaling-out the approach into other malaria-endemic countries. The 1,7-malaria Reactive Community-based Testing and Response (1,7-mRCTR) which is a locally-tailored approach for reporting febrile malaria cases in endemic villages was developed to stop transmission and *Plasmodium* life-cycle. The (1,7-mRCTR) utilizes existing health facility data and locally trained community health workers to conduct community-level testing and treatment.

Methods: The pilot project was implemented from September 2015 to June 2018 in Rufiji District, southern Tanzania. The study took place in four wards, two with low incidence and two with a higher incidence. One ward of each type was selected for each of the control and intervention arms. The control wards implemented the existing Ministry of Health programmes. The 1,7-mRCTR activities implemented in the intervention arm included community testing and treatment of malaria infection. Malaria case-to-suspect ratios at health facilities (HF) were aggregated by villages, weekly to identify the village with the highest ratio. Community-based mobile test stations (cMTS) were used for conducting mass testing and treatment. Baseline (pre) and endline (post) household surveys were done in the control and intervention wards to assess the change in malaria prevalence measured by the interaction term of 'time' (post vs pre) and arm in a logistic model. A secondary analysis also studied the malaria incidence reported at the HFs during the intervention.

Results: Overall the 85 rounds of 1,7-mRCTR conducted in the intervention wards significantly reduced the odds of malaria infection by 66% (adjusted OR 0.34, 95% CI 0.26,0.44, $p < 0001$) beyond the effect of the standard programmes. Malaria prevalence in the intervention wards declined by 81%

(from 26% (95% CI 23.7, 7.8), at baseline to 4.9% (95% CI 4.0, 5.9) at endline). In villages receiving the 1,7-mRCTR, the short-term case ratio decreased by over 15.7% (95% CI − 33, 6) compared to baseline.

Conclusion: The 1,7-mRCTR approach significantly reduced the malaria burden in the areas of high transmission in rural southern Tanzania. This locally tailored approach could accelerate malaria control and elimination efforts. The results provide the impetus for further evaluation of the effectiveness and scaling up of this approach in other high malaria burden countries in Africa, including Tanzania.

Keywords: Malaria, 1,7-mRCTR approach, Community-based, Testing, Treatment, Response, Health facilities, Control, Intervention

3.2 Background

In recent decades, there has been a substantial increase in financial and political commitment supporting the fight against malaria. Specifically, investments have gone into the scaling-up of vector control tools such as long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS) (Alonso and Tanner 2013, Feachem et al. 2019, Feachem et al. 2010, Murray et al. 2012, Walker et al. 2016, WHO 2019). Additionally, significant improvements have been made in case management by the introduction of artemisinin-based combination therapy (ACT) (Bhattarai et al. 2007, Steketee and Campbell 2010). Such interventions have produced a massive reduction in the malaria burden and prevented several million deaths worldwide (Bhatt et al. 2015, Bhattarai et al. 2007, WHO 2019). Globally, it is estimated that 228 million malaria cases were reported in 2018, with Africa bearing the brunt of this burden (WHO 2019). Over the last two decades, malaria control programs in Tanzania have become larger and more widespread, with a national scale-up of preventive strategies and improved quality and access to testing and treatment (Bhattarai et al. 2007, Ministry of Health and Social Welfare 2014, National Malaria Control Programme et al. 2013). As a result, the prevalence has declined from an average of 18.1% in 2008 to 7.3% in 2017 (Ministry of Health 2007, Ministry of Health Community Development Gender Elderly and Children (MoHCDGEC) [Tanzania-Mainland] et al. 2017). Despite these notable achievements, the fight is far from over. More than 93% of the Tanzanian population remains at risk of malaria (Ministry of Health and Social Welfare 2014, Ministry of Health Community Development Gender Elderly and Children (MoHCDGEC) [Tanzania-Mainland] et al. 2017). Sustaining the gains and making progress towards elimination remain the main challenges owing to financial gaps to ensure universal coverage, access to health services, and epidemiological challenges.

To guide malaria elimination, the World Health Organization (WHO) has released the Global Technical Strategy for Malaria 2016–2030, which emphasizes the importance of transforming the malaria surveillance response strategy into a core intervention (WHO 2015a). The national malaria control programme (NMCP) is advocated to take into account the epidemiology and diversity of malaria in each country using malaria burden stratification, and tailoring interventions to the local context (malEra Consultative Group on Monitoring Evaluation Surveillance 2011, WHO 2015a). Likewise, WHO's Test-Treat-Track (T3) (WHO 2012c) initiative for malaria surveillance and the response has been in place to guide the goals of universal coverage of preventive tools and eliminate malaria deaths and eradicate the disease. In China, professionals have developed the ′1-3-7′ approach (Zhang et al. 2018, Zhou et al. 2015b). In this surveillance system, confirmed cases must be reported within one (1) day, origin (imported or domestic) investigated within three (3) days, and appropriate intervention to reduce the chance of onward transmission must be done within seven (7) days. This highly personnel-intensive approach has been used in China's national malaria elimination programme (Cao et al. 2014a), with the effect of near-elimination of domestic cases (Feng et al. 2018, WHO 2019). Several studies have shown that targeted interventions could hasten malaria elimination (Bousema et al. 2012, Landier et al. 2016, Landier et al. 2018, Sturrock et al. 2013a, Sturrock et al. 2013b). However, the question remains open regarding what intervention optimization strategies are applicable and what would be the best model to introduce intervention in higher- transmission settings.

In Tanzania, a review of the most recent population-based malaria indicator survey and health facility (HFs) information has shown the high heterogeneity of malaria endemicity within regions across the country (Chacky et al. 2018, Ministry of Health and Social Welfare 2014, National Malaria Control Programme 2018, National Malaria Control Programme (NMCP) 2012, Runge et al. 2020),

underscoring the need to deploy appropriate interventions carefully. New approaches for malaria control are needed to sustain and accelerate progress towards elimination, and synthesis of the WHO-T3 initiative and the Chinese experience of surveillance and response offers a great opportunity for the identification of new approaches.

The main objectives of the China-UK-Tanzania tripartite pilot project were: (i) to reduce the malaria burden by 30% in 2018 compared to that of 2015; (ii) to strengthen the capacity of malaria control at the local level; and, (iii) to explore the appropriate model and mechanism to develop scalable anti-malarial programmes for Tanzania and other African countries. Taking the cues from China's domestic success and the WHO-T3 initiative, the Chinese and Tanzanian teams jointly developed a new approach for malaria surveillance and response. The 1,7-malaria reactive community-based testing and response (1,7-mRCTR) approach operates at the village level. It entails reporting of any confirmed malaria cases at the HFs within 24 h combined with a follow-up the next week consisting of focal treatment of holo-endemic villages to stop transmission at the same phase of the Plasmodium life-cycle. This targeted approach aligns with the WHO's high-impact initiative for countries with moderate and high transmission (WHO 2018), tailoring the Chinese experiences and the WHO-T3 initiative into the local settings of Tanzania. The overriding objective of this particular paper is to establish the effectiveness of the 1,7-mRCTR approach by observing changes in community-level malaria prevalence, by comparing changes from baseline to endline surveys within and between study areas, in areas where the burden of malaria infection is high. As a secondary objective, the changes in malaria incidence reported at the health facilities after interventions in the villages were also studied.

3.3 Methods

Study design and setting

The study area was the Rufiji District, located in southeastern Tanzania, which has been described previously (Khatib et al. 2018, Wang et al. 2019). A pilot project was implemented from September 2015 to June 2018. Two control wards (Bungu and Kibiti) and two intervention wards (Chumbi and Ikwiriri) were selected. Based on the malaria incidence rates recorded the preceding year by staff at the local HFs, each arm contained one high-transmission and one low transmission-ward. In this study, malaria incidence $< 20/1000$ cases and $\geq 20/1000$ cases were considered as low and high transmission wards, respectively. Since these wards (except Chumbi) had been part of the previous Health and Demographic Surveillance System site (HDSS), they were considered well prepared for testing and treatment evaluation of the proposed model under programme conditions (Habicht et al. 1999). The two control wards received no interventions beyond what was provided by the NMCP, primarily LLINs. Fourteen facilities were located in the control wards, eight in Bungu and six in Kibiti, but only one per ward was a proper health centre, the others being dispensaries. The intervention wards contained 11 HFs covering 18 villages, again with one proper health centre per ward, and the rest being dispensaries. Nearly 89% of the people in Rufiji live within 5 km of an HF (Shabani et al. 2010). Since the approximate distance between the centres of Ikwiriri (intervention ward) and Kibiti (control ward) was 30 km, it is unlikely that people from the control wards attended the screenings in the intervention wards. Based on the census of 2012, the total populations of the intervention and control wards in 2012 were 72,163 and 53,292, respectively (National Bureau of Statistics (NBS) 2013). The average household size in Rufiji was 4.4, and 45% of the total population was under 15 years of age (National Bureau of Statistics (NBS) 2013). Figure 3.1 shows a map of the study area with the location of the pilot project wards.

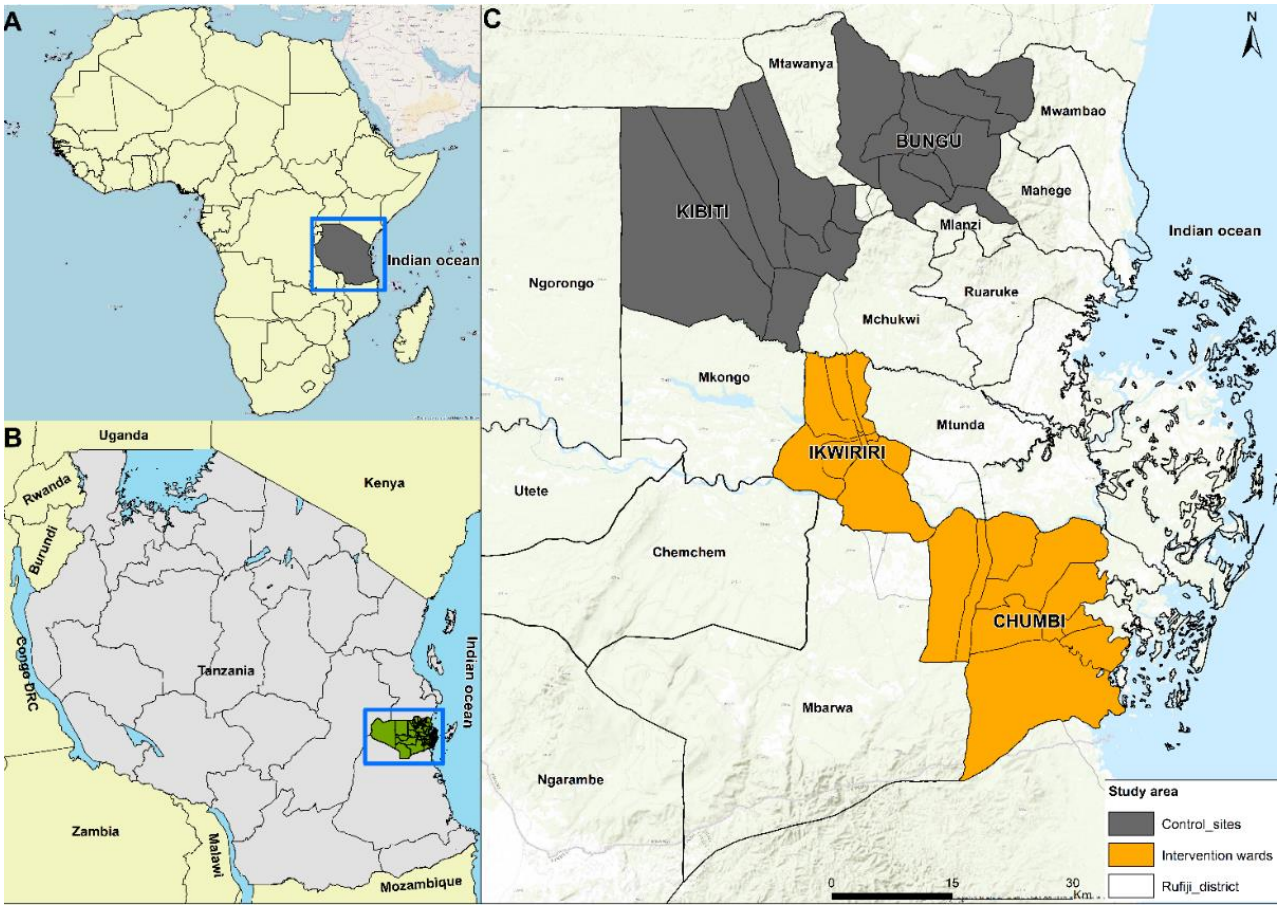

Figure 3.1. Location of the study area in, Rufiji district, Tanzania. [A] Overview map of Africa showing Tanzania location, [B] overview location of Rufiji District in Tanzania, [C] overview map of Rufiji district indicating the intervention (Ikwiriri and Chumbi) and control wards (Bungu and Kibiti). Base Map was obtained from OpenStreetMap through the ArcGIS plugin.

Intervention

Implementation of the project started with workshops and kick-off meetings held by expert teams from both implementing partner countries in China to share and exchange knowledge on malaria control and experiences from the two countries, which also involved field visits to both Tanzania and China. The visit involved consultations with central and local government authorities for an understanding of health system issues related to the provision of malaria services and identification of project sites. Subsequently, technical review of the Tanzanian health information systems and health facility-based malaria service provision both revealed huge variations in terms of the data

structure (individual versus aggregated case reporting), timeliness and completeness of the information, the precision of the information in terms of mapping the precise location of the malaria cases to allow for finer micro stratification down to the sub-district level for targeting the intervention and to top it all the variation in malaria burden. While 1-3-7 is best suited for very low transmission areas with a relatively very low number of cases, the pilot project was to be implemented in a moderate transmission site with a huge burden of malaria, hence the decision to adopt the 1,7-mRCTR approach.

The locally tailored 1,7-mRCTR surveillance and response approach was the main intervention in the intervention communities, in addition to the existing malaria control prevention implemented by the Ministry of Health through NMCP. While the package of this project was deployed the intervention arm only, the existed health intervention by the government through the ministry of health continued equally in both arms. LLINs are the main malaria vector control in the district. In May 2016, LLINs were distributed in the district through Universal Coverage Campaign (UCC). Besides community screening and treatment, the 1,7-mRCTR approach included quality control supervision of case detecting capability through increasing parasitological examination rate of all suspected malaria cases at the corresponding community-level.

All village members through community health education campaigns were advised to seek treatment at a health facility for any febrile illness. Furthermore, information, education, and communication (IEC) materials were developed purposely with local-tailored key messages for the targeted community.

Within both the intervention and control wards, data quality assurance and malaria service availability

and provision surveys were regularly conducted by the NMCP and Council Health Management Team (CHMT) as an integral part of their mandate and responsibility. The project team had special emphasis on the intervention sites and communicated any deficiencies observed to either the CHMT or NMCP for correction. On a random day of the week, the quality control team conducted a spot check survey at HFs to cross-check the quality, accuracy, and consistency of data and status of malaria supplies (diagnostics and antimalarials). These spot check visits were envisaged to increase the ensure compliance of the service providers to the standard operating procedures for malaria service provision at HFs as well as validate the quality of the data being submitted and used for decision making.

Weekly, all malaria suspects presenting to local HFs were tested for malaria by RDT or microscopy, were allocated to the villages of patient(s) residence. The response was mounted in the village with the highest ratio of the number of confirmed malaria positive cases/the number of suspects. There was no specified cut-off. The highest village specific malaria incidence ratio varied with time. Monday-Friday of the following week teams of community-based health care workers (CHCWs) set up community-based mobile test stations (cMTS) in different hamlets (sub-villages) of the 'hot spot' village, starting with those presumed to have the highest case ratio, but moving around to ensure the village-wide coverage of community members. The detailed activities for the 1,7-mRCTR implementation are provided in the Additional file 1 and study protocol which has been published elsewhere (Wang et al. 2019).

Implementation

Before the study began, formal meetings were held between the researchers, the District Medical Officer's (DMO's) office, the CHMT staff, and local community leaders to discuss the study objectives, procedures, and timelines. Accompanying printed materials in Swahili were distributed at

this meeting to provide complementary project information. To maximize project acceptance after a village had been identified as a hotspot, weekly social mobilizations were initiated, i.e., the field supervisor and village community leaders held meetings to discuss the logistics and cMTS locations. Upon deciding on the locations, village leaders and CHCWs informed the rest of community members about the presence of the cMTS, emphasizing that testing and treatment were free. Although only the hotspot villages were targeted, people from neighbouring villages within the intervention sites, who came for testing were also tested and treated. When a village re-appeared as a hotspot, test station locations were chosen using information based on the previous time (s) of response.

Village members above 6 months of age were invited to be screened for malaria. On the day of screening, the participant's informed consent was taken and registered. Finger-prick blood was collected from participants and used for both RDTs (CareStartTM Malaria Pf/PAN (HRP2/pLDH) Ag Combo RDT) and blood slides to test malaria parasitaemia. For prompt treatment, only RDTs results were used, and, if positive, treated with dihydroartemisinin-piperaquine (D-ARTEPP) following the national policy guidelines for malaria treatment (Ministry of Health and Social Welfare 2006). The blood slides were used for quality control, and to determine the malaria species (Khatib et al. 2018). In case of complications or severe cases, the participants were referred to the nearby health facilities. The participants' demographic information, travel history for the previous two weeks, medical histories such as medications taken, and vital signs were also recorded. Due to security problems in the study area, the activities stopped for 8 months from January to August 2017 and resumed from September 2017 to April 2018. Figure 3.2 illustrates the schematic diagram of the 1,7-mRCTR implementation in the intervention area.

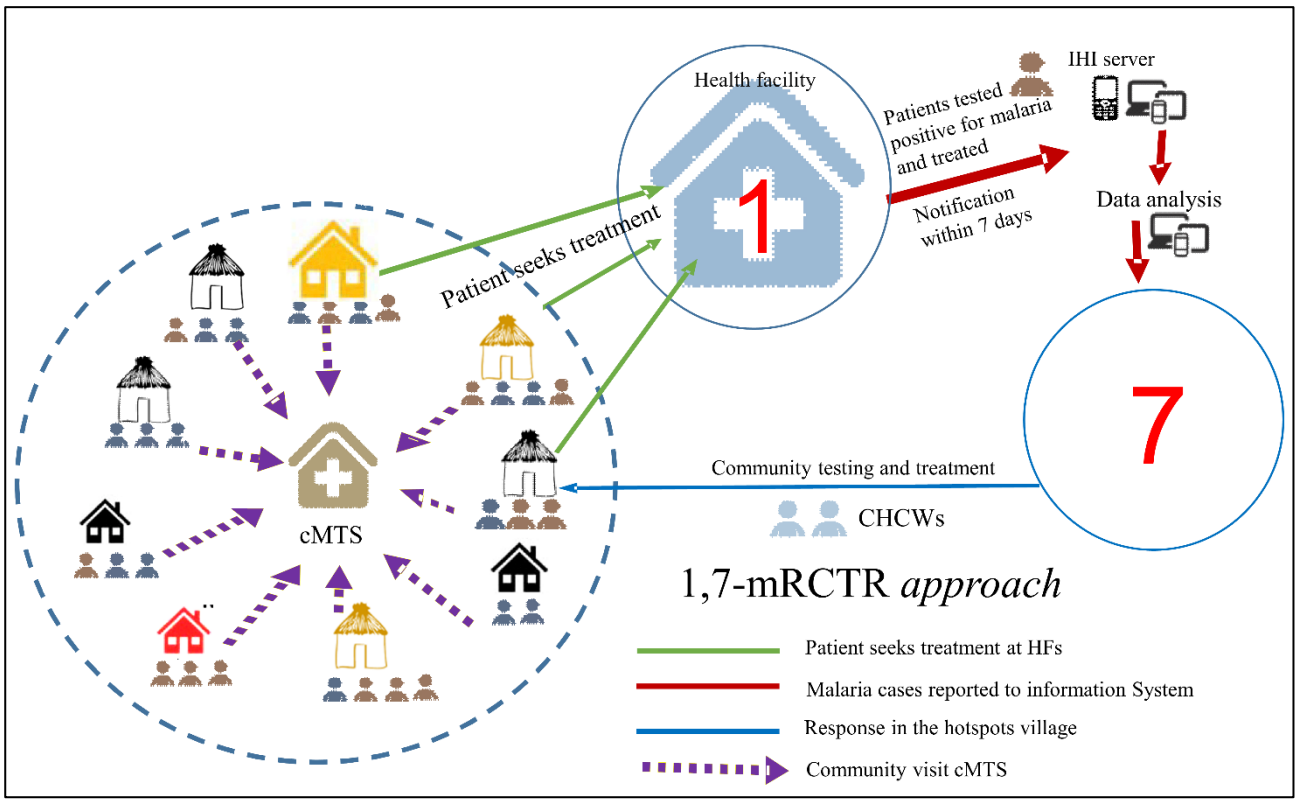

Figure 3.2. Diagrammatic representation of the 1,7-mRCTR approach as implemented in the intervention arm.

Evaluation

The primary measure of the effectiveness of 1,7-mRCTR, determined in advance, was the adjusted comparison of the changes in malaria prevalence from before the project to after the intervention in the control and intervention areas. This was a non-experimental study, the entire evaluation was based on the baseline and endline household cross–sectional surveys with independent samples conducted in both intervention and control areas. Figure 3.3 shows the number of participants sampled for baseline and endline cross-sectional household surveys for the 1,7-mRCTR approach evaluation.

The baseline was created using data collected from September to November 2015, with the endline survey done from February to April 2018. A random sample of 2000 households was selected based on community census data for each of the baseline and endline surveys. The sample size and power

calculation for this evaluation can be found in the previously published protocol (Wang et al. 2019). A structured questionnaire was designed based on the standard RBM-MERG guidelines with modification to fit the study area (Roll Back Malaria Monitoring and Evaluation Reference Group et al. 2005). It was developed in English, translated into Swahili, and installed on tablets using the Open Data Kit software.

A full description of the study's aim and the objective was given to the head of the household at the first visit. All participants were provided with a written informed consent form describing the risks, benefits, and the participant's rights to free diagnosis and treatment. The right to refuse participation without penalty was explained and guaranteed. If a household in the list could not be located or did not wish to participate, a nearby house with similar features was selected for replacement. At the household level, each occupant present was tested in situ for parasite infection using an RDT, blood smear, and filter papers. Only RDT results were considered in the analysis. Other people were not pricked because they only accepted to participate in the interviews without consenting to invasive procedures necessary for blood collection. However, this was not considered a serious problem that could bias the study because it was expected and addressed during the design stage where 20% of the calculated sample was added. The detailed methods for the baseline survey have been reported previously (Khatib et al. 2018).

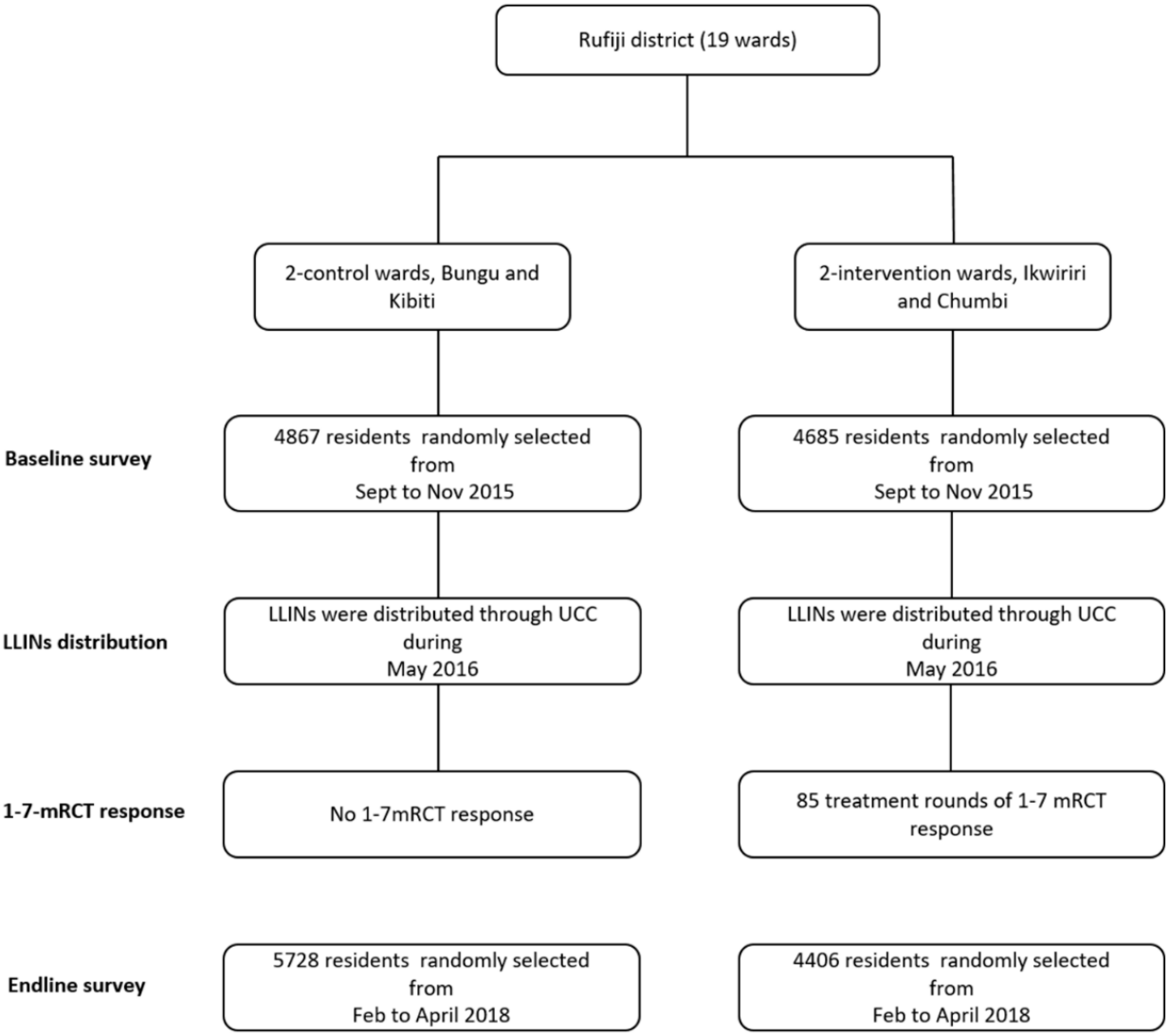

Figure 3.3. Schematic diagram of the study design, intervention activities, and the number of participants sampled for baseline and endline cross-sectional household surveys for the 1,7-mRCTR approach evaluation.

Statistical analysis

Baseline and endline prevalences were computed as the values of the intercepts in generalized estimating equations (GEE) clustering on household and using the identity link, with their standard errors. Univariate analyses were done to test the relationships between different potential explanatory variables and prevalent malaria. Comparisons between the intervention and control arms were done similarly for each survey. Malaria prevalence was modelled using GEEs with the logit link, clustering

at the household level. The effect of 1,7-mRCTR was estimated by comparing the changes from the baseline malaria prevalence to that at the endline surveys (main effect 'time') in the two areas (main effect 'area'), using the interaction term of area and 'time' (baseline vs endline) as the measure of programme effect (difference-of-differences). When the interaction effect is included in the model, the main effect of the area describes the difference between the two areas at baseline, and the main effect of time gives the 'average' change in odds of malaria from baseline to endline. The interaction effect represents the difference between the changes in the two areas.

Categorical variables were presented as numbers (percentages), while continuous variables were presented as mean (confidence interval)/medial (quartile range), respectively. Potential confounders included age (categorized as under 5 years, 5 to 14 years and above 15 years), sex, LLINs use the previous night, and socio-economic status (SES). The wealth index (SES) as a potential risk factor for malaria infection was generated using principal component analysis on a list of assets possessions to produce the SES quintiles (Filmer and Pritchett 2001).

For the duration of the project, routine data were available only for the intervention wards, and the only routinely collected case-related numbers were in HFs. Therefore, the case ratios (HFs cases/population) were analysed rather than true incidence values. A mixed-effects regression model with the village as a random effect was used to analyse the impact of the 1,7-mRCTR in reducing HFs case ratios between villages receiving malaria intervention and those not receiving it. The detailed analytical procedure for the health facility data analysis is described in Additional file 2. Statistical analyses were performed using STATA software (version 15.1, College Station, TX, USA) and SAS software (version 9.4, Cary, NC, USA).

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3.4 Results

Community impact of 1,7-mRCTR on the reduction of malaria prevalence

Overall 9522 and 10,134 participants were surveyed during the baseline and endline surveys, respectively. A total of 7691 and 7989 individuals agreed to provide finger-prick blood for malaria testing for each respective survey (Table 3.1). The median household size for the baseline and endline survey population was 6 (interquartile range IQR 4–8) and 5 (IQR 4–7), respectively. All age groups were included in the study, and people ≥ 15 years of age accounted for more than 52% of all participants, followed by the 5–15 years age group (31%). In both surveys, females accounted for 55% of the total surveyed participants. The disease burden recorded in both intervention and control wards at the baseline survey significantly declined by the time of the endline survey. Malaria prevalence in the intervention wards declined by 81% (from 26.0% (95% CI 23.7–27.8), at the baseline to 4.9% (95% CI 4.0–5.9) at the end of the study) (Table 3.1). In the control wards, malaria prevalence was reduced by 52% from 28.1% (95% CI 26.1–30.2) at the baseline to 13.4% (95% CI 12, 12–14.7) at the endline survey. Both intervention and control wards showed a significant increase in LLIN use over the time of the study as a whole. In the intervention wards, the use of LLINs increased from 66% (95% CI 62.6–69.1) at the baseline to 83% (95% CI 81.3–85.3) at the final survey. In the control wards, the use of LLINs increased from 49.4% (95% CI 46.4–52.4) at the baseline survey to 80% (95% CI 77.9–81.5) at the end.

Table 3.1. Demographic and characteristics of participants in the baseline and endline community surveys

	Baseline survey		Endline survey	
Characteristics	**Control**	**Intervention**	**Control**	**Intervention**
Population*, n (%)	4,867	4,685	5,728	4,406
Age group, years				
<5	908 (18.7%)	852 (18.2%)	986 (17.2%)	702 (15.9%)
5-15	1,602 (32.9%)	1,425 (30.4%)	1,727 (30.2%)	1,307 (29.7%)
>15	2,357 (48.4%)	2,408 (51.4%)	3,015 (52.6%)	2,397 (54.4%)
Gender, n (%)				
Female	2,698 (55.4%)	2,509 (53.6%)	3,310 (57.8%)	2,464 (55.9%)
Male	2,169 (44.6%)	2,176 (46.4%)	2,418 (42.2%)	1,942 (44.1%)
Malaria infection[1], n (%, 95% CI)				
Positive	1,103 (28.1, 26.1-30.2)	967 (25.7, 23.7-27.8)	621 (13.4, 12.12-14.7)	163 (4.9, 4.0-5.9)
Negative	2,827 (71.9, 69.9-73.9)	2,794 (74.3, 72.2-76.3)	4,029 (86.6, 85.3-87.9)	3,176 (95.1, 94.1-96.0)
Bed-net use[2], n (%, 95% CI)				
Yes	2,316 (49.4, 46.4-52.4)	2,969 (65.9,62.6-69.1)	4,568 (79.7, 77.9-81.5)	3,673 (83.4, 81.3-85.3)
No	2,375 (50.6, 47.6-53.6)	1,534 (34.1,30.9-37.4)	1,160 (20.3, 18.5-22.2)	733 (16.6, 14.7-18.7)

*Number of individuals surveyed; [1]based on malaria rapid testing using RDT; [2]Reported insecticide-treated bed-net use the previous night.

Multivariate analysis

Multivariate analysis using GEEs is presented in Table 3.2. The baseline malaria prevalence was lower in the intervention wards, adjusted odds ratio (aOR) 0.41 (95% CI 0.35–0.48, $p < 0.001$), and both wards had much lower odds of malaria at endline compared to baseline, aOR 0.90 (95% CI 0.77–1.04, $p = 0.14$) (Table 3.2). The aOR of the endline/baseline was 0.34 (95% CI 0.26–0.44, $p < 0.001$). The decline in prevalence odds in the intervention wards was much greater than that in the control wards. LLIN use was associated with significantly lower odds of having malaria: aOR 0.71(95% CI 0.63–0.80). The highest wealth quintiles (i.e., those better off) people were less likely to be infected by malaria, aOR 0.21 (95% CI 0.17–0.26, $p < 0.001$)) as compared to the lowest (i.e., the poorest).

The 5–15 years old participants had twice as high odds of malaria infection compared to those under five, aOR 2.13 (95% CI 1.89–2.40, p < 0.001)) (Table 3.2).

Table 3.2. Univariate and multivariable analysis describing the effects of the 1,7-mRCTR and risk factors for malaria infection

Variables	Univariable model		Multivariable model	
	cOR(95% CI)	p-value	aOR((95% CI)	p-value
Survey years				
Baseline	1(ref)	--	1(ref)	--
Endline	0.29(0.26-0.33)	<0.001	0.41(0.35-0.48)	<0.001
Site				
Control wards	1(ref)	--	1(ref)	--
Intervention wards	0.74(0.66-0.84)	<0.001	0.90(0.77-1.04)	0.14
Comparison of endline to baseline				
Control	1(ref)	--	1(ref)	--
Intervention	0.17(0.14-0.21)	<0.001	0.34(0.26-0.44)	<0.001
Gender				
Female	1(ref)	--	1(ref)	--
Male	1.44(1.32-1.57)	<0.001	1.24(1.13-1.36)	<0.001
Age group, years				
<5 years	1(ref)	--	1(ref)	--
5-15 years	2.09(1.87-2.34)	<0.001	2.13(1.89-2.40)	<0.001
>15 years	0.67(0.60-0.76)	<0.001	0.67(0.59-0.76)	<0.001
Bed-net use[1]				
No	1(ref)	--	1(ref)	--
Yes	0.43(0.38-0.48)	<0.001	0.71(0.63-0.80)	<0.001
Wealth index				
Lowest	1(ref)	--	1(ref)	--
Second	0.86(0.74-1.02)	0.076	0.75(0.64-0.88)	<0.001
Middle	0.62(0.52-0.73)	<0.001	0.56(0.47-0.66)	<0.001
Fourth	0.55(0.46-0.65)	<0.001	0.50(0.42-0.60)	<0.001
Highest	0.23(0.19-0.29)	<0.001	0.21(0.17-0.26)	<0.001

cOR=crude odds ratio; aOR=adjusted odds ratio; CI=confidence interval; [1]Insecticide-treated bed-net use previous night.

Changes noted in the intervention communities

The Chumbi high-transmission ward had a total population of 26,631 people (per census), with 15,317 malaria cases (reporting to the HFs) during the study period. The Ikwiriri moderate-transmission ward had a total population of 45,532 people (per census), with 21,254 reported HF malaria cases (Table 3.3). The average case ratios (total number of positive cases per total population) were 5.34 and 4.38 (per 1000 population per week) for Chumbi and Ikwiriri, respectively. While both wards had roughly the same case ratio in the low transmission season (August-April), they diverged in the high transmission season (May–July), with a more considerable increase in Chumbi. A total of 50 rounds of 1,7-mRCTR visits were conducted in Chumbi, during which 6511 cases were treated. In the Ikwiriri ward, 35 rounds of 1,7-mRCTR visits were conducted, with 2924 cases treated. The median age of the participants subjected to the 1,7-mRCTR rounds was 15 years (IQR 7–28). One village never received a 1,7-mRCTR. No important adverse reactions were reported during the study period.

Table 3.3. Characteristics of participants screened and number of health facility cases and case ratios by ward, season and year during the 1,7-mRCTR project in the intervention wards

Characteristics	Ikwiriri[1]	Chumbi[2]	Overall
Total population, n	45,532	26,631	72,163
Number of treatment rounds	35	50	85
Population screened	17,160	21,246	38,406
Malaria infection (%)*	2,924 (17.0)	6,511 (30.6)	24.57
Fraction of village population tested (mean (standard error))	10.5 (1.3)	12.0 (1.7)	11.4(1.1)
Fraction of those tested who were positive	17.5 (1.7)	31.8 (2.6)	25.9(1.8)
Total number of health facility cases, n	21,254	15,317	36,571
Number of health facility cases, (n (Weekly case ratio/1,000 popn) (%))			
Low transmission season[$] 2016	7,728 (4.47)	5,180 (3.96)	12,908(4.25)
2017	5,578 (3.22)	2,825 (2.16)	8,403(2.77)
High transmission season [$$] 2016	4,127 (6.47)	4,049 (8.40)	8,176(7.30)
2017	3,821 (5.99)	3,263 (6.77)	7,084(6.33)

*Tested positive for malaria infection by RDT; [$]September to April, [$$]May to August, popn=population, std err=standard error. [1]Moderate-low transmission ward, [2]High transmission ward

There was a substantial decrease in weekly case ratios per 1000 population from 2016 to 2017 during both the low and the high season (Table 3.3). Weekly case ratios from 2016 to 2017 decreased proportionately more in the low season (Table 3.3). In Ikwiriri, the case ratio during the high season barely decreased at all (6.5 to 6.0%,), while in Chumbi the case ratio decreased proportionately less in the high season (8.4 to 6.8%, a 19.4% decrease) than in the low season (4.0 to 2.2%, a 45% decrease).

Changes in reported HFs malaria cases at the village level

A mixed-effect regression model analysis of the routine HFs data controlling for the season, wards, their interaction and number of times the village was previously treated indicated that in the week after a 1,7-mRCTR visit in the village, the case ratio decreased by over 15.7% (95% CI − 33, 6) but was not significant (Table 3.4). From 2 to 5 + weeks after village treatment, the case ratio varied among weeks but was mostly below that during the week of treatment. The analysis separating the two intervention wards (Chumbi and Ikwiriri) showed the same trend of low-level case ratio reductions.

Table 3.4. Estimated change in malaria incidence case ratios compared to the hotspot week, by week after 1,7-mRCTR response in the village of the intervention wards

Weeks since treatment	**Exchangeable model**			
	Estimate %	**95% CI**		**p-value**
	Ref			
Week of treatment	13.6	-7.1	38.9	0.22
Week following treatment	-15.7	-33.0	5.9	0.14
2 weeks after treatment	-3.1	-24.5	24.3	0.80
3 weeks after treatment	5.3	-17.9	35	0.69
4 weeks after treatment	9	-18.5	45.8	0.56
5-13 weeks after treatment	8.7	-7.1	27.2	0.30

*Based on a mixed model, weighted by the inverse probability of being in the designated week of or after the 1,7-mRCTR and controlling forward, season, time since the beginning of the project.

3.5 Discussion

Surveillance is recognized as an intervention and considered instrumental in accelerating global malaria elimination efforts. However, all existing evidence to date does support the incorporation of surveillance as in intervention in low endemicity areas and no evidence comes from moderate to high endemicity areas. 1-3-7 model which inspired the development of this project and subsequent adopting of the 1,7-mRCTR approach, is a unique approach to implementing the recommended WHO-T3 and surveillance as an intervention for eliminating malaria. Nevertheless, the 1-3-7 model mainly worked in China whose target is elimination as opposed to Tanzania majority of which still experiences moderate to the high transmission and hence the target is to reduce the burden. The adopted 1,7 mRCTR has demonstrated beyond doubt that, a locally tailored surveillance-response strategy can successfully result in a dramatic reduction of disease burden and hence accelerate elimination efforts. The study offers the first attempt at establishing an appropriate surveillance-response model that will fit most African settings in driving the malaria elimination agenda.

The 1,7-mRCTR intervention substantially reduced the community malaria burden in the areas characterized by moderate to high malaria transmission in southeastern Tanzania. The dramatic reduction in the intervention wards (81%) compared to the control areas (52%) produced clear and practical evidence underlining the usefulness of the 1,7-mRCTR intervention, which was bolstered by the multivariate analysis showing that the reduction of the malaria prevalence (66%) was beyond the impact of LLINs alone. Importantly, current malaria interventions, including the most advanced ones using the novel vaccination approach, have only reported a 30–50% effect beyond that of LLIN use (Maher 2008).

The results are consistent with other studies demonstrating the effect of early diagnosis and community treatment in reducing the burden of malaria infection in sub-Saharan African countries and elsewhere (Aidoo et al. 2018, Deutsch-Feldman et al. 2018, Landier et al. 2018, Larsen et al. 2015). However, contrary to these studies, the 1,7-mRCTR for screening and treatment was based on using health facility-based data to geographically map the patients and identify village as the index of observation, evaluation, and targeting instead of individuals. The advantage of this approach was that it provided a chance for all community members to participate, which is in line with the current WHO-recommended focus and strategy on the high burden and high impact (WHO 2018). Also, the fact that the 1,7-mRCTR involved local CHCWs provides a strong foundation for the sustainability of addressing the essential systemic key issue to project implementation. Furthermore, though it is slightly beyond the scope of this paper, the intervention has demonstrated capable of not only conferring protection to the beneficiary communities but also has delivered short term impact on the health system's service provision by reducing the number of the hospital attendance in subsequent weeks following the intervention week. However this effect needs to be evaluated further to establish the exact magnitude and duration of effect.

Moreover, looking at the intervention design the success of the 1,7-mRCTR was mainly contributed by the daily collected and reviewed HFs data and used to identify weekly priority areas for priority screening and treatment by local CHCWs teams. This though tedious exercise, led to a positive outcome through effective engagement of all involved parties service providers to provide data and the communities to receive the intervention. This reduction of malaria burden using the 1,7-mRCTR approach does highlight the feasibility and opportunity of simply emphasizing using HFs data for microstratification of cases and devising appropriate accessible, prompt, and effective malaria interventions, especially in remote, underserved areas with moderate-high malaria transmission

(Bejon et al. 2010, Maher 2008, WHO 2012a). Furthermore, the involvement of the local CHCWs has been instrumental in optimizing the awareness, acceptability, and coverage of the intervention since most of the CHCWs were recruited and worked from the project area where they were familiar to geographical settings and the culture.

Despite the success demonstrated by the adopted approach in Tanzania, key lessons from the project team would be to be observant. While the combination of the WHO-T3 initiative and the Chinese 1-3-7 model could be easily taken up consideration must be made for locally tailoring in most malaria endemic settings across Africa requiring more modification. The disease epidemiology and the differences in health systems' such as lack of proper individual tracking systems versus transmission status as well as the inability of existing information systems to allow for sub-district level microstratification would hamper the adaptability of such strategies in most settings. Therefore, as exemplified by our team the process of crystallizing and making some minimal essential adaptions, such as the inclusion of parameters allowing isolation (in the village of residence) of cases testing positive and the development of an electronic platform for individual cases reports is essential to ensure the success of the strategy. The modified platform was able to capture all individual malaria daily, map the individual patient down to the village level allowing for micro stratification and assessment of the magnitude of the burden comparing the villages within the catchment area before launching the response by the team of CHCWs. It should be noted here that the 1,7-mRCTR approach was successfully deployed local community-based personnel, including field interviewers, nurses, laboratory technicians, under the oversight of clinicians who serviced the entire catchment area. This approach was adopted to address both the acceptability of the intervention as well as the shortage of human resources for health.

The findings from this study are limited in terms of spatial and temporal coverage. The project was implemented in only one district of the country, which has several other settings with varying epidemiological, ecological, socio-economic, and cultural. There is still a need to further explore whether this intervention package would lead to similar results in other areas, which are epidemiologically, ecologically, and socio-economically different. Extending this intervention in other settings could validate the findings of the pilot project and further build confidence in possible uptake by national programmes and subsequently scale-up for impact. Other potential limitations include that the study was a before-after assessment of which no adequate control of study participants is conducted which may compromise the strength of the evidence, also it was implemented in the area where other programmatic activities were going on as usual, which, despite our rigorous analysis some of the observed impacts might have been altered. Indeed, the 1,7-mRCTR could potentially be an innovative and effective approach to accelerate malaria elimination in Africa, however, this assertion is based on the epidemiological impact assessment of the intervention only. The cost-effective analysis of the project looking at the implementation of the 1,7 mRCTR approach is being looked at and it is a work in progress that will be submitted for publication.

3.6 Conclusion

Implementation of the 1,7-mRCTR contributed convincingly to reducing the malaria burden in areas of moderate and high transmission in southern Tanzania and offers the first attempt at implementing surveillance as an intervention in areas with high malaria burden. Appropriately structured and defined health facility data is instrumental in allowing sub-district level microstratification and targeting resources and interventions more appropriately. The results encourage a broader evaluation of the 1,7-mRCTR approach and the strategic approaches for accelerating malaria control and elimination efforts. Furthermore, lessons learned from implementing the 1,7-mRCTR approach with

the community-based capacity building and local health system strengthening are shaping the Chinese aid efforts to support African countries in accelerating malaria control and elimination.

Acknowledgements

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Ethics approval and consent to participate

The Medical Research Coordination Committee of the National Institute for Medical Research granted the permit to conduct this study (NIMR/HQ/R.8a/Vol.IX/2005). Institution ethical approval was also obtained from the Ifakara Health Institute Institutional Review Board (IHI/IRB/No: 18-2015) and the Chinese Centre for Disease Control (201505). Informed consent was obtained directly from the head of

the households, and for the participants >18 years, consent/assent was obtained from parents or guardians for children who are >13 but <18 years and live with a parent or guardian. The consent forms were prepared in English and translated into Kiswahili (the local language). For adults who were not able to read the form, the informed consent form was read out by the local CHCWs in the presence of a community witness (Balozi) and the participant was asked to mark a thumb impression on the form, and the witness signed it.

Consent for publication

Not applicable

Availability of data and materials

All relevant data can be made available upon receipt of official requests while ensuring participant and community data privacy and confidentiality.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

XNZ, NX, and SA conceived and designed the project. DQW and PPC designed and implemented the project. YPM, DQW, and PPC drafted the manuscript. YPM, KR, HMM, EH, and SA performed the statistical analysis of the study. SA, GT, ET, MT, SFR, PV, XNZ provided further revisions. YPM, PPC, DQW, TG, MGM, MT, SA, XNZ, and all the other authors implemented the study and

reviewed the manuscript. All authors read and approved the final manuscript.

Additional file 1: Survey organization and Implementation

Survey organization and selection of study areas

Introduction of the program

This collaborative program was implemented by the Ifakara Health Institute (IHI) in Tanzania and the National Institute of Parasitic Diseases (NIPD) at China CDC. The China-United Kingdom-Tanzania pilot project on malaria control was the first project to pilot the feasibility of how Chinese models, in combination with the WHO-T3 initiative, could be effectively used to reduce malaria and fast track elimination efforts in Africa. The program aimed to reduce malaria disease burden by 30% in comparison with what was at the beginning of the project, through strengthening capacity for malaria control at the local level and implementation of the adopted Chinese experiences in combination with the World Health Organization T3 strategy in the proof of concept areas(Wang et al. 2019).

The design of this project started with workshops and kick-off meeting held by technical personnel from potential partners followed by field visits in Tanzania. Before study implementation, the field visits involved consultations with central and local government authorities for the identification of project sites. Based on the availability of prior data, epidemiological parameters, and logistical convenience, Rufiji district was selected. The selected study area covered four wards. Of four wards, two were assigned to the intervention arm, and the other two were controls. The identification of the project sites was followed by a baseline survey to establish parameters upon which the impact of implementing the project would be evaluated. After the baseline survey, the implementation of the project started. Intervention package of the project involved the application of a modified Chinese "1-3-7" (Zhou et al. 2015a) model for malaria surveillance and response in combination with the

WHO-T3 Initiative and the local resources. The local resources here included a platform of health system infrastructures, manpower, funds, and supplies that existed to provide the base of the intervention. Both malaria experts from China and Tanzania worked cooperatively on this community-based pilot project to provide the platform for expanding Chinese malaria experiences gained and transferred into innovative 1-7 mRCT approach development and integration in strengthening community engagement and mobilization.

Stakeholder engagement

The project designing and implementation was a collaborative effort by multiple individuals from local and international malaria stakeholders. At the national level, the study team was composed of members from the IHI and NIPD, together with the National Malaria Control Programme (NMCP) of Tanzania and the National Institute of Medical Research (NIMR) of Tanzania. The approved protocol was shared with NMCP and NIMR for discussion and agreement on the proposed intervention. Subsequently, at the district level, the local government officers (District Medical Officer, District Malaria focal person, Vector control officer, and Council Health Management Team) were consulted, and the study design was discussed in detail.

At the local community level, engagement activities were conducted before and during the screening campaigns to broaden and strengthen community awareness, to raise the general knowledge of malaria and to promote the intervention. Meetings involving; community leaders, school teachers, and children and key informants at the district, wards, villages, and sub-village levels were held.

As part of working collaboration between Chinese and Tanzania, during field implementation, at least 36 Chinese teams of malaria expertise (epidemiologist, medical entomologist, laboratory scientist,

and anthropologist) were deployed at the local community to provide malaria technical and scientific assistance on study design, feasibility, and practical workflow coordination. Different from some international projects, the on-site Chinese staff for technical support were dispatched to the pilot areas and worked with local stakeholders throughout the pilot project to find out the practical issues and obstacles lying in the malaria control process and cope with them sharing Chinese experience, in a mutual learning-by-doing way. Chinese staff in the field of epidemiology, entomology, anthropology, lab sciences were selected in China nationwide to work with IHI and other local partners. Importantly, the malaria experts from China jointly working with Tanzania worked on this community-based pilot project was purposely to provide the platform for expanding Chinese malaria experiences gained and transferred into other settings like Tanzania.

The on-site Chinese staffs were twinned together with local staff from IHI, NMCP, and other partners in the filed communities, jointly working on a specific aspect (e.g., surveillance & treatment, or vector control activities, etc.) for work plan designing, local staff training, field implementation, and supervision, etc. They mainly supervised and gave guidance to local training and field implementation. The working teams regularly conducted community mobilization campaigns with more than 200 local stakeholders, including the local government leaders and health staff from 36 administrative villages in the 4 communities. Besides the supervision and guidance, they also ensured the steady progress of the project implementation by jointly taking solutions on the field level.

For implementing the 1,7-mRCTR, the project recruited and trained 35 community-based health care workers (CHCWs) on malaria surveillance and treatment activities. Detailed training included the fundamental skills for malaria case diagnosis and treatment, vector control, and health education. The CHCWs were divided into four teams, which were referred to as surveillance response teams. Each surveillance response team comprising of at least one laboratory technician, a clinician, a nurse, field

interviewers, and a field supervisor. The teams were deployed to the two intervention wards to conduct 1,7-mRCTR. Furthermore, a community sensitization team was formed from each respective village to raise the community's awareness and compliance with a 1,7-mRCTR. The size of the sensitization team depended on the number of sub-villages units, including the hamlet leader and village community health volunteers.

The role of each team member in the cMST

Teams of CHCWs, including supervisors, lab technicians, nurses, field workers were recruited from the village where this study was conducted. The CHCWs were recruited from the community to serve as a bridge between the community and the research team and other stakeholders of the project. We envisaged this approach will lead to a reduction in recruitment costs as compared with recruitment from other regions which could increase the cost to the management through additional costs such as accommodation. However, this is yet to be proved since this paper did not evaluate the cost-effectiveness of the intervention. This is planned for the next paper.

Supervisor's tasks: Supervisor's responsibilities were to ensure all field workers have the necessary materials for the day, including enumeration number for the selected household (ids) to be visited by each and ensuring that every participant visiting the cMST is registered with a unique identification. Supervisors were also required to inform the pre-inform the village leaders when the village identified as hotspots. Furthermore, the supervisors had the role of ensuring that all forms were cross-checked for completeness and are accurately recorded following the standard operating procedure.

Laboratory personnel: This was the person responsible for receiving the samples and forms from the field, prepare the slides for reading, parasite identification, recording the results, and send the results forms to the field supervisor for further management.

Field workers: This was a frontline public health worker whose role was to administer the questionnaire and collecting all demographic details of participants attended the cMST. They were also responsible for conducting community education on malaria prevention. Furthermore, they were also responsible for a day to day activities of ensuring that all field equipment, logistics are in place before the field to start. All of these were recruited from the village; this was to ensure the trusting relationship between the research team and community members.

Additional file 2: Analytical procedure for HFs data

Statistical Analysis

To examine whether the 1,7-mRCT affected the number of health facility cases in the treated wards, the total number of cases diagnosed at health facilities each week for each ward were considered and computed case ratios (the number of cases at the HF per population base). Seasons were divided into the high season (weeks 18-31 of the year, roughly May to July) and low season (all other weeks) based on case count. The weekly case ratios per population base were considered as replicates of the situations within the wards. GEE models of the annual effects (2017 versus 2016 - the only full years in the project) controlled for the season were fitted. To make sure that our modeling methods did not unduly influence the results, the logarithmic case ratios (with identity link) using both independent and exchangeable correlation structures were modelled. Also, the case ratios using identity link and independent and exchangeable correlation structures was modelled. Thus, four ways of examining the outcomes were prepared. Moreover, the possible interaction of year and season, i.e., whether or not the approach tested was more or less effective depending on the season, was considered.

To examine the length of time, the case ratio per population was suppressed after a village was treated, the logarithm of the case ratio using mixed models with the identity link, the exchangeable working

covariance structure, and the empirical variance was modelled. Each village-week was considered to be a replicate within the village (random effect). The exposure of interest was the (integer) number of weeks post-treatment. If the last treatment exceeded 13 weeks, the time was reset to 'pre-treatment'. If a village was treated within the 13 weeks, the 'clock' restarted. In addition, to a ward and season (which was modeled harmonically), a linear term for time since the project started was included. Interaction terms between the ward and this term and the season variables were included. Since the treatment was not allocated randomly but based on being a hotspot, we needed to weight the observations to reflect the probability that an individual village would be treated in a particular week. The method of Hernan (Hernan et al. 2000) was followed to produce stabilized weights using season, ward, and linear time for the numerator model and adding the number of times a village had been previously treated, and the previous week's incidence ratio for the denominator model. Since the stabilized weights had a large range,.005 to observations with computed weight below 0.01 and 101 to observations with computed weight over 100 was assigned.

Chapter 4: Epidemiological characterization of malaria in rural southern Tanzania following China-Tanzania pilot joint malaria control baseline survey

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4.1 Abstract

Background: Malaria is an important public health problem in Tanzania. The latest national malaria data suggests rebound of the disease in the country. Anopheles arabiensis, a mosquito species renowned for its resilience against existing malaria vector control measures has now outnumbered the endophagic and anthrophilic Anopheles gambiae sensu stricto as the dominant vector. Vector control measures, prophylaxis and case management with artemisinin-based combination therapy (ACT) are the main control interventions. This paper presents and discusses the main findings from a baseline household survey that was conducted to determine malaria parasite prevalence and associated risk exposures prior to piloting the T3-initiative of World Health Organization integrated with Chinese malaria control experience aimed at additional reduction of malaria in the area.

Methods: The study was conducted from 4 sub-district divisions in Rufiji District, southern Tanzania: Ikwiriri, Kibiti, Bungu, and Chumbi. Malaria transmission is endemic in the area. It involved 2000 households that were randomly selected from a list of all households that had been registered from the area. Residents in sampled households were interviewed on a range of questions that included use of long-lasting insecticidal nets (LLINs) the night prior to the interview and indicators of socio-economic status. Blood drops were also collected on blood slides that were examined for malaria parasites using microscopes.

Results: The study observed an average malaria parasite prevalence of 13% across the selected site. Its distribution was 5.6, 12.8, 16.7, and 18% from Ikwiriri, Kibiti, Bungu, and Chumbi wards, respectively. The corresponding LLIN use discovered were 57.5% over the district. The highest

usage was observed from Ikwiriri at 69.6% and the lowest from Bungu at 46.3%. A statistically significant variation in parasitaemia between socio-economic quintiles was observed from the study. Males were more parasitaemic than females (p value = 0.000).

Discussion and Conclusion: The findings have been discussed in the light of results from Tanzania Demographic and Health Survey-Malaria Indicator Survey, 2015–2016 and other related studies, together with goals and targets set for malaria control. The paper also discusses the observed parasitaemia in relation to reported LLIN use and its distribution by some important factors as they were explored from the study. It has been concluded that malaria burden is now concentrated on the fringes of the settlements where the poorest section of the population is concentrated and LLIN usage is lower than the national average and targets set by national and global malaria control initiatives.

Keywords: Long-lasting Insecticidal Nets (LLIN), Malaria Parasite Prevalence, Rufiji District, LLIN Users, Chumbi

4.2 Background

Malaria is one of the communicable diseases accounting for major health burden in Tanzania. More than 90% of the population is at risk of transmission. Tanzania Demographic and Health Survey- Malaria Indicator Survey (TDHS-MIS) 2015 – 2016 for under-fives using malaria rapid diagnostic test (mRDT) shows average parasite prevalence of 14% (Ministry of Health 2016). This figure suggests that that the disease has rebound in the country as prevalence was less than 10% in 2012. The main vector species are *Anopheles gambiae sensu stricto* that has currently been outnumbered by *Anopheles arabiensis*, and *Anopheles funestus* is also active in some areas(Killeen 2014, Lwetoijera et al. 2014). The dominant parasite is *Plasmodium falciparum* (Ministry of Health 2016). The stated prevalence reported for the country is contrary to milestones set in the country's national strategic plan for malaria that was 5% in 2016 and a decrease to less than 1% in 2020 (Ministry of Health and Social Welfare 2014).

The major control strategies in place are long-lasting insecticidal nets (LLINs), indoor residual spraying (IRS), larviciding of mosquito breeding sites, intermittent presumptive therapy in pregnant women (IPTp), quality-assured diagnostic testing and treatment of malaria cases with artemisinin-based combination therapy (ACT) (Ministry of Health and Social Welfare 2014). Coverage level for all these interventions fell in 2016 against the progress that had been made in 2012 (Ministry of Health 2016). Against this background, the China-Tanzania joint malaria control project selected Rufiji district, Coast region in southern Tanzania for piloting the T3-initiative of the World Health Organization-integrated with Chinese malaria control experience aimed at additional reduction of malaria in the area.

The project conducted a baseline household survey across Rufiji district to determine some key metrics of malaria epidemiology in the area. Milestones and targets set by the project will be measured using these baseline parameters. This paper aims at shedding light on these baseline parameters in the area and they will be discussed in the light of the overall malaria condition in the country as highlighted from the TDHS-MIS 2015-2016 (Ministry of Health 2016).

The study aimed at identifying the baseline malaria parasite burden and related risk factors in four wards of Rufiji District, Coast Region.

4.3 Methods

Study site

Rufiji is a district located in Coast region, Tanzania. It lies about 200 km south of Dar es Salaam extending between 7.470 and 8.030°S and 38.620 and 39.170°E along the Dar es Salaam-Lindi and Mtwara Highway. It occupies a land area of 14,500 sq. km (divided into 19 wards and 100 villages), which is almost half of the land of the administrative region to which it belongs and bigger than the two smallest regions on Tanzania mainland. The district is named after the country's largest river, Rufiji River, through which its longest stretch passes, and its huge valley and flood plain defines its ecology, settlement pattern and economic activities.

The district's current population is 248,230 scattered around nearly 100 villages. The major settlements in the district are Utete, the district headquarters and Ikwiriri, Kibiti, Bungu, and Jaribu mpakani, all located along the above-mentioned highway (Fig. 4.1). The dominant economic activities in the area are smallholder farming (largely conducted along the river valley), carpentry,

artisanal fishing, retailing, and of late, animal keeping. The main crops grown in the area are cassava, rice, maize, fruits, vegetables, cashew nuts, and coconuts.

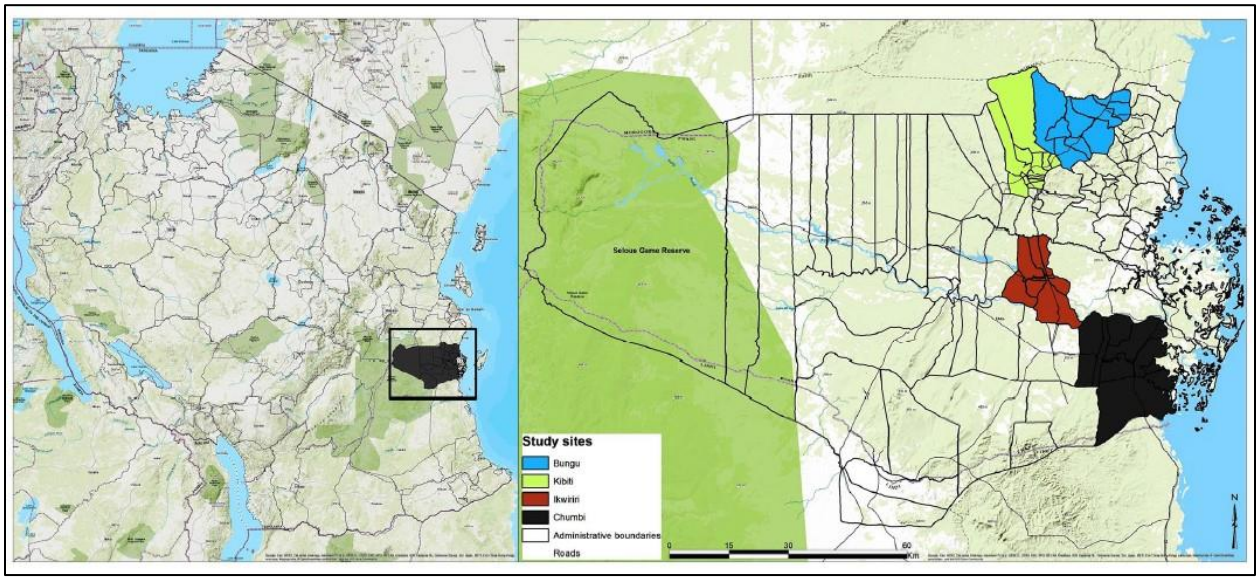

Figure 4.1. Study area location

The district is part of hot, humid, coastal plain with varying tropical climatic conditions. It normally gets rain twice a year; the short season, which is more uncertain, is September and October and the longest rainfall happens from February to May. The river gets most of its water during the long rainfall which normally swells and floods a large area of the valley and lasts up to August and September, which is the period that is most favourable for mosquito breeding and when malaria transmission is most intense.

In terms of epidemiologic and health systems studies, the district is famous for the Demographic and Health Systems Surveillance Systems Site (HDSS). At the time preceding this study, Ifakara Health Institute was hosting one of its two HDSS sites in the district. The other one was Ifakara HDSS site in Kilombero district, Morogoro region. Rufiji HDSS activities were conducted in 6

contagious wards composed of 31 villages to the north of Rufiji River, covering an area of 1,813 sq km. The site was staffed by a network of 52 paid field workers and supervisors connected to a team of 118 voluntary informants. It created and maintained a database of all households in the villages and their respective residents who were continuously monitored for vital demographic and health events such as birth, migration and death. Cash flow challenges triggered the suspension of the site activities a short time before the start of this study.

Malaria is the key disease in the district. Its transmission is still endemic. It is most common during and after the period of long rain. It is responsible for the majority of out-patient health facility attendance. Young children and pregnant women are population groups at highest risk of transmission (Khatib et al. 2012). However, the latest progress in its control has extended the burden to school aged children (Ishengoma et al. 2013). Other important ones are waterborne disease, soil-transmitted helminths and lower tract respiratory infections, including TB and AIDs. Health care delivery in the district is dominated by 2 hospitals, 5 health centres and 48 dispensaries. They are predominantly owned by the Government. There are several privately owned and operated retail drug outlets authorized by the Government, known as Accredited Drug Dispensing Outlets (ADDOs) which are commonly concentrated in places with relatively large population centres. They are important for increasing access to some key interventions especially for malaria. Malaria control and delivery strategies depend on same interventions provided by national policy (Ministry of Health and Social Welfare 2014).

Study design and procedures

Data were collected using cross-sectional household survey from September to December 2015 and January 2016. Field activities were conducted in 2 phases.

Phase I

The expansion of project activities to areas beyond the HDSS villages forced the team to conduct a census of households and people in the new area before implementation of the survey. The exercise enabled the study to compile a database for sampling selection. The sampling frame was already available in villages covered by HDSS site. The HDSS site wards that were included in the study were Ikwiriri, Mgomba, Umwe, Kibiti, and Bungu. A new non-HDSS ward was added to the study: Chumbi.

Phase II

Using the database from both the HDSS and the new enumeration, the survey randomly sampled 2,000 households from the 6 wards with an estimated 10,000 members. Two modules of questionnaire were prepared. Module 1 was a questionnaire that collected household information, such as household characteristics and asset ownership. This form was addressed to the head of a household and if he was not available, another senior household member was interviewed. The second module targeted every member of the selected household. Once the household was selected, every member of the selected household was interviewed. As for children aged 16 and below, their parents and caretakers consented and were interviewed on their behalf. A total of 9,522 individuals, equivalent to 95.5% of the target population, were interviewed. However, only 7,056 individuals, equivalent to 73.5%, were pricked for blood collection. Other people were not pricked because they only accepted to participate in the interviews without consenting to invasive procedures necessary for blood collection. Among the main data collected from the interviews were household

asset ownership and household characteristics. They were used to generate household socio-economic status.

Blood drops which were collected were stained on glass slides and stained with Giemsa. They were read by trained microscopists using standard procedures for preparation, interpretation and reporting. Both *P. falciparum* and non-falciparum asexual parasites and gametocytes were identified, but over 98% of malaria infections in these areas were due to P. falciparum and prevalence of non-falciparum infection is not reported. Asexual parasites were quantified by counting number of parasites per 200 white blood cells. Parasite density was estimated by assuming a count of 8,000 white blood cells per ul of blood. Five per cent of slides read by each microscopists were read again by a senior laboratory technician for quality control; discordant readings were consistently less than 14%.

All two-form modules were prepared and pre-tested in *Swahili*. They were then installed in tablet computers. The data were recorded in these tablets. Members of the field team were recruited from laid-off HDSS staff. They were familiar with the villages and the households that were collected; because they had worked in this kind of study before using tablets computers, it was easier for them to be trained.

Data analysis

Data sets were transferred into STATA version 10 software (Stata Corp, College Station, TX, USA) for merging, cleaning and performing analyses. To account for unequal probability of selection, all results were weighted (weight = 1/probability of selection) and were adjusted for

clustering with households as the primary sampling unit. The analysis were done with svy: command in STATA. The main outcome measure was the proportion of observed participants with malaria parasites for the whole study. The prevalence was then compared by sex, age group and socio-economic status (SES). SES was estimated using the scores calculated from the household characteristics and asset ownership that were collected from the study. It was generated using Principal Component Analysis (PCA). The prevalence was also analysed for each ward involved in the study. The corresponding distribution of parasitaemia from each ward and sex, age group and SES were also analysed. Comparison of these outcomes within and between wards and the stated risk factors was made using Chi square test. Multivariable logistic regression was used to assess the importance of the selected risk factors for malaria parasitaemia in the study. The Concentration Index formula by (Kakwani et al. 1997) as adapted in STATA was used to generate concentration indices and the respective confidence intervals from the study to identify existence of socio-economic inequality in malaria parasite prevalence in the study area. The concentration curves were created using MS Excel version 10.

4.4 Results

Table 4.1 displays respondents that participated in the study and their distribution by basic socio-economic characteristics. Six wards were involved in the study. However, because of many similarities between Ikwiriri, Umwe and Mgomba wards, as they are all and situated at one contagious location, the analysis pooled them as one ward and designated them as Ikwiriri. Ikwiriri will carry the findings for the 3 wards throughout this paper.

Table 4.1. Observed sample from each selected ward and its distribution by a sex, age group and socio-economic status

Ward	N=9552	Gender		Age groups			Socio-economic status				
		Male n (%)	Female n (%)	<5 n (%)	5–15 n (%)	>15 n (%)	Poorest n (%)	Second n (%)	Third n (%)	Fourth n (%)	Least poor n (%)
Ikwiriri	2595	1172 (45.2)	1423 (54.8)	452 (17.4)	792 (30.5)	1351 (52.1)	300 (11.6)	510 (19.7)	531 (20.5)	508 (19.6)	746 (28.8)
Kibiti	2568	1127 (44.0)	1441 (56.0)	479 (18.7)	823 (32.1)	1266 (49.3)	491 (19.1)	394 (15.3)	544 (21.2)	427 (16.6)	712 (27.7)
Bungu	2303	1045 (45.4)	1258 (54.6)	433 (18.8)	779 (33.8)	1091 (47.4)	347 (15.1)	567 (24.6)	569 (24.7)	557 (24.2)	263 (11.4)
Chumbi	2086	1001 (48.0)	1085 (52.0)	396 (19.0)	633 (30.4)	1057 (50.7)	773 (37.1)	445 (21.3)	286 (13.7)	393 (18.8)	189 (9.1)

Table 4.2 displays malaria parasite prevalence observed from the study and its magnitude from each of the 4 wards. It also shows the distribution of the burden by gender, age group and SES. The overall observed prevalence was 13.0%. The highest prevalence was recorded from Chumbi at 18.4%, which was 41% above the district-wide average. The lowest burden (5.6%) was observed from Ikwiriri: 43% below that of the district. According to Table 4.2, males were in general significantly more parasitaemic than females (p = 0,000). The burden was consistently higher for school-aged children, 5-15 years compared to under-fives (p = 0.000). Consistent with many other observations, the findings from this study suggest that parasite prevalence was the lowest among the relatively richest individuals than among the poorest (p =0.000) (Table 4.2).

Table 4.2. **Observed parasitaemia in Rufiji district and its distribution from each selected ward across sex, age group and socio-economic status**

Ward	n = 915 (13.0)	Gender		Age group			Socio-economic status				
		Male n = 438 (15.2)	Female n = 477 (11.6)	< 5n = 214 (14.8)	5–15 n = 468 (21.1)	> 15 n = 233 (6.9)	Poorest n = 273 (19.6)	Second n = 198 (14.2)	Third n = 189 (13.7)	Fourth n = 168 (11.8)	Least poor n = 87 (6.1)
Ikwiriri	106 (5.6)	49 (6.4)	57 (5.1)	22 (5.9)	54 (9.4)	30 (3.2)	19 (9.6)	24 (6.1)	24 (6.5)	19 (5.0)	20 (3.7)
Kibiti	241 (12.8)	115 (15.2)	126 (11.2)	64 (15.9)	132 (22.6)	45 (5.0)	84 (21.6)	49 (16.6)	49 (13.4)	28 (9.0)	31 (6.0)
Bungu	290 (16.7)	146 (20.5)	144 (14.1)	62 (17.2)	144 (24.1)	84 (10.8)	57 (21.3)	79 (19.0)	71 (16.3)	68 (16.4)	15 (7.2)
Chumbi	278 (18.4)	128 (18.7)	150 (18.1)	66 (21.6)	138 (29.7)	74 (9.9)	113 (20.7)	47 (15.2)	45 (21.2)	52 (17.2)	21 (14.5)

Overall males p = 0.000

Kibiti sex p = 0.019

Bungu sex p = 0.0001

5–15 group p = 0.000

Poorest p = 0.000

Table 4.3 presents results generated from multivariate analysis that associates malaria and gender, age group, SES and ITN use. Unlike in univariate analysis as presented in table 2 where males were more parasitaemic than females (p=0.000), it is shown in Table 4.3 that gender had statistically significant relationship with malaria parasitaemia only from Bungu where males were likely to be 40% more parasitaemic than females (95% CI: 1.1-1.8. It is similarly shown from the table that people above 15 years and above were less likely by 60% to be infected by malaria parasites compared to under-fives (95%CI: 0.3-0.5). The observation was consistent in all of the wards involved in the study. School-aged children (5 – 15 years) were at higher risk of malaria transmission than under-fives (see Table 4.3). However, by comparing the two variables according to the wards that the respondents came from, observations were statistically significant only from Kibiti and Bungu.

Table 4.3. Factors related to parasitaemia in Rufiji district by wards

	Districtwide			**Ikwiriri**			**Kibiti**			**Bungu**			**Chumbi**		
	OR	**95% CI**	**p value**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Gender															
Female	Baseline														
Male	1.1	1.0–1.3	0.130	1.1	0.8–1.7	0.500	1.1	0.8–1.5	0.580	1.4	1.1–1.8	0.010	0.9	0.7–1.2	0.572
Age group															
< 5	Baseline														
5–15	1.4	1.2–1.8	0.000	1.6	1.0–2.7	0.056	1.5	1.03–2.1	0.036	1.5	1.1–2.2	0.018	1.4	0.9–2.1	0.096
> 15	0.4	0.3–0.5	0.000	0.5	0.3–1.0	0.045	0.3	0.1–0.5	0.000	0.6	0.4–0.9	0.018	0.4	0.3–0.6	0.000
Socio-economic status															
Poorest	Baseline														
Second	0.7	0.5–0.9	0.007	0.6	0.3–1.4	0.273	0.7	0.4–1.2	0.179	0.8	0.5–1.4	0.474	0.7	0.4–1.2	0.164
Third	0.6	0.5–0.8	0.005	0.7	0.3–1.6	0.395	0.6	0.3–1.0	0.040	0.6	0.4–1.1	0.097	1.1	0.7–1.7	0.725
Fourth	0.5	0.4–0.7	0.000	0.6	0.2–1.3	0.196	0.4	0.2–0.6	0.001	0.7	0.4–1.3	0.248	0.8	0.4–1.6	0.388
Least poor	0.3	0.2–0.4	0.000	0.4	0.2–1.0	0.043	0.3	0.2–0.5	0.000	0.3	0.1–0.7	0.003	0.8	0.4–1.6	0.535
Fever*															
No	Baseline														
Yes	2.4	1.9–2.9	0.000	2.1	1.2–3.7	0.015	3.2	2.1–4.8	0.000	1.8	1.2–2.8	0.009	1.5	1.1–2.1	0.012
ITN use															
No	Baseline														
Yes	0.6	0.5–0.7	0.002	0.6	0.4–0.9	0.045	0.6	0.4–0.8	0.001	0.6	0.4–0.8	0.004	0.8	0.6–1.1	0.159

*Fever presence over the past 14 days

In terms of SES, the wealthiest individuals in the district were observed to be less vulnerable to malaria parasites compared to the poorest (95% CI: 0.2- 0.4). These district-wide results were comparable to those from Kibiti and Bungu where the least poor were less parasitaemic than the poorest by 70%.

The results suggest an overall 60% reduction in malaria parasitaemia in people sleeping under an LLIN compared to people who do not use them. Protection provided to LLIN users was maintained in every ward selected for the study, except from Chumbi. Fever prevalence also predicted parasitaemia from the study. People that reported fever 14 days preceding interview were twice as parasitaemic as others who did not report the condition.

Table 4.4 reports LLIN use for the district and from each selected ward and its distribution by gender, age group and SES. Overall, LLIN use from the district was 58%. Females reported higher LLIN use than males ($p=0.000$) and children younger than five years reported the highest LLIN use of all other age groups ($p < 0.05$), and school-aged children had the smallest proportion of LLIN use ($p=0.000$). The highest LLIN coverage was observed from Ikwiriri and the lowest was observed from Bungu. Females consistently reported higher LLIN coverage than males in all wards ($p < 0.05$). School-aged children were least protected in every ward. In terms of wealth quintiles, the least poor segment of the population in every community enjoyed higher ITN coverage than the poorest ($p < 0.05$).

Table 4.4. Insecticide treated net use in Rufiji district and its distribution from each selected ward across sex, age group and socio-economic status

Ward	n = 5285 (57.5)	Gender		Age group			Socio-economic status				
		Male n = 2241 (54.2)	Female n = 3044 (60.2)	< 5 n = 1095 (63.6)	5–15 n = 1427 (48.4)	> 15 n = 2763 (61.1)	Poorest n = 543 (39.2)	Second n = 691 (51.2)	Third n = 772 (55.7)	Fourth n = 887 (60.0)	Least poor n = 1080 (80.1)
Ikwiriri	1728 (69.6)	727 (66.0)	1001 (72.4)	341 (76.3)	490 (64.1)	897 (70.6)	67 (34.5)	233 (62.8)	257 (71.2)	294 (76.8)	434 (83.0)
Kibiti	1289 (52.2)	522 (48.7)	767 (55.0)	279 (60)	341 (42.5)	669 (55.7)	579 (57.8)	92 (34.0)	170 (49.6)	179 (58.5)	379 (76.9)
Bungu	1030 (46.3)	441 (44.1)	589 (48.0)	215 (51.1)	287 (37.4)	528 (50.9)	89 (34.5)	178 (41.8)	179 (40.3)	224 (56.3)	160 (76.6)
Chumbi	1238 (61.4)	551 (57.3)	687 (65.2)	260 (66.7)	309 (50.4)	669 (66.0)	249 (45.7)	188 (66.9)	166 (70.0)	190 (68.6)	107 (87.0)

Overall sex p = 0.000

Ikwiriri sex p = 0.001

Kibiti sex p = 0.002

Chumbi sex p = 0.003

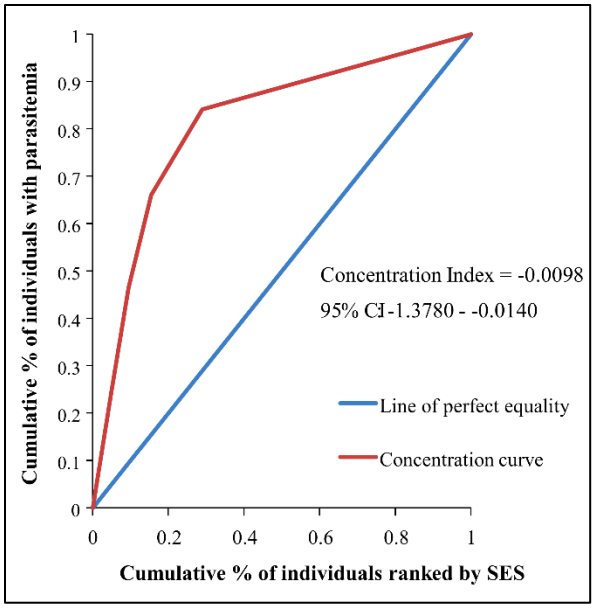

Figure 4.2. Socio-economic inequality in malaria parasitemia as generated from the national malaria survey 2015-2016

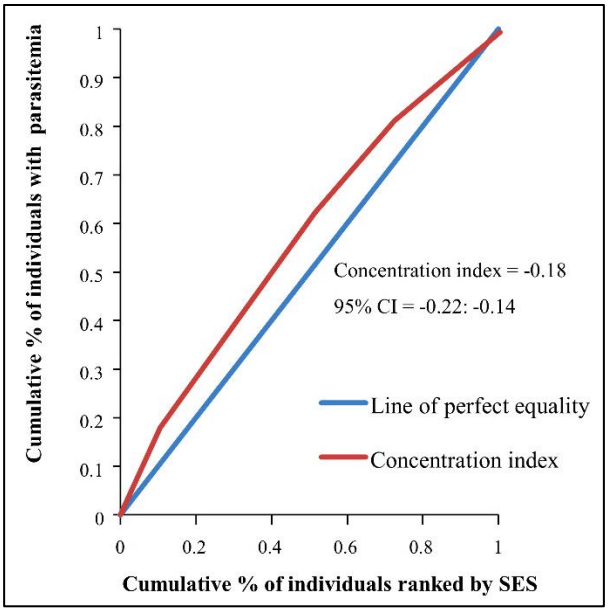

Figure 4.3. Socio-economic inequality in malaria parasitemia in Rufiji generated from the study survey

The concentration curves plotted using data from the national survey as depicted in Fig. 4.2 lie above the line of perfect equality, suggesting the existence of disproportionate inequality in malaria parasite prevalence against the poorest population in the country. This is supported by the negative CIX (-0.0098) that corroborates the curve. However, since the index is so small it suggests that the concern is not so serious and it can easily be fixed. Fig. 4.3 represents the overall situation from the study and follows the national pattern. In contrast, the CIX is larger away from 0 showing a bigger magnitude of parasitaemia inequality afflicting the poorest population in Rufiji district versus the country. The overall pattern from the study was repeated in all wards (Figs 4.4-4.6) involved in the study, except Chumbi (Fig. 4.7). The CIX from all wards showing concentration curves above the line of equality suggests inequality in malaria burden that is more severe than the national average.

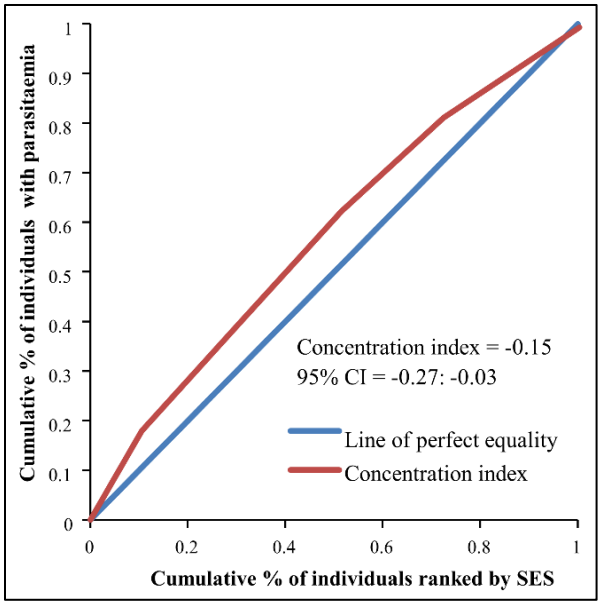

Figure 4.4. Socio-economic inequality in malaria parasitemia in Ikwiriri generated from the study

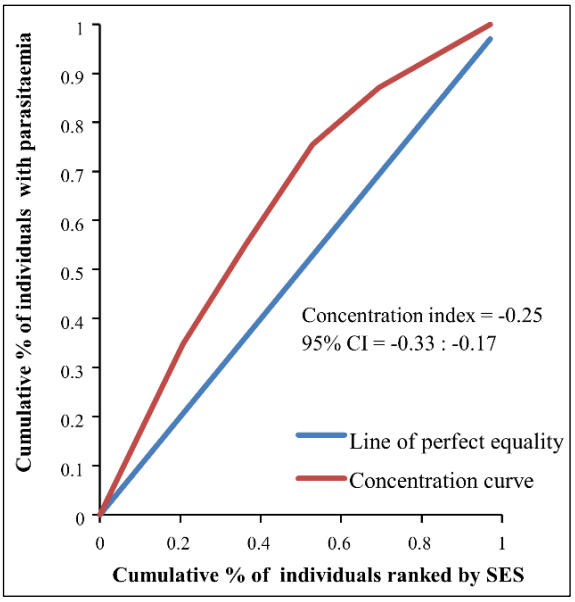

Figure 4.5. Socio-economic inequality in malaria parasitemia in Kibiti generated from the study

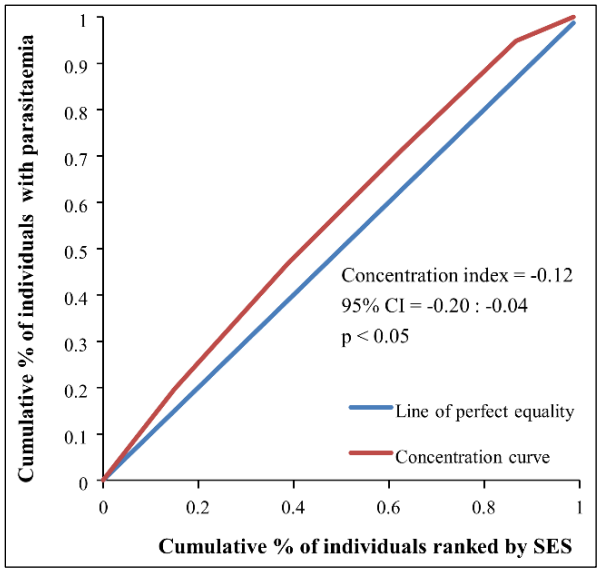

Figure 4.6. Socio-economic inequality in malaria parasitemia in Bungu generated from the study

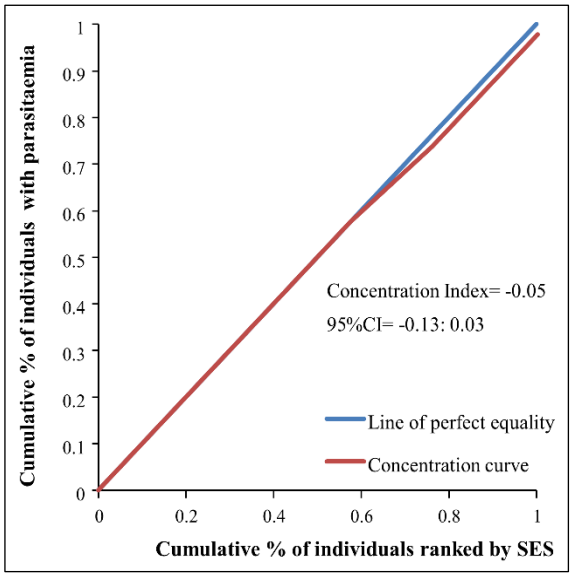

Figure 4.7. Socio-economic inequality in malaria parasitemia in Chumbi generated from the study

Fig. 4.8 rules out the existence of average meaningful socio-economic inequality in LLIN use in the country. The fact that all curves lie below the diagonal supported by positive values in CIX with confidence intervals to the right of 0 from Figs 4.9-4.13 demonstrates that national data are

hiding the true condition of LLIN use inequality in some narrow geographical settings. The figures reveal the weakness of the aggregate data presented in the national survey in evaluating equality of coverage in malaria interventions.

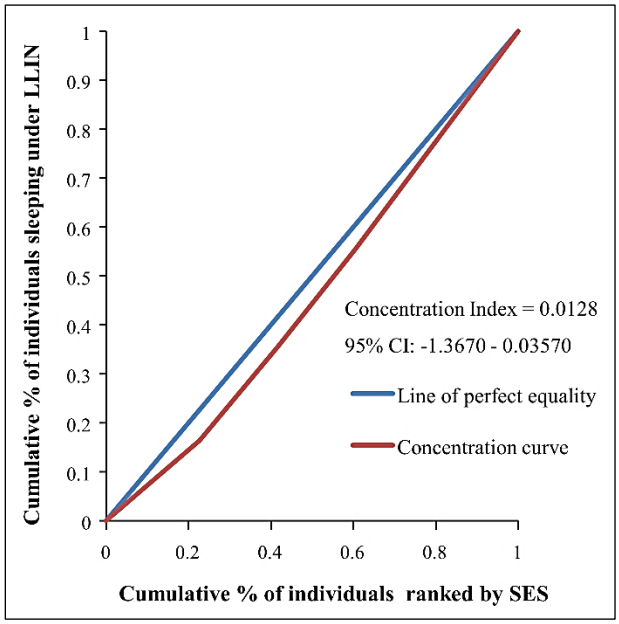

Figure 4.8. Socio-economic inequality in LLIN generated from nationa survey 2015-2016

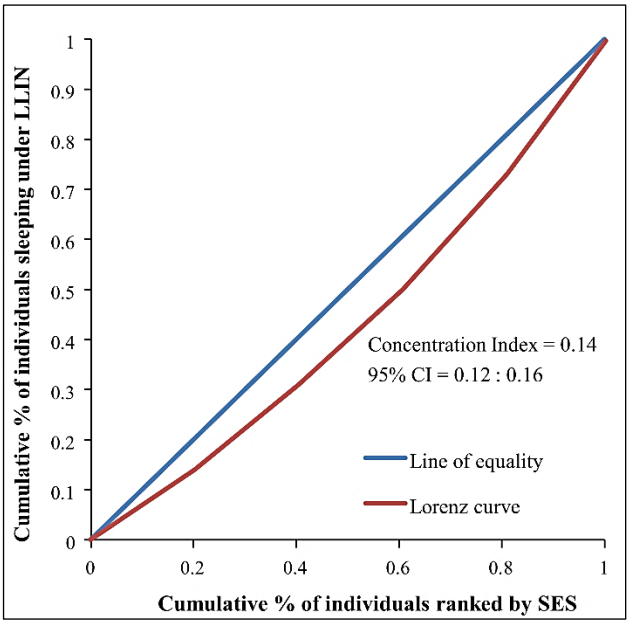

Figure 4.9.Socio-economic inequality in LLIN use in Rufiji district generated from the study

Figs 4.4-4.7 demonstrates concentration curves and indices that depict equal socio-economic inequality based on malaria parasitaemia and ITN coverage from the study. Fig. 4.2 shows the concentration curve lying above the perfect line of equality, which can be interpreted as higher exposure to malaria parasite prevalence for the poorest. The overall magnitude of inequality for the district and across the wards is reflected by concentration indices below 0 (-0.1; 95% CI: -0.21--0.13). This disproportionate distribution of parasitaemia discriminating against the poor was statistically significant in the district. Concentration curves presented in Figs 4.2-4.6 lie below the diagonal generated from data observed from the study, and supports other findings from the national survey. The concentration curve from this graph was above 0 (0.13; 95% CI: 0.11-0. 15).

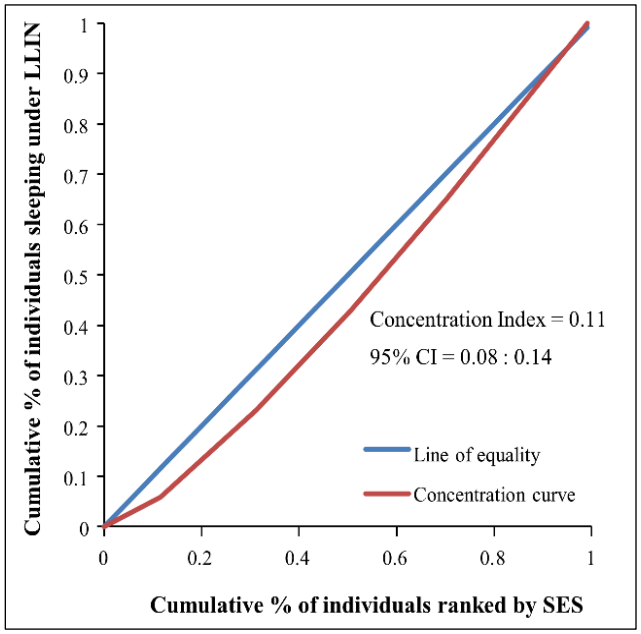

Figure 4.10. Socio-economic inequality in LLIN use in Ikwiriri generated from the study

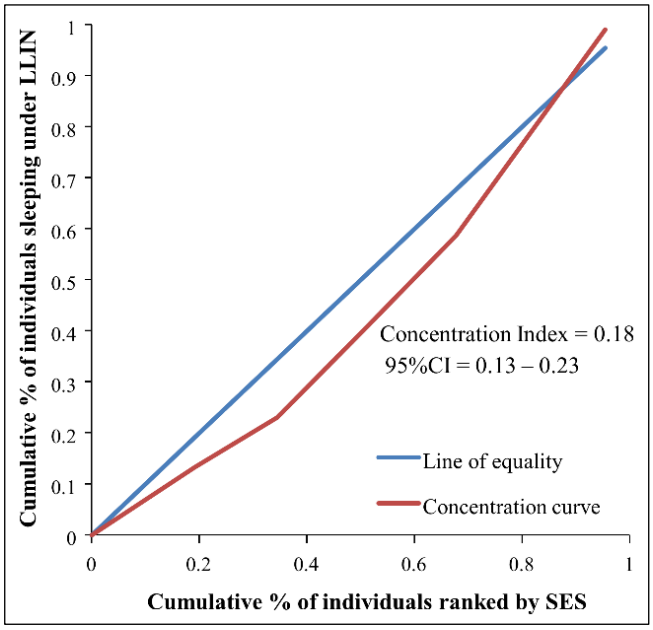

Figure 4.11. Socio-economic inequality in LLIN use in Kibiti generated from the study

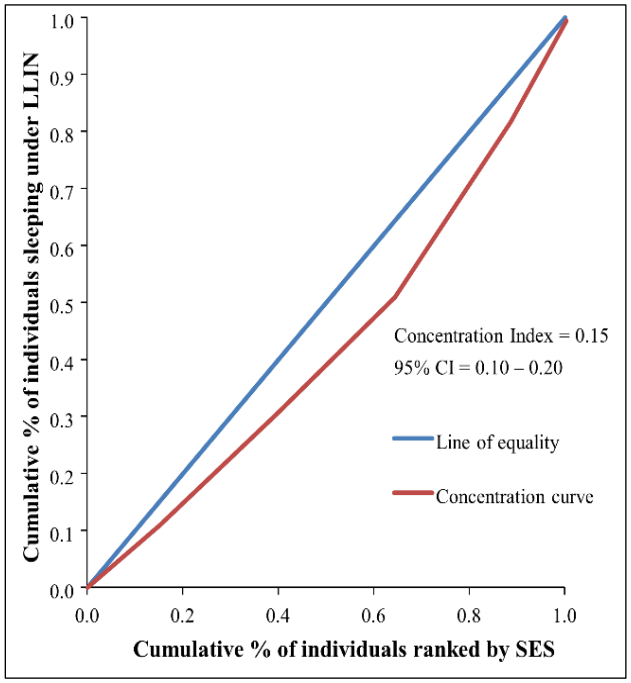

Figure 4.12. Socio-economic inequality in LLIN use in Bungu generated from the study

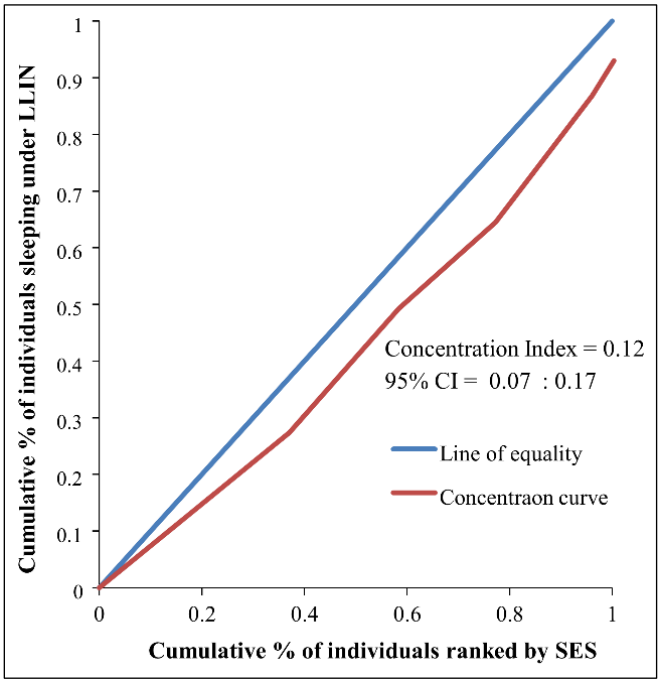

Figure 4.13. Socio-economic inequality in LLIN use in Chumbi generated from the study

4.5 Discussion

This is the first study demonstrating malaria parasite prevalence in a narrow geographic setting in Tanzania since the TDHS–MIS 2015–2016 (Ministry of Health 2016). The average parasitaemia observed from the study was larger than the national average. National malaria prevalence as measured using microscopy reported for 2016 was 6%. However, the national malaria data were limited to under-fives and disaggregated down to only regional level. Pwani, a region to which Rufiji district belongs, reported malaria parasite prevalence for under-fives of only 5.8%. Under-five parasitaemia from this study was 14.8%. This is a large variation between the national and district level data that demonstrates that even if the overall country's malaria burden is in decline as in some countries in Africa (WHO 2016b), the problem is shifting towards certain geographical locations in the same country. This variation was reported even between various regional divisions. Some regions in the central, northeastern and southern highland zones had parasite prevalence lower than 1% while in regions around Lake Victoria, such as Geita, parasitaemia was 17.7% (Ministry of Health 2016)

It is here been presented this kind of variation in parasitaemia between the 4 sub-district divisions that were selected for the study. While an average parasitaemia was 13%, Ikwiriri showed parasite prevalence lower than 6% and Chumbi, which was the most parasitaemic ward, had a prevalence of 18%. Variation was expanded to include some other factors that were in many other studies associated with malaria transmission. It has been reported that parasitaemia was more common for school-aged children compared to other groups, including under-fives who, together with pregnant women, are still considered to be at highest risk of malaria (WHO 2016b). It is because of this prevailing knowledge that most malaria-evaluating studies, including malaria indicator surveys, are concentrating on under-fives (Galactionova et al. 2017, Ministry of Health 2016, Snow et al.

2010). The changing malaria risks that are expanding or shifting to older children have been reported in several other studies (Gonçalves et al. 2014, Ishengoma et al. 2013). Unequal malaria distribution based on SES has also been highlighted in this study. The disease is most common among poorest groups in the community. Poverty as a risk exposure to malaria has been reported elsewhere (Galactionova et al. 2017, Khatib et al. 2012, Taylor et al. 2017, Teklehaimanot and Mejia 2008, Victora et al. 2012). The lowest parasitaemia observed from the study was in a ward with largest proportion of least poor, and possessed the largest features of an urban settlement. This observation is consistent with other studies on malaria epidemiology in Africa (Wang et al. 2006). It can, therefore, be deduced that malaria is a disease of poverty and is more concentrated on the fringes of a population. Additional progress on control and subsequent elimination requires efforts that will concentrate on the poorer populations in poorer settlements.

Long-lasting insecticidal net use is scaled up as a control tool for vectors responsible for malaria transmission. Many and different programmes have been implemented in Tanzania and in many other places that are at risk of malaria (Bonner et al. 2011, Paaijmans et al. 2010, President's Malaria Initiative 2012). Effective LLIN coverage can provide both personal and community protection against malaria (Hawley et al. 2003, Khatib et al. 2008, Killeen et al. 2007b) even though its validity is counter-indicated by an increasing population of *An. arabiensis,* a sister species of An. gambiae complex which poses a major setback to existing vector control strategies(Killeen et al. 2016). It has been shown in a number of studies that LLIN roll out is responsible for the decline of malaria burden observed in many places (Bhattarai et al. 2007, Curtis et al. 2003, Eisele et al. 2012). Three major strategies used for rolling out LLINs in Tanzania are a universal coverage campaign (in 2010–2011), private sector distribution and School Net Programme (Bonner et al. 2011, Ministry of Health 2016). From a 2015–2016 survey, an average

50.7% was collectively achieved for the country (Ministry of Health 2016). This study has reported higher average LLIN use than national figures. It has been shown that malaria prevalence was not homogenous across the study. With the exception of one location, whose case will be discussed in a separate paragraph, malaria parasite prevalence was inversely related to LLIN use. The burden was largest where LLIN use was the lowest and it was the lowest where LLIN use was the highest. This observation cannot and is not supported at every place because malaria transmission functions in a multitude of conditions and its control is multifactorial (Galactionova et al. 2017, Ishengoma et al. 2013). A number of studies have demonstrated a significant decline in malaria that was not explained in terms of high LLIN coverage (Galactionova et al. 2017, Ishengoma et al. 2013). Achieving effective coverage, under certain conditions, leads to lower malaria burden. However, there are interventions, including changes in environmental conditions and secular trend, which can bring the malaria burden down independent of LLIN coverage (Aregawi et al. 2014, Lynn and Bossak 2017). For example, a TDHS–MIS report showed that not all regions reported with highest malaria parasite prevalence had the lowest LLIN coverage (Ministry of Health 2016). Indeed, the Government and its partners strive to achieve LLIN coverage over 80% by 2020 (National Malaria Control Programme et al. 2013). This goal has not yet been achieved as the current coverage is 49% (Ministry of Health 2016).

As for larger parasite burden observed from school-aged children versus under-fives and other population groups, LLIN follow the same pattern. This age category possessed the lowest LLIN coverage in the study. This observation is supported by results from the TDHS–MIS that suggest LLIN use was highest for under-fives and among people living in urban areas (Ministry of Health 2016). Females were also associated with higher LLIN use than males. The variation can be associated with LLIN distribution programmes targeting under-fives and pregnant women as the

existing knowledge singles them out as biologically most vulnerable to malaria transmission (Ministry of Health and Social Welfare 2014). However, it is important for new malaria control plans to be aware of this new reality, as success in sustaining gains and accelerating progress towards end goals in the fight against malaria will depend on clearing parasitaemia from everyone. This is so important for the prevention of onward transmission. Programmes intended to improve malaria interventions for the currently recognized vulnerable groups should be modified to include other groups observed with highest parasitaemia.

It has been stated that a high malaria parasitaemia observed from Chumbi ward presents a paradox for a pattern that shows an association between high LLIN use and low malaria parasitaemia and improved SES and high LLIN coverage. The ward was characterized by the lowest proportion of residents in the highest SES but had higher LLIN use next to Ikwiriri. However, being in the top league of LLIN users was not reflected in parasitaemic status which was the highest of all wards in the study. Various studies have reported that massive roll out of existing malaria vector control interventions have a devastating impact on mosquito species *An. gambiae sensu stricto* that formerly played a leading role as a malaria vector in Africa (Bayoh et al. 2010a, Emami et al. 2017, Killeen et al. 2016). Implementation of LLINs alone or in combination with IRS has successfully reduced the population of this mosquito species bringing many malaria-endemic countries close to goals of malaria control. However, the emergence of *An. arabiensis*, a sister species of *An. gambiae* complex, which can survive on both bovine and human blood, poses a new challenge to eliminating malaria. Their susceptibility to control has been attenuated by their ability to feed outdoor whether at dusk or dawn on both humans and animals, in the case of indoor human protection with existing vector control interventions (Killeen and Smith 2007). Being zoophagic, it has been shown that they are more abundant in areas with large animal populations as was the

case in Chumbi ward where domestication of animals was one of its major economic activities (Killeen et al. 2016, Killeen and Smith 2007). A substantial number of residents in the area are pastoralists who tend to spend prolonged hours with their animals which likely exposes them to opportunistic malaria vectors, and which have exhibited insecticide avoidance behaviour. Malaria protection potential of LLINs, whose usage in Chumbi had surpassed several other locations in the study, could hardly be optimized due to conditions discussed. This paradox was not limited to this study area. TDHS–MIS also shows the highest malaria parasite prevalence in regions that are predominantly pastoralists (Ministry of Health 2016). However, LLIN coverage was higher than in some other regions, reporting relatively low parasitaemia. This could vindicate entomological models demonstrating decreased protection potential of conventional vector control measures in the face of changing dynamics of vector composition (Killeen et al. 2016, Killeen and Smith 2007, Okumu and Moore 2011).

Many studies have identified inequality as an important barrier to achieving universal coverage of malaria control interventions that is necessary for achieving total control of the disease (Alonso et al. 2011, Okumu et al. 2013). The findings from the study have shown various forms of inequality. The most important one that has consumed enormous resources to fix was inequality based on SES. Logistic regression model presented in results section supported by concentration curves and concentration indices has demonstrated the presence and significant magnitude of wealth-based inequality in parasitaemia and LLIN use. All concentration curves generated using malaria parasitaemia data are hovering above the line of perfect equality. All CIX lie to the left of 0 and can be interpreted that malaria is concentrated in the poorest population. Concentration curve from national malaria data is no different from that observed in this study. Equally important, several evaluation studies conducted in Africa have demonstrated that poverty is a risk factor for malaria

(Gallup and Sachs 2001, Khatib et al. 2013, Teklehaimanot and Mejia 2008). Poor access to malaria control interventions has often been cited as a valid explanation for this. Of all interventions in place, the study paid attention to LLINs only. It showed the lowest LLIN use among the poorest study participants as reflected in concentration curves lying below the diagonal.

The question to ask is, what did happen to the LLIN universal campaign aimed at addressing poverty as an obstacle to access? Is the investment worth pursuing? TDHS–MIS and other studies following up sources of nets providing coverage to different socio-economic groups found that LLINs from mass campaigns were responsible for the largest proportion of nets used by the poorest population (Russell 2004). These nets were commonly reported from rural areas. Conversely, private sector distribution was responsible for the majority of nets used by the least poor population (Khatib et al. 2008). This was commonly reported in urban areas. A source of LLINs in this type of setting is a function of SES that trickles down to urban and rural areas. It is evident that mass distribution campaigns are universal and periodic while the private sector is continuous but only active in urban areas. Time intervals between mass campaigns is longer than LLIN lifespan which can account for a variation in reported LLIN use between the quintiles and between rural and urban areas. In addition, publicly funded mechanisms intended for sustaining high level LLIN coverage for vulnerable populations is delivered in formal sector sources whose access in rural areas and to poor populations in urban areas is narrow. Consequently, it is largely beneficial to relatively better off people concentrated in urban areas.

4.6 Conclusion

The study has shown malaria parasite prevalence based on microscopic examination higher than the national average. It has shown substantial variations in parasitaemia between sub-district

locations. This condition gives an impression that malaria control efforts in the study area have yielded varying impact on malaria burden. It appears that the burden is concentrated in areas and among groups with limited access to control interventions. It suggests that implementation of malaria control activities are favourable in easy-to-reach areas and to groups able to afford the costs involved in accessing interventions targeted by publicly subsidized programmes. These are areas that are characterized by relatively good healthcare services that provide better access to such key malaria control interventions as LLINs and subsidized healthcare facilities. Population groups with economic strength can afford the high prices charged for malaria control interventions. The fact that LLIN use was highest in population centres, among under-fives, women, and the highest socio-economic quintile provides reasonable evidence to this conclusion.

It is evident that inaction is not an option for national malaria control programmes striving for progress in malaria control and malaria elimination. For success in malaria control in some areas and in some population groups, while leaving out peripheral areas and other marginal groups, will undo gains made and take the country back to where it was over a decade ago. It is important to identify and implement strategies that have worked elsewhere. Programmes that have worked to increase LLIN coverage for under-fives and pregnant women can be expanded to include school-aged children, adult males and non-pregnant females. The study has overall provided a broad picture of populations based parasite burden in Tanzania at sub-national level. However, its strength may have been in some ways been affected by the limitation of cross-sectional surveys. Data were collected in December and January, which are the peak season for malaria transmission in the area, but can hardly represent all of the remaining months of the year. Members of some sampled households could not be interviewed because they were not present at their homesteads during the time of the study. Their absence could have biased the results in some ways. Sample

selection was based on households and therefore some population groups might have disproportionate representation and this would also have swayed the results.

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Author's contributions

RAK contributed to the design of the study, supervised the field surveys, analysed and interpreted the data, and wrote the manuscript in consultation with the other authors. YPM, EK, TG and MGM participated in the design of the study, execution of the field surveys, interpretation of the data and editing of the manuscript. PCC, DW, NX, XZ and SA oversaw all aspects of the study, including design and execution of the field work, analysis and interpretation of the data and drafting of the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication: Not applicable.

Ethics approval and consent to participate

Ethics approval for the study was granted by the institutional review boards of Ifakara Health Institute (IHI) (IHI/IRB/No: 18-2015, and by the National Tanzanian Medical Research Co-ordinating Committee of the National Institute for Medical Research (NIMR) (certificate No. NIMR/HQ/R.8a/Vol.IX/2015). Study participants were individually asked for written informed consent. For children less than 16 years old, the consent was obtained from the parent or guardian.

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Chapter 5: Reduced human-biting preferences of the African malaria vectors Anopheles arabiensis and Anopheles gambiae in an urban context: controlled, competitive host-preference experiments in Tanzania

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5.1 Abstract

Background: Host preference is a critical determinant of human exposure to vector-borne infections and the impact of vector control interventions. Widespread use of long-lasting insecticide-treated nets (LLINs) and indoor residual spraying (IRS) across sub-Saharan Africa, which protect humans against mosquitoes, may select for altered host preference traits of malaria vectors over the long term. Here, the host preferences of *Anopheles arabiensis* and *Anopheles gambiae sensu stricto* (s.s.) were experimentally assessed in the field, using direct host-preference assays in two distinct ecological settings in Tanzania.

Methods: Eight Ifakara Tent Trap (ITT), four baited with humans and four with bovine calves, were simultaneously used to catch malaria vectors in open field sites in urban and rural Tanzania. The numbers of mosquitoes collected in human-baited traps versus calf-baited traps were used to estimate human feeding preference for each site's vector species.

Results: The estimated proportion [95% confidence interval (CI)] of mosquitoes attacking humans rather than cattle was 0.60 [0.40, 0.77] for *An. arabiensis* in the rural setting and 0.61 [0.32, 0.85] for *An. gambiae s.s.* in the urban setting, indicating no preference for either host in both cases (P=0.32 and 0.46, respectively) and no difference in preference between the two (Odds Ratio (OR) [95%] = 0.95 [0.30, 3.01], P=0.924). However, only a quarter of *An. arabiensis* in the urban setting attacked humans (0.25 [0.09, 0.53]), indicating a preference for cattle that approached significance (P=0.08). Indeed, urban *An. arabiensis* were less likely to attack humans rather than cattle when compared to the same species in the rural setting (OR [95%] = 0.21 [0.05, 0.91], P =0.037).

Conclusion: Urban *An. arabiensis* had a stronger preference for cattle than the rural population and urban *An. gambiae s.s.* showed no clear preference for either humans or cattle. In the urban setting, both species exhibited stronger tendencies to attack cattle than previous studies of the same species in rural contexts. Cattle keeping may, therefore, particularly limit the impact of human-targeted vector control interventions in Dar es Salaam and perhaps in other African towns and cities.

Keywords Malaria, Vector, Anopheles, Host preferences, Residual transmission, Entomological surveillance, Tanzania.

5.2 Background

Apart from the distributions of bites between inside and outsides the houses and at different times of the night (Finda et al. 2019, Monroe et al. 2020), what mosquitoes feed upon critically determines the choice and impact of human-targeted vector control interventions (Killeen Gerry F 2014, Killeen et al. 2017b, Kiware et al. 2017, Lyimo and Ferguson 2009, Sherrard-Smith et al. 2019, Tirados et al. 2006). For example, both historical and recent reports (Bayoh et al. 2010b, Draper et al. 1972, Gillies and Smith 1960, Kaindoa et al. 2017, Lwetoijera et al. 2014, Sharp and le Sueur 1996) show that the widespread use of long-lasting insecticide-treated nets (LLNs) or indoor residual spraying (IRS), which directly target humans or houses they live in, strongly suppressed or virtually eliminated the population of the main malaria vectors *Anopheles gambiae sensu stricto (s.s.)* and *Anopheles funestus s.s*. These two species preferentially feed upon human blood across sub-Saharan Africa (SSA) (Bayoh et al. 2010b, Derua et al. 2012, Draper et al. 1972, Kitau et al. 2012, Padonou et al. 2012, Smith 1962). Beyond Africa, *Anopheles darlingi* was eliminated in British Guiana following three years of IRS with DDT (Giglioli G 1951). This same species appears to have disappeared in Suriname in response to the scale-up of LLINs (Hiwat et al. 2012). These vectors are highly vulnerable to insecticide-based interventions for protecting humans because these species rely heavily upon human blood for their survival (Giglioli G 1951, Killeen et al. 2001, Kiszewski et al. 2004, Kiware et al. 2012, Kiware et al. 2017).

While *Anopheles arabiensis* is commonly known to exhibit flexible host-feeding, switching biting between humans and domestic animals (Massebo et al. 2015, Meza et al. 2019, Torr et al. 2008, White GB 1974), recent evidence suggests that even the historically most inflexible human-feeding mosquito species in Africa, *An. funestus s.s*. can now attack non-human hosts, specifically cattle

(Lobo et al. 2015, Meza et al. 2019). This newly observed behavioural plasticity allows the mosquito to evade human-targeted insecticide-based interventions by allowing it to access safer alternative blood sources (Pluess et al. 2010, Pryce et al. 2018). This behaviour may help vector species sustain its population and contribute to residual malaria transmission by evading fatal contact with existing front-line interventions (Govella and Ferguson 2012a, Killeen et al. 2017b, Waite et al. 2017).

Inherent host preference is an innate behavioural trait of a mosquito population that is assessed in the field by allowing mosquitoes to freely select between two or more different host species experimentally presented in equal numbers simultaneously. Host choice, however, is a more complex function of both host preference and the availability of different host species that can be accessed locally and is assessed by surveying the sources of mosquito bloodmeals collected after they have fed (Lefèvre et al. 2009, Takken and Verhulst 2013). However, because the host choices exhibited by any given mosquito population can vary across spatial scales of only a few metres (e.g., in a cattle shed versus the house nearby), experimentally-controlled host preference measurements are a more reliable means of making direct comparisons between populations. Despite its critical importance as a metric to inform the selection of impact vector control interventions, there remains a paucity of data on vector host preference and its potential change over time.

Here, the inherent host attack preferences of *An. arabiensis* and *An. gambiae s.s.* only was assessed in two distinct ecological settings (urban versus rural) in Tanzania. A competitive preference experimentally-controlled assay, baited with either a human or calf, was simultaneously presented

to malaria vectors. This study focused only on these two vector species because they are both important primary malaria vectors across Tanzania and elsewhere in Africa. Other, mostly secondary, malaria vector species were caught in insufficient numbers to be reliably assessed.

5.3 Methods

Study sites

This study was conducted at two different Tanzania regions: the urban Dar es Salaam and the rural village within the Kilombero valley in the Morogoro region. Dar es Salaam is the largest City of Tanzania, situated at 6° 51′S, 39° 18′E along the Indian Ocean with an estimate of 5 million people according to the national census of 2012 (National Bureau of Statistics (NBS) 2013). A detailed description of the study area has been previously published elsewhere (Geissbühler et al. 2007, Msellemu et al. 2016). The main malaria vectors are *An. gambiae s.s.* and *An. arabiensis,* but *Anopheles merus* and *An. funestus s.s.* are also available, though existing in very low numbers throughout the year (Geissbühler et al. 2009). *Anopheles gambiae s.s.*, which is often regarded as the most anthropophagic vector (rely feeding heavily upon human blood), feeds predominantly in the middle of the night (Geissbühler et al. 2007, Govella et al. 2010). In contrast, its sibling species, *An. arabiensis,* which is commonly referred to as zoophagic (prefers feeding on cattle) mosquito throughout SSA (Kiszewski et al. 2004), starts actively feeding in the early evening and mainly outdoors, time which coincides with the period when most residents of this city are still outside (Geissbühler et al. 2007, Govella et al. 2010). This overlaps overtime, and outdoor space between mosquito and human activity potentially increases the risk of human exposure to malaria transmission, which cannot be effectively addressed by using indoor-targeted interventions such as LLINs (Govella et al. 2010). During this study, human *Plasmodium falciparum* malaria

infection was around 10% among residents in all age groups (Msellemu et al. 2016), and with the strong reduction in malaria vectors densities of *An. gambiae* complex and *An. funestus* group (Killeen et al. 2019). This was achieved due to the scaling-up of larvicides (Maheu-Giroux and Castro 2013) and LLINs (Geissbühler et al. 2007, Msellemu et al. 2016). The scaling-up of larvicides and LLINs coincided spontaneously with the wide use of window screening across the city of Dar es Salaam (Killeen et al. 2019). The average annual rainfall ranging from 800mm to 1300mm with a 25ºC annual temperature (Dar es Salaam City Council 2004).

The second study site was at Kilombero valley, Lupiro village (8°23'03.8" S, 36°40'26.7" E), which is located 40 km south of Ifakara town within the Kilombero Valley, south-eastern Tanzania (Killeen et al. 2007a). The detail of an area can be found elsewhere (Kaindoa et al. 2017, Killeen et al. 2007a). The area is located at 300 meters above sea level on the floodplains of Kilombero valley. The average annual rainfall ranges between 1200 to 1800 mm between December to May, and the temperature is recorded at ranges from 20 to 32.6°C. The most resident lives on subsistence farming of rice, fishing, and sparse livestock keeping. *An. arabiensis* and *An. funestus* group are the primary malaria vectors in the area, but the latter exist in relatively very low numbers throughout the year (Lwetoijera et al. 2014). The historically-important malaria vector *An. gambiae s.s*. had been virtually eliminated, following the widespread use of LLINs (Kaindoa et al. 2017).

Experimental design

Eight Ifakara Tent Trap version C (ITT-C) (Govella et al. 2010) baited with either humans or calves were simultaneously used to catch wild malaria vectors in urban Dar es Salaam and rural

Kilombero Valley. In each site, an open field ground measuring more than 500m long was selected. Four (human versus calf) pairing catching stations, spaced about 50m apart, were established within these field grounds. Within each pair, the host was spaced 5m apart, allowing for a competitive host preference assay. A Latin square design involving the movement of trap-host combinations between positions was implemented to minimize possible biases associated with each position and natural variations in individual hosts' attractiveness to mosquitoes (Lindsay et al. 1993, Mukabana et al. 2002). Each pair was rotated after each experimental night through four stations. Four nights were required to make a complete round of experimentation (Fig. 5.1). After each round of four nights, the actual human volunteers and calves were replaced. The calf within each ITT-C was tethered to lure the mosquito entry inside the trap. Each morning, calves were taken out of the tent for daily grazing. There was no exchange of host between traps (calf-baited versus human-baited) because it was not acceptable to expect human participants to sleep in traps soiled by a calf. Trapping was conducted from 19:00 hours to 06:00 hours, and trapped mosquitoes were emptied from the trap every morning using a mouth aspirator. The details on how to empty mosquitoes inside the ITT-C can be found in the previous article (Govella et al. 2010). In urban Dar es Salaam, 104 (60 nights between May to August 2009 and 44 nights between March and June 2010), experimental nights were conducted. In rural Kilombero Valley, only 16 nights (from August to September 2010) was conducted. It took longer in Urban Dar es Salaam due to the limited number of malaria vector densities.

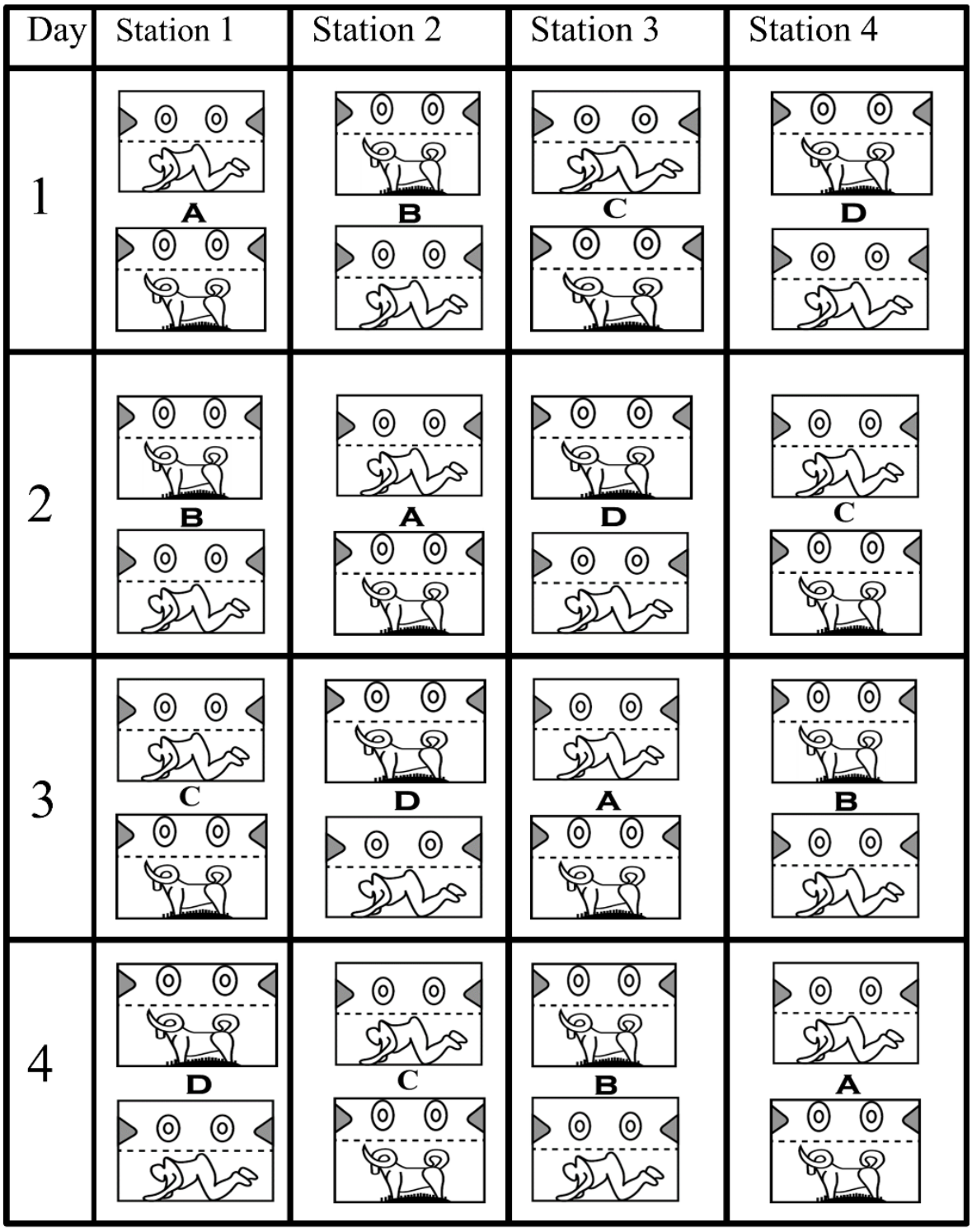

Figure 5.1. The schematic illustration of a typical 4x4 Latin square experimental design with one complete round of experimentation through four mosquito-capturing stations in the field area. The dashed line indicates a screen bisecting the upper and lower part of the trap, which protects volunteers from being exposed to mosquito bites. The ring and the funnel shape on the side illustrate the mosquito entry point.

Mosquito identification

Every morning, trapped adult mosquitoes from each trap were collected by mouth aspirator, placed in a respective paper cup prior labelled according to the host, and killed using chloroform. Morphological identification was conducted based on the keys of Gillies and Coetzee (Gillies and Wilkes 1965). All collected *An. gambiae sensu lato (s.l.)* were stored individually in Eppendorf tubes (1.5 ml) with silica gel desiccant and cotton before transport for Polymerase chain reaction (PCR) assay for species identification. The field-collected data were recorded and linked with laboratory results using the designated forms adapted from Kiware et al. (Kiware et al. 2016).

Statistical analysis

Statistical analyses were carried out using the R statistical software version 3.6.1, augmented with the matrix, lattice, and lme4 packages. To test the effect of species-specific on attacking human host, only PCR confirmed individuals from the *An. gambiae complex (An. gambiae s.s.* and *An. arabiensis)* were used. Because the response variable for each species is binary (that is, an individual mosquito can only attack a single host at a time and not both), a Generalized Linear Mixed Effect Models (GLMMs) (Franco et al. 2014), using binomial distribution and logit link function, was applied. The proportion of mosquitoes caught attacking humans was treated as the response variable, with a variable combination of PCR confirmed species and sites as a fixed effect. The experimental night and stations were fitted as a random effect. The model was run first without fitting an intercept so that the absolute proportion of mosquitoes attacking the human for each species and from each site can be estimated and compared. This was followed by fitting models that included intercept to obtain the contrast in human feeding preference between species with *An. gambiae s.s*. in urban Dar es Salaam treated as a reference species in the model. This

detailed statistical analysis on the effect of species on the propensity of attacking upon human host species was restricted to *An. arabiensis* and *An. gambiae s.s*., partly because of their importance in driving malaria transmission in these settings, and their number captured was sufficient to detect the effect.

5.4 Results

Species composition

In urban Dar es Salaam, 197,155 mosquitoes were collected. 42,929 (21.8%) and 154,226 (78.2%) mosquitoes were collected from human and calf baited traps, respectively. The taxonomic group of mosquito collected included: *An. gambiae s.l.* (n=97, 0.05%), *Anopheles coustani* (n=2,144, 1.1%), *Culex spp*. (n=192,836, 97.8%), *Mansonia spp*. (n=1633, 0.8%) and *Coquillettidia spp*. (n=460, 0.2%). All *An. gambiae s.l.* were subjected for PCR test, and 88 (88/97, 91%) specimens successfully amplified. Of which, 25 (28%) were *An. gambiae s.s*. and 63 (72%) *An. arabiensis*.

In rural Kilombero Valley, 41,876 mosquitoes were collected. 22,093 (53.0%) and 19,783 (47.2%) mosquitoes were collected from human and calf baited traps respectively. The taxonomic group of mosquito collected included: *An. gambiae s.l.* (n=334, 0.8%), *An. funestus* group (n=6, 0.01%), *An. coustani* (n=185, 0.44%), *Anopheles ziemanni* (n=31, 0.07%), *Culex spp* (n=9539, 22.8%), Mansonia spp. (n=31,749, 75.8%) and Coquillettidia spp. (n=32, 0.08%). All *An. gambiae s.l.* were again subjected for PCR test, and all successful amplified specimens 313 (94%), confirmed to be *An. arabiensis.*

Based on the logistic model fitting to these data, the estimated proportion [95% confidence interval (CI)] of mosquitoes attacking humans rather than cattle was 0.60 [0.40, 0.77] for *An. arabiensis* in the rural setting and 0.61 [0.32, 0.85] for *An. gambiae s.s*. in the urban setting (Fig. 5.2), indicating no preference for either host in both cases (P=0.32 and 0.46), respectively, with no evidence for any difference in preference between the two (Odds ratio (OR) [95%] = 0.95 [0.30, 3.01], P=0.924)). However, only a quarter of *An. arabiensis* in the urban setting attacked humans (0.25 [0.09, 0.54]; Fig. 5.2), indicating a preference for cattle that approached significance (P=0.081). Indeed, *An. arabiensis* in the urban setting were less likely to attack humans rather than cattle when compared to the same species in the rural setting (OR [95%] = 0.21 [0.05, 0.91], P =0.037).

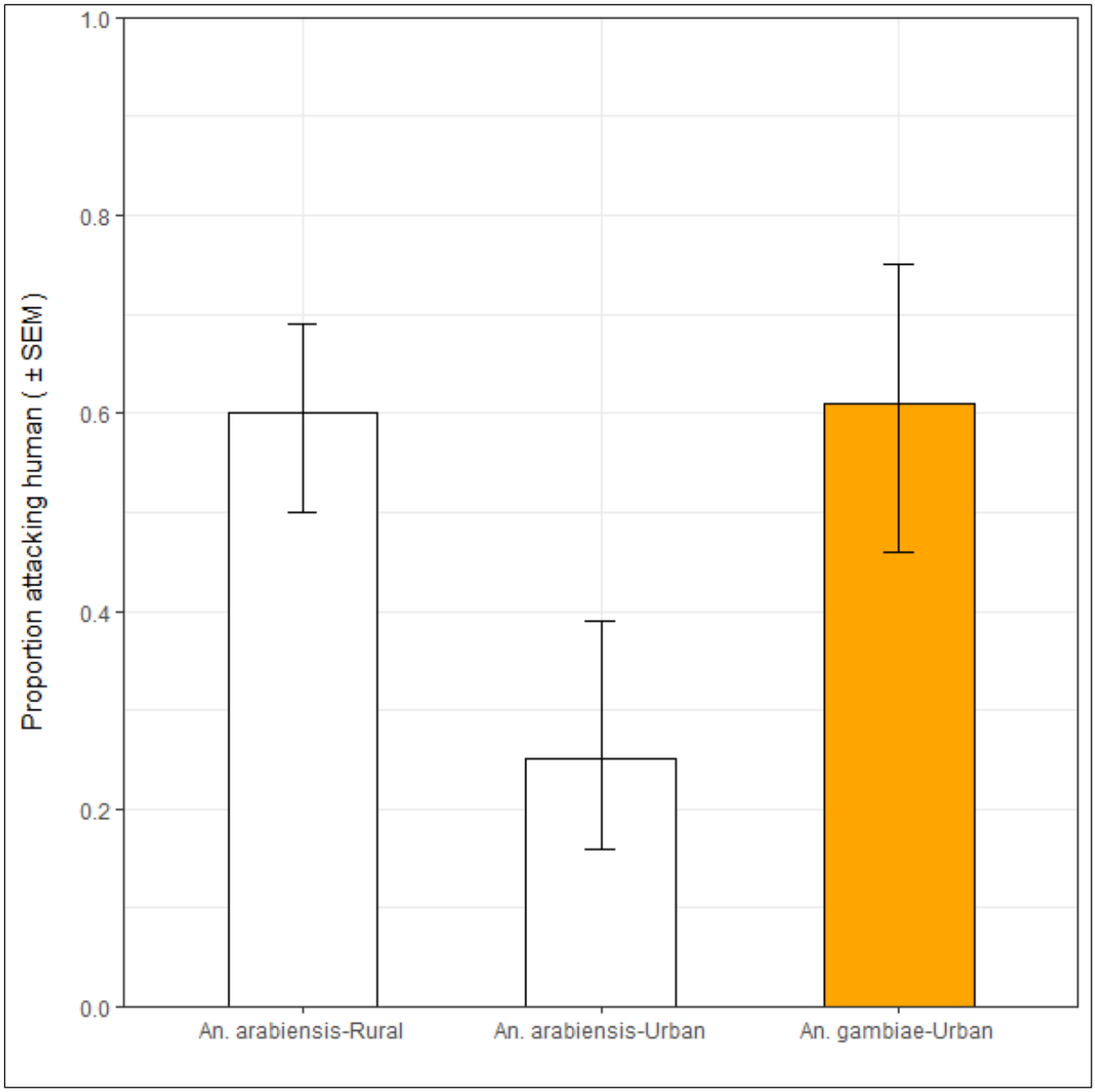

Figure 5.2. The proportion estimates (mean and standard error) attacking humans by the *An. gambiae s.s* and *An. arabiensis* captured in urban Dar es Salaam and rural Kilombero Valley.

5.5 Discussion

The findings indicate variation in the preference for feeding upon humans rather than cattle between two populations of *An. arabiensis,* in urban Dar es Salaam, and rural Kilombero. These observations become more interesting and seem to suggest an effect of urban environments on both *An. arabiensis* and *An. gambiae s.s*., compared with preceding studies that also measured host preference through carefully controlled experiments. The rural Tanzanian *An. arabiensis* population studied here had no strong preference for humans or cattle. Indeed these results compared particularly well with those of Meza et al. (Meza et al. 2019) (Fig.5. 3), which also used juvenile cattle with relatively low biomass, therefore, similar levels of attractiveness (Port et al. 1980). However, in urban Dar es Salaam, *An. arabiensis* appeared to exhibit a strong preference for cattle over humans and significantly different from the same species in rural Kilombero over approximately the same period (Figs. 5.2 and 5.3). Also unexpectedly, *An. gambiae s.s*. collected in Dar es Salaam, lacked its notoriously strong preference for humans compared with equivalent indices derived from a previous study of the same species in rural Tanzania (Killeen et al. 2001). It appears that both siblings species have a stronger preference for non-human hosts in this urban context than in previously reported studies of rural populations of the same species (Killeen et al. 2001, Meza et al. 2019, Torr et al. 2008) (Fig. 5.3).

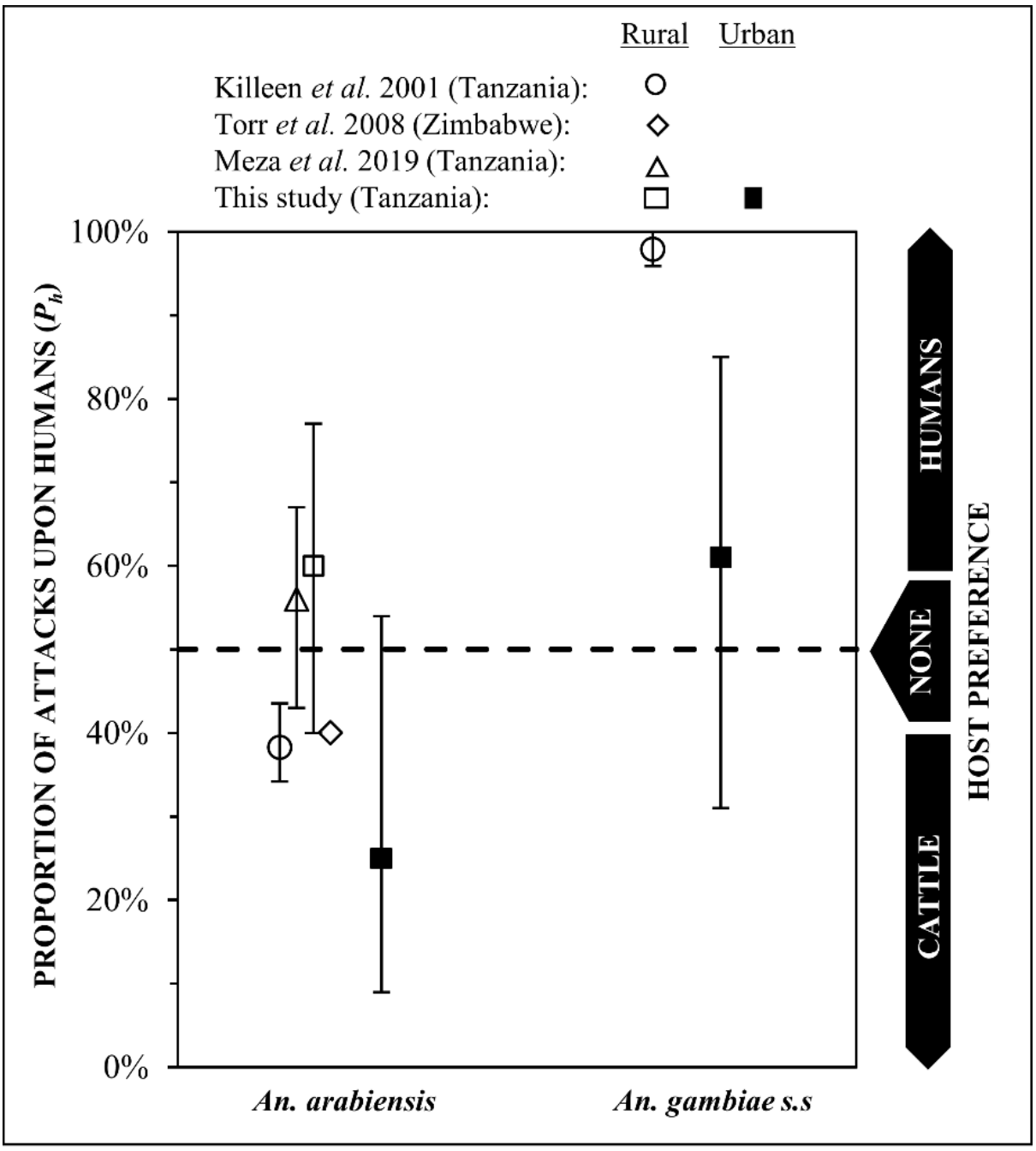

Figure 5.3. Previously estimated proportion of attacks on humans versus cattle (P_h)) when offered a direct choice between one of each host species (mean and 95% confidence intervals, for *An. arabiensis* in rural Tanzania (data extracted from Fig 4 in (Meza et al. 2019), and rural Zimbabwe (data extracted from Fig 7 in (Torr et al. 2008)), and the estimated proportion of attacks on humans for *An. arabiensis* and *An. gambiae s.s*. obtained from historical records in the rural coastal region of Tanzania (Killeen et al. 2001) compared to those obtained by this study in Kilombero, rural southern Tanzania, and Dar es Salaam, urban coastal Tanzania. The estimated proportion of attacks on humans (P_h) from historical records were derived from modelling analysis of the relative availability of humans versus cattle (λ) models: $P_h = 1/(1 + \lambda)$(Killeen et al. 2001).

The flexible feeding behaviour exhibited by the *An. arabiensis* in rural Kilombero is consistent with that reported by previous studies from the same setting (Meza et al. 2019) and beyond (Torr et al. 2008) that employed similarly direct, experimentally-controlled, host attack preference measurements but used different capture methods. It is also reassuring that fitting host preference and availability models to historical blood meal host choice data for the same species across entire villages (Killeen et al. 2001, White et al. 1972) yields similar indirect estimates, indicating only a slight preference for cattle (Fig. 5.3) even though such natural herds are dominated by larger adult cattle that may be reasonably expected to be more attractive (Port et al. 1980). Indeed the Torr et al. (Torr et al. 2008) direct host preference experiments using electric grids similar to Meza et al. (Meza et al. 2019), which also used adult cattle, yield almost identical estimates to these indirectly inferred from modelling analyses, confirming a slight preference of rural *An. arabiensis* for fully-grown cattle over humans. Such biologically and methodologically plausible triangulation of results from such different studies with such different methods suggests that the experimental approach applied here, including the first use of ITT-C (Govella et al. 2010) for experimental host preference studies, provides reliable and readily comparable indices of host preference. Therefore, it is reasonable to interpret the findings that *An. arabiensis* had a stronger preference for cattle in urban Dar es Salaam than in rural Kilombero or any previous studies population of the same species (Fig. 5.3) at face value.

It is also telling that a similar, and perhaps more surprising, the pattern was observed for the notoriously anthropophagic (Coetzee et al. 2000, Killeen et al. 2017b, Takken and Verhulst 2013, White GB 1974) *An. gambiae s.s.* compared with a previous study of the same species in a rural Tanzanian context (Fig. 5.3). The lack of a clear preference for humans over cattle by *An gambiae*

s.s. in this contemporary urban context contrasts starkly with historical records from Segera, only 258 km away from Dar es Salaam (Killeen et al. 2001). This unusually flexible feeding behaviour for *An. gambiae s.s*. in Dar es Salaam may also contribute to the persistence of this species in this settings, unlike other nearby ecological settings where it was virtually eliminated (Bayoh et al. 2010b, Derua et al. 2012), following widespread use of LLIN (Bayoh et al. 2010b, Derua et al. 2012, Kaindoa et al. 2017, Lwetoijera et al. 2014). The increasingly widespread use of LLINs (National Bureau of Statistics (NBS/Tanzania) 2011), and high coverage of house window screening in urban Dar es Salaam (Killeen et al. 2019), which limit safe access of mosquitoes to human blood, may have forced this species to develop a strategy which enables them to evade personal target protective interventions for humans by exploiting animal blood whenever they can find it.

Urban Dar es Salaam generally has fewer cattle than Kilombero, and probably in most other rural settings. It is, therefore, interesting that *An. arabiensis* now appears to have a stronger preference for feeding on cattle and perhaps on other non-human hosts that were not assessed here. It will be important to investigate whether the two populations are genetically distinct or not (Gillies and De Mellion 1968, Main et al. 2016, Reddy et al. 2011). This may be especially important following the recent surge of interest in genetic manipulation approaches for malaria vector control (Gantz et al. 2015)**.** Regardless of the underlying basis for this apparent trend towards greater zoophagy in both vector species in Dar es Salaam, on the one hand, it will limit the impacts of existing malaria vector control interventions like LLINs and mosquito-proofed window screening. On the other hand, it may provide opportunities for complementary approaches like veterinary insecticide

treatments for livestock (Chaccour and Killeen 2016, Chaccour et al. 2018, Imbahale et al. 2019, Killeen et al. 2017b, Kiware et al. 2017, The Ivermectin 2020).

While this study was quite limited in terms of scale and sample size, it does raise some important questions that merit consideration beyond Dar es Salaam and Tanzania. Urbanization is known to influence host preferences in other mosquito taxa (Rose et al. 2020), and similar effects to those reported here might also occur in other African settings where *An. gambiae s.s*. and *An. arabiensis* continue to mediate malaria transmission, despite widespread use of LLINs (Reddy et al. 2011). Indeed, it is notable that few experimentally controlled host preference studies could be found to populate Fig. 5.3, despite the vital role that this trait plays in malaria transmission and control. Therefore, this finding strongly encourages more widespread measurement of mosquito feeding preferences across a diversity of ecological settings through routine programmatic surveillance (Killeen et al. 2018). This may help inform the selection and evaluation of complementary vector control interventions, ideally in an ecologically stratified manner.

5.6 Conclusions

Urban *An. arabiensis* had a stronger preference for cattle than the rural population in this or previous studies. Furthermore, the urban *An. gambiae s.s*. assessed here had a weaker preference for humans over cattle than reported by a previous study of the same species in a nearby rural context. Cattle keeping may limit the impact of human-targeted vector control interventions in Dar es Salaam, and perhaps in other African towns and cities. Generalization of mosquito species host preferences across broad geographies or assuming that they may remain static traits may be misleading with respect to the selection of effective vector control interventions. Therefore, the

characterization of vector feeding preferences across distinct ecological settings is recommended as a critical component of routine programmatic surveillance to inform the effective design, selection, implementation, and assessment of complementary new vector control interventions, ideally on an ecologically stratified basis.

Ethics approval and consent to participate

The permission to carry out this study was approved by the Ethical Committee of the National Institute of Medical Research [NIMR/HQ/R.8a/Vol.IX/279 and 324] and from the Institutional Review Board of the Ifakara Health Institute [IHI-IRB-A.50]. The volunteer was provided with informed consent after a verbal explanation about study design in the local language. Before participation and after the experimentation days, participants were screened by a trained clinician for malaria parasite using a rapid diagnostic test (mRDT), and none was found positive. In case they were found positive, they would be treated free of charge following the national guideline of malaria treatment and withdrawn from the study. Information sheets of the informed consent included assurance of confidentiality, voluntary participation, potential risks, and benefit associated with the study. They also had the right to withdraw from the study at any time without justification.

Consent for publication

As part of the consenting procedure and information sheet's content, they also included a request that results obtained will be disseminated through scientific articles to reach broad audiences, including academics. The permission to publish was thereafter obtained from the National Institute of Medical Research (NIMR), Tanzania that has the legal mandate to approve publications of results from public health research data.

Availability of data and materials

The Ifakara Health Institute, on behalf of the United Republic of Tanzania, owns all data. Data can be shared upon reasonable request in line with the Ifakara Health Institute's data management and sharing policy.

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Authors' contributions

GFK, SM, PPC, and NJG conceived the study and designed experiments. YPM, AM, and DJM contributed to the study design, trained the mosquito collectors, implemented and supervised the field activities. YPM, NJG, and GFK performed the analysis. YPM and NJG drafted and revised the manuscript. SM, PC, DJM, and MT reviewed the manuscript. All authors read and approved the final manuscript.

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Chapter 6: High-resolution community-based mapping of residual malaria vector densities to support malaria elimination efforts in Southeastern Tanzania.

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Working paper

6.1 Abstract

Introduction: Several sub-Saharan African countries have embraced an agenda of malaria elimination, but their current intervention must be rethought and redirected to locate residual sources of transmission. For efficient and effective vector control interventions, entomological characterisation and description of vector composition at a high resolution will be essential.

Methods: Between December 2015 and April 2018, we conducted intensive surveillance of malaria vectors, covering 37 villages of the entire project area. Mosquito trapping was done concurrently across all the villages, using CDC light traps and resting bucket traps.

Results: A total of 24,715 (21.13%) female Anopheles mosquitoes,87,478(74.78%) Culex, 4,297(3.67%) Mansonia, 487(0.42%) Aedes, and 1(0.0009%) Coquilettidia were collected during the study period. Molecular identification confirmed eight (8) subspecies of *Anopheles gambiae s.l.* and *Anopheles funestus*. *Anopheles arabiensis* (62.1%), *Anopheles gambiae s.s* (23.63%), and *Anopheles merus* (14.25%) were identified in *An. gambiae s.l*. *Anopheles funestus s.s* (96.25%), *Anopheles leesoni* (2.98%), *Anopheles rivulorum* (0.66%), and *Anopheles parensis*(0.11%). Different wards,villages, and months had different mosquito species compositions and densities. Human biting rates varied considerably between wards (2 =1201.2, df = 3, p 0.01). 0 to 73 bites/person/night varied among communities (2 = 9906.8, df = 36, p 0.01). The maximum overall vector densities and HBR were reported in May (10.1 bites/person/night), after which they fell below 2 bites/person/night in most locations (2 = 1837.6, df = 5, p 0.01), except in *An. funestus s.l*-dominated areas.

Conclusion: Entomological indices of malaria transmission in the Rufiji district varied significantly among villages. This fine scale entomological description highlights how small areas at village levels differ in terms of malaria transmission indicators may be used as a guide towards an evidence-based decision for targeted intervention.

Keywords: Malaria, malaria vectors, Human biting rates, *Anopheles gambiae s.l.* and *Anopheles funestus*, residual transmission

6.2 Background

Like other sub-Saharan countries that have made progress in malaria reduction, the nature of transmission in Tanzania appears to be highly spatially heterogeneous at the sub-national level (Alemu et al. 2013, Chacky et al. 2018, Kamau et al. 2020, Thawer et al. 2020). When considering the presence of heterogenous transmission, the goal of malaria elimination, and limited operational resources, interventions would ideally and preferentially target higher burden areas to further reduce transmission towards maximizing resources (Raman et al. 2016). Spatial heterogeneity of malaria incidence requires more focused, locally tailored strategies (Bousema et al. 2010, Loha et al. 2012). However, the current approaches of delivering interventions, which are based on either large area epidemiological stratification or "one size fit all" model (Ministry of Health and Social Welfare 2014) such as universal bed net coverage, may not be efficient and effective (Taconet et al. 2021, Tediosi and Penny 2016).

The most recent entomological survey in the Rufiji revealed vector species diversity and distribution between 2003 and 2004 (Kigadye et al. 2011). The area's primary vector control method, ITNs, had less coverage than it does now (Khatib et al. 2018, Khatib et al. 2008). In Tanzania, bed net distribution in mass distribution began in 2004 (Hanson et al. 2009, Ministry of Health 2002). Since then, there has been an increase in the use of ITNs and other malaria control measures, primarily diagnostics and treatments(Khatib et al. 2012, Khatib et al. 2013). The prevalence of the disease has significantly decreased attributable to these successful malaria control measures. After more than ten years of using ITNs in this district, we hypothesized that increased ITN use would have an impact on transmission intensity, vector dynamics, including densities, species composition, distribution, behavior, and the contribution of various species to malaria transmission at the village level compared to Kigadye research (Kigadye et al. 2011).

Village level characterisation and how entomological indices varied among villages were deemed to be significant for targeted and successful vector management in the area, especially given that the disease load has been greatly reduced (Farnert et al. 2014, Khatib et al. 2018, Selemani et al. 2015).

Using mosquito data collected for six consecutive months during the project's implementation, we provide a fine-scale (village level) entomological description of the area. Presented in this paper are 1) general mosquito species occurrences, composition, and densities, 2) the main malaria vector species in the area and their proportions of composition,3) spatial distribution of the vector species among villages, and 4) distribution of malaria vectors biting rates among villages and months. The vectors' biting activity, host preference based on analysis of blood meal sources, susceptibility status of the vectors against insecticides, infection rates, and the impact of the implementation of 1-7-mRCT response the reduction of infections in the vectors will be reported subsequently.

6.3 Methodology

Study area description

A longitudinal mosquito surveillance study was conducted in the Rufiji District, Coastal region "Pwani" (Figure 6.1). Rufiji is located between latitude 7.470°- 8.030°S and longitude 38.620° - 39.170°E. The total area of the District is approximate 14,500 square kilometers elevated to 500m above sea level. The District is characterized with a bimodal rainfall, the short rains occuring between October and December, and the long rains between February and May. The annual mean temperature ranges between 24 and 31°C. The vegetation mainly consists of dry grassland with scattered trees and bushes, and subsistence crops. A prominent feature of the District is the the

Rufiji River Basin stretching to 177,429 square kilometres forming Rufiji River, which forms the largest and most extensive flood plain and delta in Tanzania. . The extensive valley and flood plain the river haves influenced the ecology of the area, settlement human pattern, and economic activities (Duvail et al. 2014). The river has a network of streams of brackish water that leads to the Indian ocean. The ecological condition in the district favors the existence of Anopheles mosquitoes responsible for malaria transmission. The district has more or less homogenous characteristics of house style with walls made of wood and mud-plastered and roofs covered with grass and corrugated iron sheet. Majortity of houses settlement is located along the main road to Mtwara region.

The transmission of malaria transmission is perennial, the highest peak observed during and after rains. Primarily malaria is transmitted by *An. gambiae s.s, An. arabiensis* and *An. funestus* as dominant vectors in Rufiji(Kigadye et al. 2011). Other Anophelines found in the area include *Anopheles pharoensis, Anopheles coustani*, and *Anopheles ziemanni*. Non-anopheline mosquitoes included Culex spp, Mansonia spp, and Aedes spp. The ITNs are the main vector control intervention in the district. The Anopheles species composition, population dynamics, density were used as entomological assessing parameters for this survey.

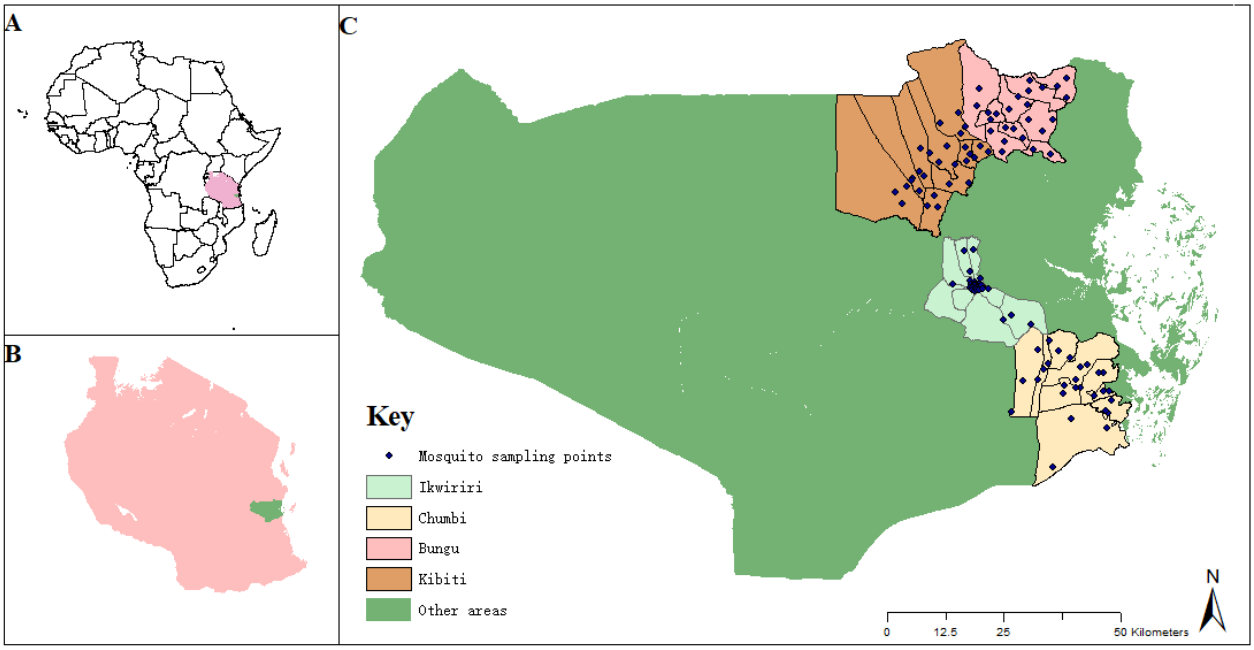

Figure 6.1. Map showing the location of the study area. **A** map of Africa showing the location of Tanzania **B** map of Tanzania shows Rufiji district **C** map of Rufiji district showing four wards where the study was conducted and mosquito collection points.

Household selection and mosquito sampling

The collection of mosquitoes was conducted into two phases. The study was conducted from September 2015 to March 2018. From November 2015 to May 2016 collections were conducted in four wards and from June 2016 March 2018 mosquitoes wee only collected from intervention communities. From June 2016 to December 2016 and from September 2017-March 2018, the data were only collected from intervention communities.

The selection of sampling household followed a stratified randomization approach taking into consideration whether the location of the household in the village is within an intervention or control wards of the 1,7-mRCTR approach (Mlacha et al. 2020). Mosquito trapping was conducted in 4 wards divided into control (Bungu and Kibiti) and intervention (Ikwiriri and Chumbi). Each ward compised with 9 villages making a total of 36 study villages for sampling, however, due to

geographical distance and logistical constraints of one, the hamlet namely Mtanange located in Ikwiriri wards was considered as villagem therefore totaling to 37 village for mosquito sampling.

The selection of houses at the village was stratified at the hamlet level which is the lowest administrative area. The stratification of houses selection to the hamlet level was to ensure eco-geographic representation of the sampling sites with regards to the spatial dispersal of the houses within the village. Three houses were then randomly selected as sentinel houses, which was maintained throughout the study period. Inclusion criteria for the house was based on three important features, 1) at least two permanent occupants, 2) at least three spaces for setting two traps and 3) Household residents sleep under bed-nets. The selection of three houses per village from each of the 37 villages made a total of 111 mosquito sampling houses spanning all over the project area.

For each house, mosquitoes were collected using two different traps (Centre for Disease Control Miniature light trap (CDC-LT) and resting bucket traps(RB-T). The CDC-LTand 1 RB-T were set indoors to capture host-seeking for estimating human biting rates (HBR) and indoor resting mosquitoes respectively. One RB-trap was set outside at five meters distance from the house for capturing outdoor resting mosquitoes. CDC-LT placed indoors, at a few cm from the ground at the foot of the sleeping space of a person sleeping under a bed-net. Collections of mosquitoes from the RB-traps was done using mouth aspirators. Collections was done from 6pm to 7am each night The trapping was done routinely for nine nights in a monthly. Live collected mosquitoes were suffocated and killed by using petroleum ether soaked into a small ball of cotton wool. Then, the immobile mosquitoes were transferred into airtight vacutainer tubes containing silica gel for storage and preservation before submission to the field entomological laboratory. Community-

based volunteers were recruited from each village and trained on how to and empty the trapped mosquitoes. For data quality assurance, the community-based volunteers received irregular supervisory visits by designated project staff. The supervisory visits were aimed at keeping the community-based volunteers reminded of the mosquito trapping procedures.

Mosquito identification

Mosquitoes were morphological identified based on the criteria of Gillies and Coetzee (Gillies and Coetzee 1987). Female mosquitoes were sorted, counted and categorized based on their abdominal status (unfed, partly fed, fully fed, and gravid). Female Anopheles mosquitoes were stored in Eppendorf tubes (1.5 ml) with silica gel desiccant and cotton before transport to the laboratory for polymerase chain reaction (PCR) assay for speciation and the Enzyme-Linked Immunosorbent Assay (ELISA) for P.falciparum sporozoites detection. All Culicines were counted, categorized as male or female, and discarded. Data collected were recorded using the designated data collection forms (Kiware et al. 2016). The polymerase chain reaction PCR used deoxyribonucleic acid (DNA) extracted from a wing or a leg of every mosquito of the sample selected for species analysis with PCR. To distinguish sibling species of the *An. gambiae* complex, PCR targeted the gene at the internal transcribed spacer region 2 (ITS 2) of the ribosomal DNA as per technique by Scott et al (Scott et al. 1993). For *An. funestus s.l*, the same gene, (ITS 2), which determines species-specific single nucleotide polymorphisms (SNP), was targeted using techniques developed by Koekemoer et al (Koekemoer et al. 2002).

Statistical analyses

Data were analyzed using R version 3.1.0 software. The total number of mosquitoes collected from each village was obtained by summing all mosquitoes collected. Human biting rates (HBR) were calculated by dividing the total number of mosquitoes collected by the number of traps used to collect host-seeking mosquitoes. In this project, only CDC-light traps were used to capture host-seeking mosquitoes. Thus, human biting rates (HBR) were calculated based on mosquitoes collected using CDC-light traps only [64]. The human biting rates per ward were calculated by dividing the total number of mosquitoes collected in the award by the number of CDC-light traps. HBR was calculated by dividing the total number of mosquitoes collected by CDC-light traps by the total number of traps. The total number of female mosquitoes and biting rates for the major malaria vectors was compared between wards, villages, and months. Comparing the HBR among wards, villages, and months for determining differences in their variability level was made using a chi-squared test. The spatial distribution of HBR using maps, the HBR data were inputted into raster maps using ArcGIS 10.5 software (ESRI, Red lands, CA USA). From PCR for species identification, the proportions of sibling species within each of two complex groups, An. gambiae s.l and An. gambiae s.l were determined.

6.4 Results

Description of density data and its distribution

Table 6.1 presents the total collected numbers of mosquitoes among the study wards. A total of 116,978 mosquitoes were collected from four wards. Culex species were the most abundant 87,478(74.78%). Anopheles species constituted 24,715 (21.13%) of all mosquitoes. Other species collected were Mansonia spp, 4,297(3.67%), Aedes spp, 487(0.42%), and Coquilettidia, 1(0.0009%).

Table 6.1. General occurrence and composition of mosquito species in the area

No. traps	Mosquito species	Number collected	Percentage
17291	*An.gambiae s.l*	20078	17.16
	An. funestus s.l	4558	3.90
	Other Anopheles species	79	0.07
	Aedesspp	487	0.42
	Mansonia spp	4297	3.67
	Culex spp	87478	74.78
	Coquilettidia	1	0.00
Total	NA	116978	100

Of all (24,715) female Anopheles mosquitoes we collected from the entire study area, 24,636 (99.68%) belonged to two species, *An. gambiae s.l* and *An.funestus s.l*, the species known to be the major vectors of malaria in Africa. *An. gambiae s.l* constituted the bigger proportion (81.5%)and the proportion of *An. funestus* s.l was 18.5%. In every ward, *An. gambiae s.l* made the highest proportion (more than 90%) except in Kibiti, where the proportion of *An. funestus s.l* was slightly higher (58.85%) than that of *An. gambiae s.l* (41.15%) (**Figure 6.2**).

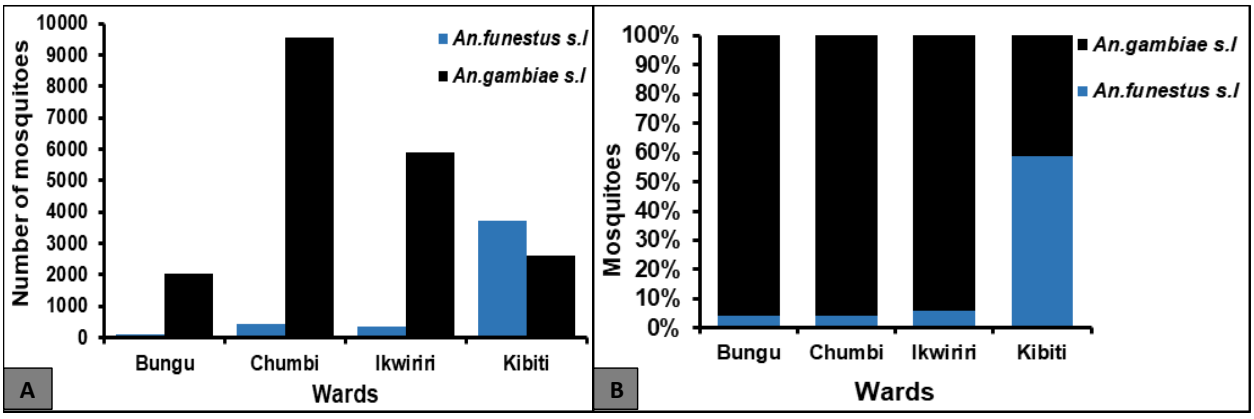

Figure 6.2. Densities and proportions of the major malaria vector species, *An. gambiae s.l* and *A.funestus s.l* among wards. A number of female *An. gambiae s.l* and *An.funestus s.l* collected per ward. B proportions *An. gambiae s.l* and *An.funestuss*.l.*An. gambiae s.l* constituted the biggest proportion >90% of all mosquitoes in all ward except Kibiti where 41.15% was recorded. Densities of the two species varied among awards.

Distribution *An. gambiae s.l* among wards

Of all (20,078) *An. gambiae s.l* collected from the four wards, the highest number 9562/20078 (47.62%) was collected from Chumbi ward and the lowest number 2035/20078(10.14%) was from Bungu ward. The other two wards, Ikwiriri and Kibiti, contributed 5892/20078(29.35%) and 2589/20078(12.90%) respectively (**Figure 6.3**).

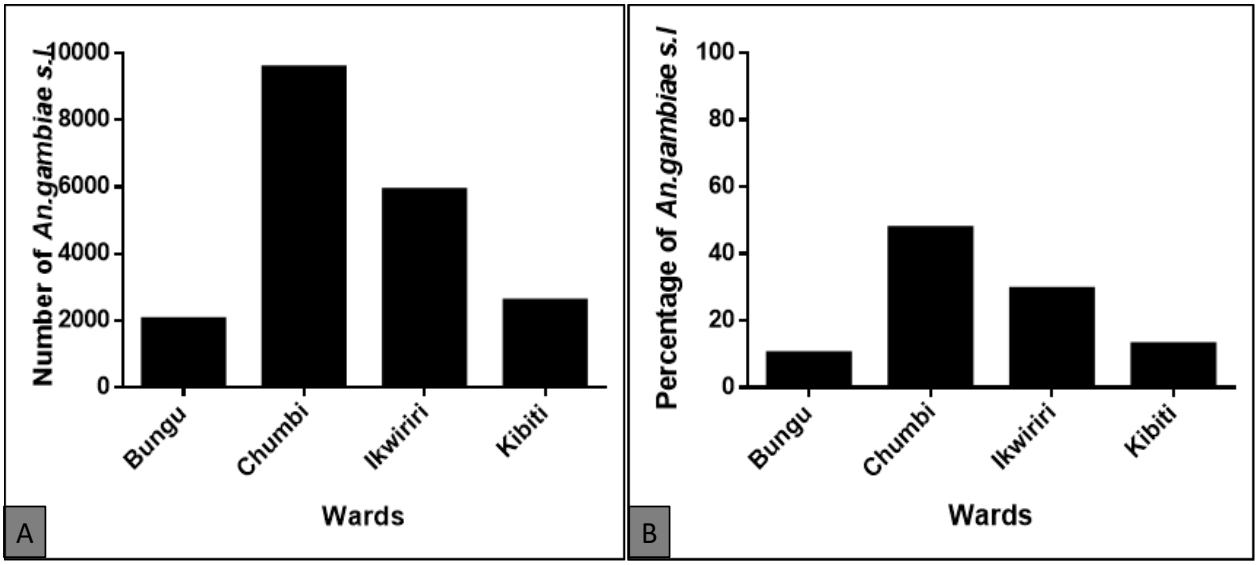

Figure 6.3. Distribution *An. gambiae s.l* among wards. A.number of *An. funestus s.l* collected per ward. B. proportional distribution of *An.funestus s.l* among wards

Distribution *An. funestus s.l* among wards

From the four wards, a total of 4,558 female *An.funestus s.l* was collected. The highest number of the mosquitoes in this group (3,703 (81.24%) was collected from Kibiti ward, and the lowest number, 84(1.84%) was collected from Bungu. Chumbi and Ikwiriri had almost equal number of the mosquitoes, 413(9.06%) and 358(7.85%) respectively (**Figure 6.4**).

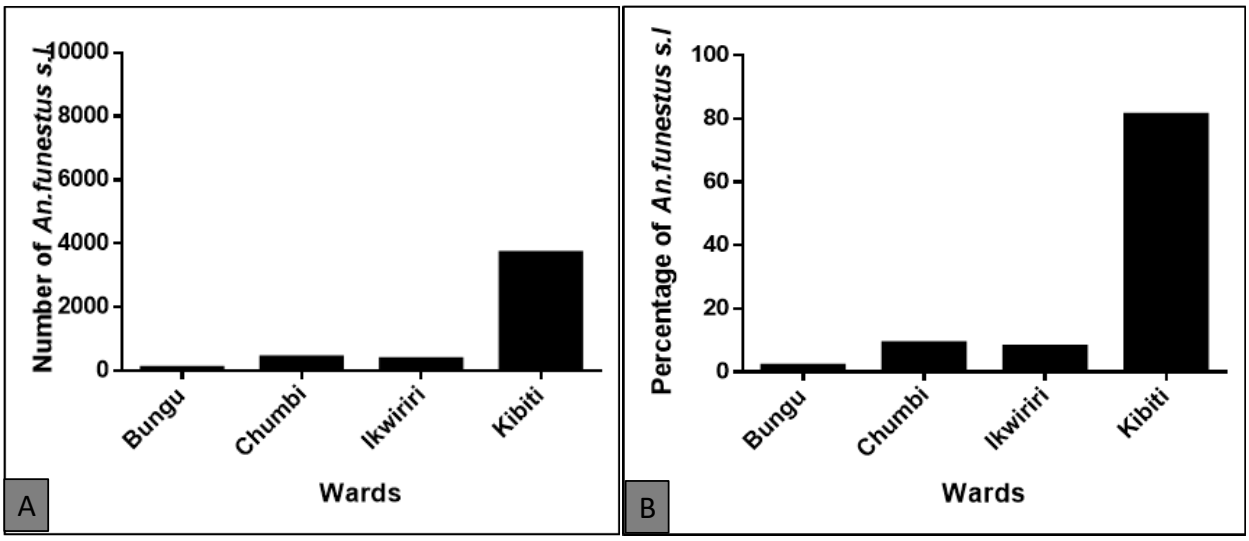

Figure 6.4. Distribution *An. funestus s.l* among wards. Anumber of *An. funestus s.l* collected per ward. B proportionsof *An.funestus s.l* among wards

Distribution of otherAnophelines

An. pharoensis and *An. ziemanni* were detected in Ikwiriri ward only, but at very low numbers, 12/6307(0.19%) and 10/6307(0.16%) respectively.*An. coustani* was detected in all the wards except Chumbi, but also at a very low density of less than 1% of all mosquitoes collected in each ward; 2 (0.09%), 35 (0.55%) and 20 (0.23%) for Bungu, Ikwiriri and Kibiti respectively.

Variation in human biting rates of *An. gambiae s.l* and *An. funestus s.l* among wards

Using CDC-light traps, we collected 24,328 female mosquitoes, which belonged to the two major malaria species; *An. gambiae s.l* 19,815 (81.45%) and *An. funestus s.l* 4513(18.55%). The results indicate that there was a significant HBR variation between species and among wards (χ^2=1201.2, df = 3, p<0.01) and villages (χ^2=9906.8, df = 36, p<0.01).

Overall biting intensities for *An. gambiae s.l* and *An. funestus s.l*

Chumbi ward recorded the highest overall HBR of 6.81bites/person/night. The HBR in Ikwiriri and Kibiti wards were almost equal; 3.98 and 4.33 bites/person/night, respectively. Bungu ward had the lowest overall HBR of 1.57bites/person/night. For *An. funestus s.l,* Kibiti ward had the highest HBR of 2.55 bites/person/night than the other three wards (χ^2=7443.9.8, df = 3, p<0.01). The lowest HBR from *An. funestus s.l* (0.06bites/person/night) was recorded in Bungu ward.Chumbi and Ikwiriri had almost equal HBR, 0.28, and 0.23 bites/person/night, respectively **(Figure 6.5).** For *An.gambiae s.l,* the highest HBR (6.53bites/person/night) was recorded in Chumbi ward followed by Ikwiriri, 3.75bites/person/night (χ^2=7213.9, df = 3, p<0.01). Bungu and Kibiti had almost equal and the lowest HBR, 1.5, and 1.78 bites/person/night, respectively **(Figure 6.5).**

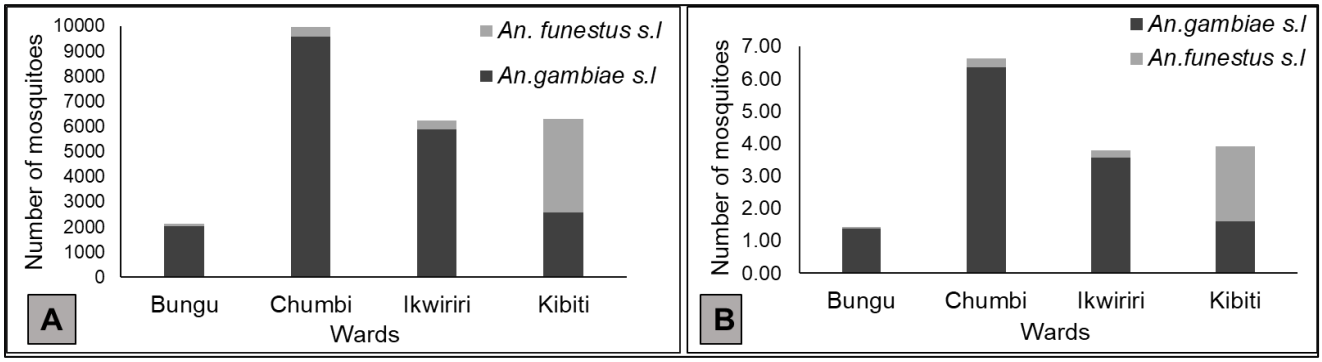

Figure 6.5. Variation in the biting intensities of the major malaria vectors among wards. **A** number of *An. gambiae s.l* and *An. funestus s.l* mosquitoes collected from each ward. **B** daily mean bites from the major malaria vectors among wards.

Variation in biting intensity among villages

Within wards, villages showed significant variations in the biting rates of *An. gambiae s.l* (χ^2=59240, df = 36, p<0.01) and *An. funestus s.l*(χ^2=23590, df = 36, p<0.01). In the Bungu ward, there a total of 2,115 mosquitoes,2031 belonging to *An. gambiae s.l* and84 to *An.funestus s.l* were collected, only one village (Nyambili) contributed>78% of all the mosquitoes. While the overall

HBR for the ward was 1.5bites/person/night, and less than 2 in each of the other villages within the ward, the HBR for Nyambili was 10.1 bites/person/night, mainly by *An.gambiaes.l.* In the Chumbi ward, where overall mosquito density (9418) was recorded, more than 50% of all the mosquitoes were concentrated in only two villages, King'ongo (30.57%) and Kiwanga (28.21%). The overall biting rates for Kiwanga andKing'ongo were 20.23 and 18.32bites/person/night, respectively. In the other ward's other villages, HBR ranged from 0.45bites/person/night in MuhoroMagharibi to 7.01 bites/person/night in Shela. In the Ikwiriri ward, only one village out of ten carried more than 75% of all mosquitoes and had the highest HBR of 38.1 bites/person/night. In contrast, in the other villages within the same ward, the HBR ranged from 0.02 to 2.18 bites/person/night. In the Kibiti ward, the HBR among villages varied from 4.65 bites/person/night(the highest) in Ngulakula village to 0.03bites/person/night, which was the lowest Mtawanya B village **(Figure 6.6 and 6.7).**

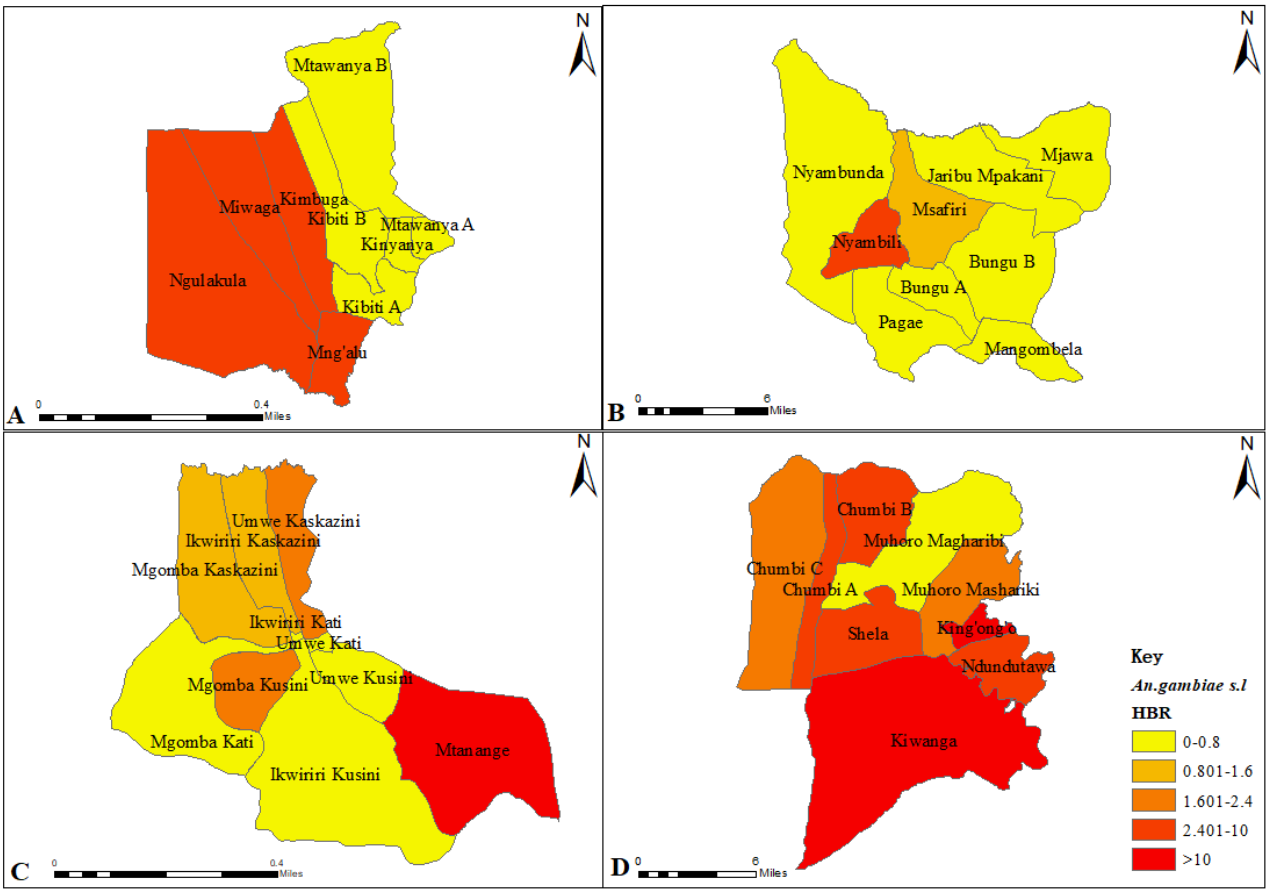

Figure 6.6. Map showing variation in the HBR of An. gambiae s.l among villages of four wards. The presented here are overall six months HBR for each village in the four wards. **A** Kibiti**, B**Bungu**, C** Ikwiriri**, D** Chumbi.

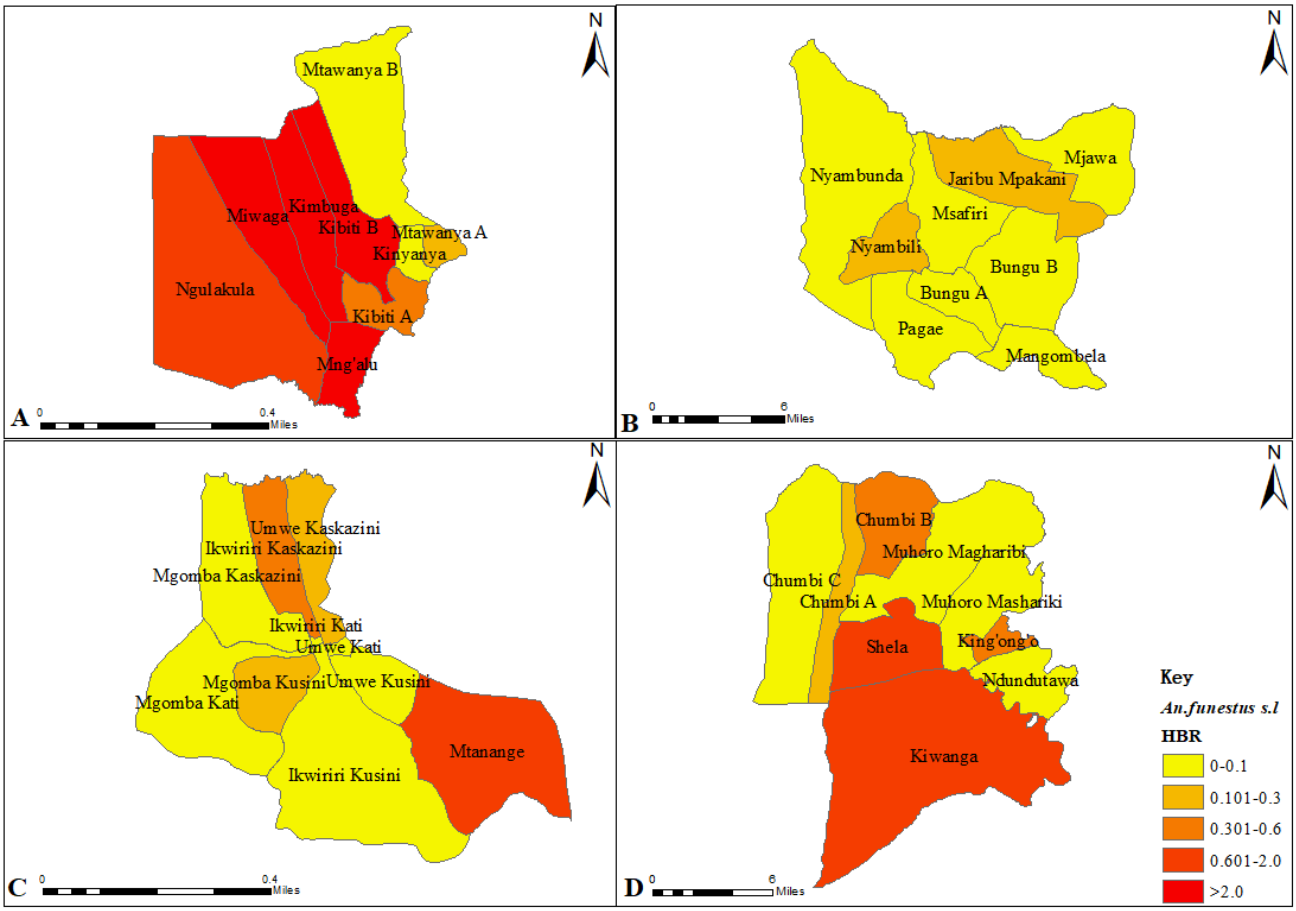

Figure 6.7. Map showing variation in the HBR of *An. funestus s.l* among villages of four wards**.** The presented here are overall six months HBR for each village in the four wards. [**A]** Kibiti**, [B]** Bungu**, [C]** Ikwiriri**, [D]** Chumbi

Temporal variation in mosquito species distribution and biting intensity among and within wards

The biting intensities of mosquitoes among villages varied significantly with months. Generally, the months of high mosquito densities and HBR were April with a peak in May. The densities and HBR declined drastically to > 5bites/person/night in many areas (χ^2=1201.2, df = 3, p<0.01)**,** except in areas with An. funestus species, where the densities remained persistently high (>5bites/person/night) in June **(Figures 6.6 and 6.7).**

Figure 6.8. Monthly variation in the human biting rates of *An. gambiae s.l* among villages

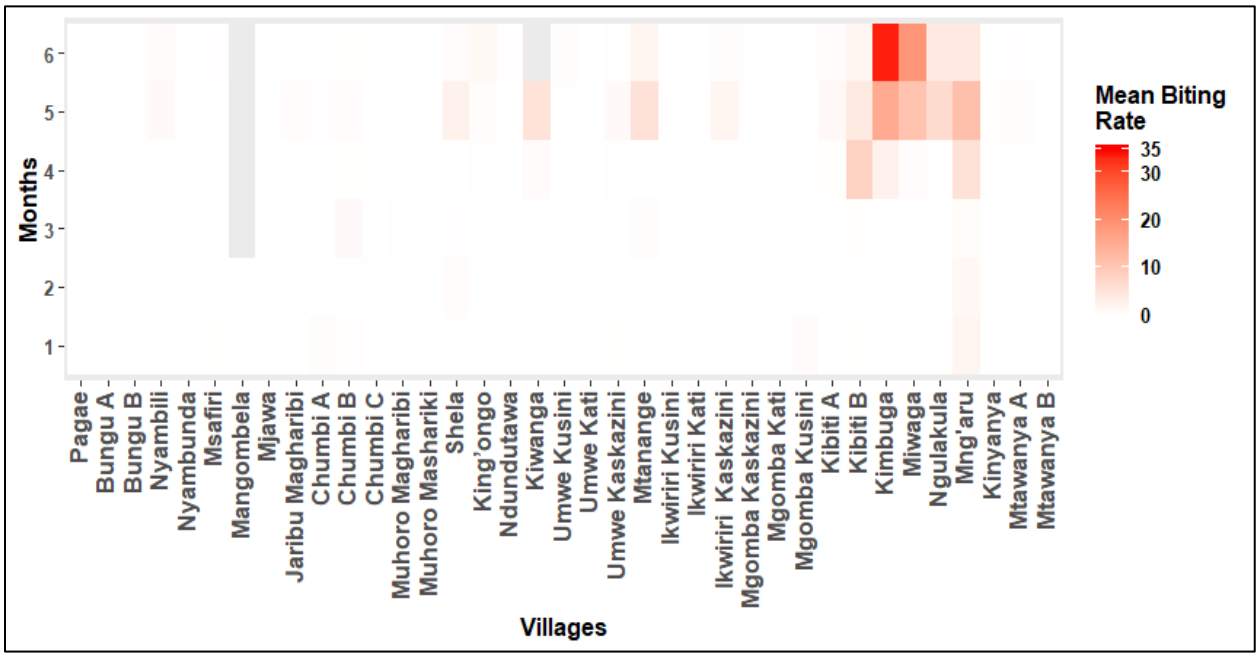

Figure 6.9. Monthly variation in the human biting rates of *An. funestus s.l* among villages

Sub-species of *An. gambiae s.l* and *An. funestus s.l* as identified by PCR

From 20,078, the total *An. gambiae s.l* we collected, 4,538 mosquitoes (22.60%) were assayed with PCR to identify the sibling species. Of all the samples tested, 91.85% amplified. *Anopheles arabiensis*, *Anopheles gambiae s.s*, and *Anopheles merus* were the sub-species identified. *Anopheles arabiensis* constituted the biggest proportion (62.11%) of all mosquito sub-species belonging to this group. *Anopheles gambiae s.s*and *Anopheles merus* constituted 14.25 and23.63%, respectively. For sibling species identification in the *An. funestus s.l*, 1060 (23.25%) samples were assayed, and 907 (85.57) amplified. The sibling species identified in this group were *Anopheles funestus s.s* (96.25%), *Anopheles leesoni* (2.98%), *Anopheles rivulorum* (0.66%), and *Anopheles parensis* 0.11%.

Distribution of the sub-species of *An. gambiae s.l* and *An. funestus s.l* among and within wards

The proportions in the sibling-species composition varied within their complex groups and among wards**(Figure 6.9).** In Bungu ward, *An. gambiae s.s* made the biggest proportion (85.2%) of all sub-species. In Chumbi and Ikwiriri wards, the largest proportion was made by *An. arabiensis*; 63.38 and 84.10%, respectively. In Kibiti, *An. funestus s.s* constituted the largest proportion (55.61) of seven species detected in the area. Of the four wards, only Bungu had the biggest proportion of *An. gambiae s.s* while in Kibiti, the largest proportion was madeAn.funestuss.s. The highest proportion of *An. merus* occurred in Chumbi, the ward, which also recorded the largest proportions of *An.arabiensis*. The variation in the proportions of the composition of sub-species among villages is as shown in **figure 6.10**.

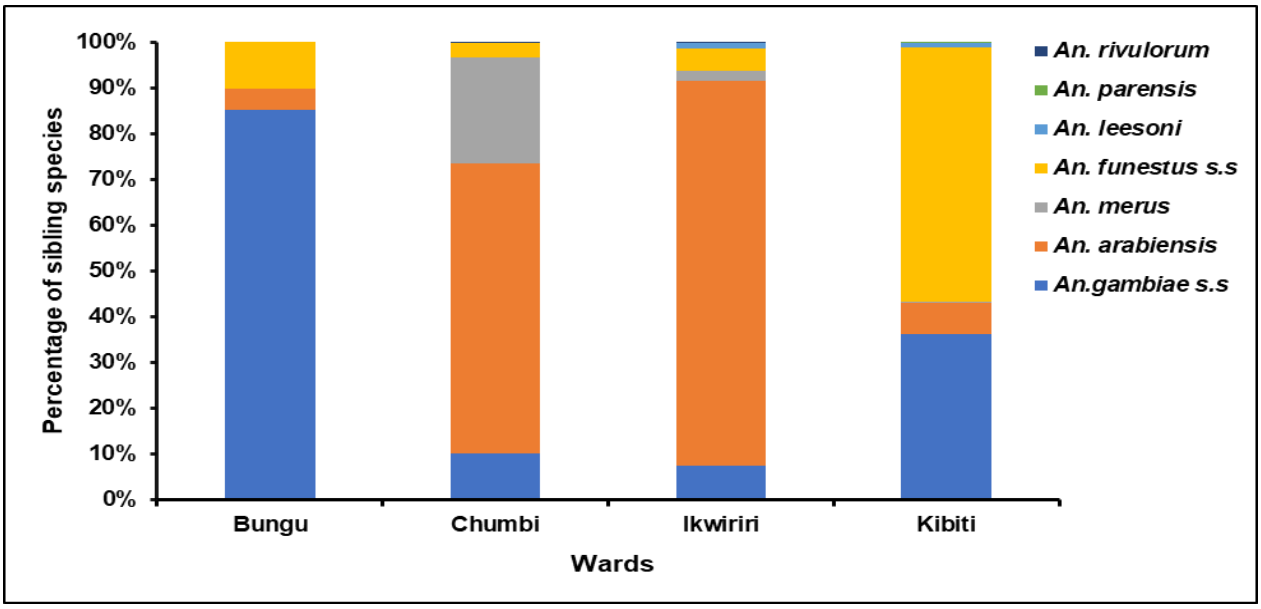

Figure 6.10. Difference in the proportions of the composition of malaria vector sub-species among wards

Figure 6.11. Proportions of the composition of in the sub-species of *An. gambiae s.l* and *An. funestus s.l* among villages

6.5 Discussion

This study examined how entomological malaria transmission indicators varied between Rufiji district wards and villages. The results demostrate spatial and temporal variations in malaria vector species, diversity, and distribution among wards and villages. More than decade ago, a research conducted in the same district found ward-level (Kigadye et al. 2011). In this study, we examined how malaria transmission entomological indicators varied between villages within wards, going beyond the ward level assessment. Indeed, there was difference in the occurrence, diversity, and concentrations of mosquito species between villages.

The findings of this study revealed that mosquito species' occurrence, proportions in their composition, and densities varied with the level of settlement development and their pattern. Based on the existing knowledge, comparatively, more developed settlements have lower densities of malaria mosquitoes and disease burden than less developed settlements(Kaindoa et al. 2016, Maghendji-Nzondo et al. 2016). For this study, villages located in or near ward centers had relatively lower numbers of Anopheles mosquitoes than other villages located away from the centers. Similarly, a study by (Finda et al. 2018) showed that areas they described as more urbanized in Ifakara town had significantly higher densities of mosquitoes than those categorized as peri-urban.

Multiple species coexisted in more than 90 percent of the study villages, although their proportions of composition varied between villages. From the existing knowledge, the identified co-existing malaria vector sub-species mainly *An. arabiensis*, *An. gambiae s.s*, *An. merus* and *An. funestus s.s* differ in terms of behavior and ecology (Kitau et al. 2012, Lwetoijera et al. 2014, Mwangangi et al. 2013). As the ITNs will continue to be used in the area , plus the pre-arranged but yet to be deployed larvicides, the diverse behavioral and ecological aspects of these species should be

considered during implementation effectiveness of interventions. The ITNs, our mainstay vector control tool are effective against mosquitoes that feed and rest indoors, such as *An. gambiae s.s* and *An. funestus s.s* but less effective against other species such as *An. Arabiensis* and *An. merus*, known to have opportunistic host choice traits and feeding and resting outdoor (Kipyab et al. 2013, Mahande et al. 2007, Tirados et al. 2006). While there is no doubt that *An. arabiensisis* an important vector of malaria (Lwetoijera et al. 2014, Mendis et al. 2000, Mwangangi et al. 2013, Temu et al. 1998), several studies have reported that *An.merus* also plays an important role in disease transmission (Kipyab et al. 2013, Pock Tsy et al. 2003). The use of bed nets alone may not be able to control the disease in locations where these two species have been detected, based on the two vector species. Since these species exhibit resilient behaviors and are less vulnerable to the currently widely utilized ITNs, vector management in the majority of Rufiji villages will necessitate the development of additional new tools to specifically target them. The description of the diversity and distribution of the vector species provided here offers fundamental information that may help with the successful implementation of a variety of vector control interventions, such as the planned larval control with *Bacillus thuringiensis israelensis* (Bti).

This study also outlined the distribution of mosquito species and densities over the course of six months of the year. HBR of *An. gambiaes.l* significantly rose from April to May, peaked in May, and then began to fall in June as the dry season started. The Kilombero valley and the surrounding area have both previously reported on a similar trend in the temporal distribution of the two vector species (Finda et al. 2018, Kigadye et al. 2011). The explanation offered here sheds light on the selection of interventions appropriate to the vectors found within the relevant time periods. Identifying and targeting the breeding habitats at the beginning and during the dry season, when the habitats' sizes have decreased, as an additional intervention, could help to suppress the vector

population that sustains malaria transmission during the dry season, for instance, in areas like the Kibiti ward, where *An. funestus s.l.* was dominant. It would be imperative to expand the reach of measures that can decrease the adult vector population from April to June in locations where we found high HBR in order to lower the biting and transmission risks, which appear to be exacerbated by seasonality.

The significant variation in entomological indicators of malaria transmission observed among villages suggests that in low and moderate transmission settings, characterization of transmission at the ward level may either underestimate or overestimate the actual spatial heterogeneity in transmission levels. For example, the ward with the most MBR had 7 bites/person/night (in Chumbi), whereas the ward with the lowest had 1.5 bites/person/month (in Bungu). In comparison, the MBR ranged from 73 bites/person/night for the village and month with the greatest MBR (Mtanange in May) to 0 bites/person/night for the village with the lowest MBR within same month (Mangombela) (Figure 6.7 and 6.8). As a result, the fine-scale entomological description offered here demonstrates how small areas at the village level may differ in terms of malaria transmission indicators. Understanding this important entomological variable provides an evidence-based decision about where to invest the limited resources for appropriate and equitable levels of intervention.

However, despite the detailed fine-scale description given here, which would be used as a baseline guide towards implementing the now very important vector control interventions in the area, some important entomological aspects remain unaddressed, thus, posing as limitations of this study. We identified more than three mosquito sub-species that are known to be important vectors of malaria. They showed that in most of the villages, the species co-existed and emphasized theneed to have

interventions that target diverse behaviors of multiple species (Govella et al. 2013, Govella and Ferguson 2012b, Killeen et al. 2017b). Nevertheless, our recommendation is based on pre-existing knowledge of the vector species' behaviors. While it is known that mosquito behaviors have been evolving (Carrasco et al. 2019) following the use of insecticides-based control tools and that understanding the current behavior of prevalent mosquitoes is important (Killeen et al. 2006, Killeen et al. 2017a, Killeen et al. 2017b) this study does not address this important aspect. Therefore, a study of the current behavior of the mosquitoes in the area and how they coincide with human activities and behavior proliferate disease transmission will add important information to the description given here.

In addition, all of the principal vector control strategies available today use insecticides, it is crucial to choose the right instruments and reduce resistance by being aware of how susceptible vectors are to insecticide-based control and the tools being used. However, this article makes no mention of the local mosquito population's current level of insecticide resistance. The majority of Tanzania's malaria vectors have evolved resistance to insecticides, according to the country's established insecticide resistance monitoring system (Kabula et al. 2014, Kisinza et al. 2017, Matowo et al. 2017). The national level characterization based on sentinel districts, however, might not address fine-scale variances among wards and villages (Matiya et al. 2019, Matowo et al. 2019, Ochomo et al. 2014, Opondo et al. 2016). The available evidence has shown that resistance status and mechanism in mosquitoes may differ spatially (Chanda 2015, Coetzee and Koekemoer 2013, van den Berg et al. 2021) and among different species (Opondo et al. 2016) and affect intervention variably (Ranson et al. 2011). In the villages of south-eastern Tanzania, (Matowo et al. 2017) described micro-level heterogeneity in the level of mosquito pesticide resistance. Understanding

the susceptibilities of the various mosquito species that are still present in the Rufiji Valley will be crucial when deciding on the best course of action.

Moreover, the variation in the distribution of the entomological indicator of malaria transmission that we have described here is consistent with the distribution of the malaria burden in the region, as reported by (Khatib et al. 2018). According to an epidemiological analysis of the region, Chumbi had the greatest parasite burden among the four study wards and Ikwiriri had the lowest. With the exception of Mtanange village, where HBR was the greatest of all the research villages, this entomological study also coincidentally recorded the highest HBR in Chumbi and the lowest in Ikwiriri (Figure 6.7). This coincident pattern of parasite and vector load at the ward level raises the prospect of a positive association between parasite and vector clustering among the local villages, which has not before been described. Despite a study in Dar es Salaam city making a different observation, this parasite-vector coincidence has also been recorded elsewhere (Mwakalinga et al. 2016). Mwakalinga et al. did not find a positive correlation between malaria parasite clustering and hot spots of vector proliferation. Nevertheless, it should be noted that Dar es salaam city, where this study was conducted, differs greatly from this study area, in the Rufiji valley, in terms of ecology, transmission levels, human settlement development level, types, and pattern. Therefore, for this study, it would be crucial to determine whether the village-level entomological indicators we describe interacted positively with the parasite prevalence in order to determine the applicability of the focused vector control actions we suggest.

Lastly, the importance of mosquito species as vectors of malaria transmission can be determined by their disease transmission role, which is captured through infection rates (Killeen 2014, Killeen et al. 2018, Lwetoijera et al. 2014). Apart from describing the species diversity and how they were

variably distributed among wards and villages, this study does not report the vectors' infection status and levels in the area and how they differed among species and villages. Understanding how much the different species identified contributed to the disease transmission and how the transmissions were distributed among different villages would help vector incrimination, estimation of transmission levels, and equitable allocation of control intervention.

6.6 Conclusion

The burden of malaria in Tanzania is declining considerably due to several interventions measures over the past two decades to control the disease. Considerably, the disease prevalence has declined below 5%, except in some regions, including the southern part. Understanding vector ecological traits and behavior and how variedly the vector species are distributed in time and space is important for deciding on the allocation of appropriately targeted interventions. The fine-scale entomological description provided here, showing the variation of malaria vector composition, forms a basis for understanding the dynamics of malaria risk to guide an evidence-based decision on how well resources should be allocated to control vectors in the area.

Ethical approval

The Medical Research Coordination Committee of the National Institute of Medical Research granted the permit to conduct the study's ethics approval (NIMR/HQ/R.8a/Vol.IX/2005). Institution ethical approval was also obtained from the Ifakara Health Institute Institutional Review Board (IHI/IRB/No: 18-2015) and the Chinese Centre for Disease Control (201505). Informed consent was obtained directly from the head of the households

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Competing interest

All the authors declare that they have no competing interests

Authors' contributions

XZ, SA, NX, WD, and PC conceived and developed the study concept. TG, PC, YM, ZZ, and LK designed the study protocols and standard operating procedures. XZ, SA, NX, PC, R K, WD, MM GC, and PC reviewed the study designs and protocols. YPM, TG, and PC supervised the implementation of the longitudinal mosquitoes surveillance study. YM, JZ, and TG analyzed data. TG and YPM drafted the manuscript. All the authors reviewed the manuscript and approved it for publication.

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Chapter 7: General discussion and conclusion

7.1 Discussion

The purpose of this PhD thesis was to examine the dynamics of malaria transmission and analyze the effectiveness of a community-based malaria reactive case detection technique in enhancing transmission-reduction of human malaria infections in areas with high LLIN coverage. The study was embedded within a tripartite pilot project between China, the United Kingdom, and Tanzania. Malaria control was the focus of the initiative, which began in September 2015 in Tanzania's Rufiji district. The project was sponsored by the UK Department for International Development and supported by the China-UK Global Health Support Programme (DFID). The pilot project deployed integrated, evidence-based strategies tailored to local malaria epidemiological profiles ensuring broad community participation. Moreover, improve local capacities to test, treat, and track using the Chinese experience surveillance and response model on malaria control and WHO-T3 strategy.

Following the particular objectives outlined in Chapter 2, each chapter of the thesis presents a full discussion, limitation, and conclusion of the findings. The significant findings are summarized in this chapter, as well as the limitations and implications of the available evidence and policy recommendations, as well as the remaining gaps that need to be researched.

7.2 Summary of the key findings

Surveillance is recognized as an intervention and is considered instrumental in accelerating global malaria elimination efforts. In chapter three of this thesis, evaluates the effectiveness of using community-based testing and treatment to reduce the malaria burden in areas with moderate to high transmission was designed and evaluated. The community-based testing and treatment

strategy was adopted by modifying the Chines surveillance and response "1-3-7" model's experience and the WHO-T3 strategy into the 1,7-mRCTR. The 1,7-mRCTR) is a locally-tailored approach for reporting febrile malaria cases in malaria endemic villages. This strategy of using surveillance as an intervention. Here, existing health facility data and locally trained community health workers conducted community-level testing and treatment. Temporal data was utilized to select high incidence villages in which follow-up testing and treatment was conducted at village leve as unit of operation. Implementation of the 1,7-mRCTR contributed convincingly to the reduction of the malaria burden in areas of moderate and high transmission in southern Tanzania and offers the first attempt at implementing surveillance as an intervention in areas with high malaria burden. This locally tailored approach strengthens health systems, reporting and response frameworks and demonstrates potential to accelerate malaria control and elimination efforts.

The success of the 1,7-mRCTR intervention is primarly attributed to its design and the respective processes. Sub-optimal case-based health facility data collection, collation and use for timely decision making for identifying and targeting foci. A common practice in most malaria endemic countries is the aggregation of individual malaria positive cases by HFs during routine passive testing and treatment. This blurs the actual burden of malaria cases at sub-national and sub-district levels eliminating the opportunity to tailor and target responses and allocate resources optimally. Additional, lack of adequate workforce capital and public buy-in for sustained solutions. Community centred approaches have demonstrated high levels of impact (Kern et al. 2011, Mlacha et al. 2020, Tiono et al. 2013). Local buy-in and ownership results in maximum participation of community members especially when receiving an intervention of choice. Top-down approaches (MoH-led) rarely include communities in decision-making resulting in a lack of awareness alongside a ‘separation’ from the implementation – often resulting in suspicion and refusals to

participate. In this project, data was timely reported and used to identify weekly priority areas for screening and treatment by local CHCWs teams. The disaggregated resident information to the near point related to the patient's home allowed the study to identify specific malaria hotspot villages for 1,7-mRCTR intervention. At the current moment, this is impossible because routine health information is being reported monthly and aggregated to HF and district levels. Furthermore, the study demonstrated the feasibility of using modestly trained community members (CHCWs) to implement the intervention and rapidly reducing the malaria burden.

In Chapter four, the household survey data was used to characterize and profile the malaria parasite burden between the study ward and identify the related malaria risk exposures. Within the current malaria sub-national stratification approach, the Rufiji district located in Tanzania's southern zone is classified as high malaria transmission strata. However, within the district, the risk of disease transmission varies significantly between wards. Despite the widespread ownership and use of LLINs in this district compared to other districts in Tanzania, malaria remains a problem for most communities. Therefore, this chapter discusses the implications of study findings in the context of current intervention on malaria control strategies referencing the TDHS–MIS 2015–2016 findings at the national and district level.

This project's findings reported an average malaria parasite prevalence of 13% across the selected site, which is higher than the national reported average of 7.3%. The transmission of malaria varies between wards ranging from the lowest of 5.6% to 18%. The study observed that the population residing far from the district centers had the lowest ownership and bed net usage. The association between SES and malaria burden was significant in our study. The lowest parasitemia was

observed in the ward with the highest proportion of the highest SES. Moreover, urbanized wards had the lowest malaria parasitemia levels compared to strictly rural wards.

In a general context, the malaria burden is now concentrated on the fringes of the settlements where the poorest section of the population is concentrated. LLIN usage is lower than the national average and targets set by national and global malaria control initiatives. Additionally, the findings pinpoint that school-age child had higher odds of malaria risk than under-fives with the lowest LLINs coverage. People who slept under LLINs had a 60% reduced malaria risk compared to non-users. The fifth chapter measured and evaluated one of the most sensitive epidemiological indices of malaria transmission (host preference by malaria vectors). In addition to being one of the most important determinants of malaria transmission dynamics, this indicator significantly influences the selection and effectiveness of malaria vector control interventions. The host preference of the principal malaria vector species, *An. arabiensis* and *An. gambiae s.s*, was evaluated in two contrasting ecological environments in Tanzania utilizing the direct host-preference experiment in open field sites. The results indicate that urban *An. arabiensis* had a stronger preference for cattle than the rural population. favored livestock more than its rural counterparts.

In contrast to historical records, urban *An. gambiae* displayed no clear preference for either humans or cattle. This research shows that mosquitoes that transmit malaria are also adapting to environmental change. Consequently, it is essential to characterize the feeding behavior of malaria vectors in a variety of ecological situations prior to applying behavior-based interventions with significant impact. It is also crucial to note that, regardless of the underlying forces for the observed changes: whether short or long term, they both highlight limit with existing interventions and provides opportunities for complementary interventions, if elimination of malaria vectors or

malaria is to be realized. To realize malaria elimination we need to more thouroughly have an understanding of the prevailing vectors, their feeding preferences. This will allow us to more appropriately design and deploy the right set of measures. Moreover, cattle keeping may limit the efficacy of existing human-targeted vector control interventions (LLINs and/or IRS), but it also offers chances for effective control using additional interventions, such as veterinary techniques including the use of endectocides (Ivermectin) (C. Chaccour & Killeen, 2016; C. J. Chaccour et al., 2018).

In chapter 6, the data illustrated the evolution of the species composition of vectors throughout time. In addition, this study demonstrates the coexistence of several vector species of malaria with ecological variety. Human biting rates (HBR) in the four wards ranged from 1.5 to 73 bites/person/night. Intriguingly, the characterization of Anopheles vectors revealed an unequal distribution of *An. gambiae s.l.*, *An. funestus*, and *An. coustani* among villages and wards. To clarify the changing vector composition in the area, additional research is required.

Accordingly, updating this information could help the ongoing targeted intervention plan. We observed different compositions and densities of the *An. funestus* group, with this species and its sibling dominating one ward. It has been found that *An. funestus* is more infectious in other environments, showing diverse behaviors and ecological niches. Sustaining the established achievements in malaria control in the Rufiji district and accelerating the elimination of malaria would require more innovative strategies to combat the variability of vector species composition.

7.3 Implications of available evidence and policy recommendations

The results given in each chapter have significant implications for the existing malaria control effort in Tanzania and other contexts with similar epidemiological characteristics.

- The 1,7-mRCTR approach could be linked to the global technical strategy malaria control framework (GTS) and national level SMMSP technical guidance for malaria control and elimination guidance. The link is related to first, provide strategic approaches to accelerate efforts toward malaria elimination and second, uplifting of surveillance to core intervention in addition to Integrated Vector control and Diagnosis & Treatment. It offers easy strategic approaches to expedite Africa's malaria elimination efforts through interventions tailored to the local context. It provides the evidence-based data to help the national malaria strategies plan to incorporate the heterogeneity of epidemiology in a country by stratifying the malaria burden for effective targeted intervention tailored to respective strata. This is consistent with the most recent reviews of the national malaria strategy plan, which have recognized the need for a more strategic allocation of scarce resources to ensure continued progress.
- Effective community engagement in malaria control will be critical for the future of malaria control in Tanzania. On the other hand, making sure that malaria is appropriately diagnosed, adequately treated, and monitored will not be an easy task. This requires strengthening the health system at all levels, particularly on access, quality, and robust surveillance. The intervention results included community participation and improved partnership international and local stakeholders involved in the malaria control program hence better prospects for sustainability.Given an extensive network of geographically distributed health facilities in Rufiji and across the country where most of the population

lives in proximity of 5 km within the HFs catchment area. Optimizing and strengthening the routine HFs, data could benefit the NMCP defining the targeted intervention area. Despite the existing limitation, the HFs data prove to be a cost-effective method.

- The considerable variability of malaria prevalence observed at wards and village level supports the evidence that as malaria decline at the national level, the burden is shifting to other geographical locations. This suggests that while designing malaria prevention measures' uptake, the geographical areas should be a priority. It is essential to assess the socio-economic status of prevention and treatment uptake to ensure the intervention's sustainability. But importantly it matches perfectly well with the need of strengthening surveillance across fine scale and highlight the need for targeted control as described above.
- The lack of a system framework with appropriate methodologies that target the highly heterogenous rates of malaria infection towards accelerating burden reduction. The systemic and appropriate distribution of vector interventions, malaria diagnostics and treatments results in more or less equitable distribution to all disease (endemicity) strata. This is usually not compatible with presently seen spatial clustering of infections and results in suboptimal targeting and resource allocation. In addition, shifting population vulnerability, with school age children harbouring the majority of asymptomatic infections results in persistence of the parasite reservoir in humans and consequent sustained transmission. Intensifying the School Net Programme, which targets students, can reduce the risk of malaria infections and improve the use of bed nets. The initiative should be implemented concurrently with other malaria control methods and Tanzania's current policy of providing free primary education, which will result in an increase in student

enrollment. Targeting the school-age children will could maximizing the community effect of bednet.

- For practical choice and assessment of the impact of interventions, it is critical to understand the vector distribution and host preference exhibited by vectors species across distinct ecology settings due to existing variation in host preference within and between species. The practical implication is based on the results provided in chapters 5 and 6 on host preference and vector composition in different ecological settings.

7.4 Prospect for future research

On the basis of the preceding discussion and policy ramifications, the findings of this study thesis have direct implications for the continuing Tanzania control effort and other epidemiological settings with comparable conditions.

- The outcomes of the 1,7-mRCTR method serve as evidence for reducing the malaria burden in moderate-high transmission areas. The results support a comprehensive evaluation of the 1,7-mRCTR approach and the strategic approaches for accelerating malaria control and elimination efforts.
- This is provide an opportunity to strengthen the surveillance-response structure of the current national malaria control program (NMCP). Even if the decision does not result in an instant change in intervention, all monitoring data must be linked to a decision. The linkage of real-time data to the decision is what makes surveillance to become an intervention.
- Adopting CHWs for community case management could alleviate the overburden of the health system and increase efficiency, resulting in a more targeted use of limited resources.

Regular training, supervision, and official recognition related to the health system structure of CHWS are needed for the program's sustainability in order to improve CHWS outcomes.

- Further progress in the control and subsequent elimination requires efforts to concentrate on more impoverished population settlements.
- This study's results have indicated the co-existence of multiple malaria vector species with high diversity within the sub-district division. The levels of susceptibility to insecticides reported in the country, and ecology variation. It is unlikely that bednet use, the only primary vector intervention in the area, will be sufficient to control such highly diverse and resilient vector species.
- The selection of effective vector control measures may be erroneously influenced by the generalization of mosquito species' host preferences across vast geographies or the assumption that they would remain constant. Consequently, the characterization of vector feeding preferences across many ecological situations is advised as a crucial element of routine program surveillance.

7.5 Conclusions

The outcomes of this project represent the first attempt to evaluate a surveillance-response model that will fit the majority of malaria-endemic settings in order to advance the malaria elimination agenda. The appropriately structured and defined health facility data is instrumental in allowing the targeting of resources and interventions more appropriately. In regions with a high incidence of transmission, such as the districts of Rufiji, the existing interventions should be sustained. Nonetheless, the district must prioritize extra focused operations aimed at finding and eliminating transmission clusters with a high rate of transmission.

To continue with the malaria reduction gain and recognize the outcome of the targeted intervention. Surveillance must be improved to allow timely identification cluster of transmission. Besides, systems to identify and treat asymptomatic must be implemented. Most importantly, community participation from the beginning of any activity is important to warrant sustainability and acceptability. Regular updates regarding malaria transmission status across settings to the community must be considered to prevent falling back into non-compliance and adherence by the affected community.

The present study's findings on a spatial-temporal variation of vector composition on a small scale of village and the host preference from other Tanzania settings characterized with distinct ecological features highlight that the enhanced surveillance must incorporate vector surveillance. The reported heterogeneity of human infections at the small scale of wards level within the district highlights the need to advance our understanding of the dynamics of malaria epidemiology transmission concerning the current malaria control guidelines provided at the global and local levels. In light of the current sub-national malaria stratification, it is important to investigate other malaria transmission contextual factors. This will determine the feasibility, compliance, and adherence of intervention package in the local context, which is important for intervention stability. Most important, strengthening surveillance systems rely on average data reported at the district level (as a practice now). Robust surveillance requires disaggregated data available weekly at district levels to guide the response to malaria elimination efforts. The linkage of real-time data to the decision is what makes surveillance to be a core intervention.

References

Aidoo, E. K., Y. A. Afrane, M. G. Machani, W. Chebore, B. W. Lawson, H. Atieli, et al. (2018) Reactive case detection of Plasmodium falciparum in western Kenya highlands: effective in identifying additional cases, yet limited effect on transmission. *Malaria Journal,* 17**,** 111.

Alegana, V. A., J. A. Wright, U. Pentrina, A. M. Noor, R. W. Snow & P. M. Atkinson (2012) Spatial modelling of healthcare utilisation for treatment of fever in Namibia. *Int J Health Geogr,* 11**,** 6.

Alemu, K., A. Worku & Y. Berhane (2013) Malaria Infection Has Spatial, Temporal, and Spatiotemporal Heterogeneity in Unstable Malaria Transmission Areas in Northwest Ethiopia. *PLoS One,* 8**,** e79966.

Alonso, P. L., G. Brown, M. Arevalo-Herrera, F. Binka, C. Chitnis, F. Collins, et al. (2011) A research agenda to underpin malaria eradication. *PLoS Med,* 8**,** e1000406.

Alonso, P. L. & M. Tanner (2013) Public health challenges and prospects for malaria control and elimination. *Nat Med,* 19**,** 150-5.

Aregawi, M., M. Lynch, W. Bekele, H. Kebede, D. Jima & H. S. Taffese (2014) Time series analysis of trends in malaria cases and deaths at hospitals and the effect of antimalarial interventions, 2001–2011, Ethiopia. *PLoS ONE.,* 9.

Baba, E., P. Hamade, H. Kivumbi, M. Marasciulo, K. Maxwell, D. Moroso, et al. (2020) Effectiveness of seasonal malaria chemoprevention at scale in west and central Africa: an observational study. *The Lancet,* 396**,** 1829-1840.

Bayoh, M. N., D. K. Mathias, M. R. Odiere, F. M. Mutuku, L. Kamau, J. E. Gimnig, et al. (2010a) Anopheles gambiae: historical population decline associated with regional distribution of insecticide-treated bed nets in western Nyanza Province, Kenya. *Malar J,* 9**,** 62.

Bayoh, M. N., D. K. Mathias, M. R. Odiere, F. M. Mutuku, L. Kamau, J. E. Gimnig, et al. (2010b) *Anopheles gambiae:* historical population decline associated with regional distribution of insecticide-treated bed nets in western Nyanza Province, Kenya. *Malar J,* 9**,** 62.

Bayoh, M. N., E. D. Walker, J. Kosgei, M. Ombok, G. B. Olang, A. K. Githeko, et al. (2014) Persistently high estimates of late night, indoor exposure to malaria vectors despite high coverage of insecticide treated nets. *Parasit Vectors,* 7**,** 380.

Bejon, P., T. N. Williams, A. Liljander, A. M. Noor, J. Wambua, E. Ogada, et al. (2010) Stable and unstable malaria hotspots in longitudinal cohort studies in Kenya. *PLoS Medicine,* 7**,** e1000304.

Bhatt, S., D. J. Weiss, E. Cameron, D. Bisanzio, B. Mappin, U. Dalrymple, et al. (2015) The effect of malaria control on *Plasmodium falciparum* in Africa between 2000 and 2015. *Nature,* 526**,** 207-+.

Bhattarai, A., A. S. Ali, S. P. Kachur, A. Mårtensson, A. K. Abbas, R. Khatib, et al. (2007) Impact of artemisinin-based combination therapy and insecticide-treated nets on malaria burden in Zanzibar. *PLoS Med,* 4**,** e309.

Bonner, K., A. Mwita, P. D. Mcelroy, S. Omari, A. Mzava, C. Lengeler, et al. (2011) Design, implementation and evaluation of a national campaign to distribute nine million free LLINs to children under five years of age in Tanzania. *Malar J,* 10**,** 73.

Bousema, T., C. Drakeley, S. Gesase, R. Hashim, S. Magesa, F. Mosha, et al. (2010) Identification of Hot Spots of Malaria Transmission for Targeted Malaria Control. *J Infect Dis,* 201**,** 1764-1774.

Bousema, T., J. T. Griffin, R. W. Sauerwein, D. L. Smith, T. S. Churcher, W. Takken, et al. (2012) Hitting Hotspots: Spatial Targeting of Malaria for Control and Elimination. *PLoS Medicine,* 9**,** e1001165.

Breman, J. G., M. S. Alilio & A. Mills (2004) Conquering the intolerable burden of malaria: what's new, what's needed: a summary. *Am J Trop Med Hyg,* 71**,** 1-15.

Bridges, D. J., A. M. Winters & D. H. Hamer (2012) Malaria elimination: surveillance and response. *Pathogens and Global Health,* 106**,** 224-231.

Bruce-Chwatt, L. J. (1984) Lessons learned from applied field research activities in Africa during the malaria eradication era. *Bull World Health Organ,* 62 Suppl**,** 19-29.

Cao, J., H. J. W. Sturrock, C. Cotter, S. Zhou, H. Zhou, Y. Liu, et al. (2014a) Communicating and monitoring surveillance and response activities for malaria elimination: China's "1-3-7" strategy. *PLoS medicine,* 11**,** e1001642.

Cao, J., H. J. W. Sturrock, C. Cotter, S. Zhou, H. Zhou, Y. Liu, et al. (2014b) Communicating and Monitoring Surveillance and Response Activities for Malaria Elimination: China's "1-3-7" Strategy. *PLOS Medicine,* 11**,** e1001642.

Carrasco, D., T. Lefèvre, N. Moiroux, C. Pennetier, F. Chandre & A. Cohuet (2019) Behavioural adaptations of mosquito vectors to insecticide control. *Curr Opin Insect Sci,* 34**,** 48-54.

Carter, R. & K. N. Mendis (2002) Evolutionary and historical aspects of the burden of malaria. *Clin Microbiol Rev,* 15**,** 564-94.

Carter, R., K. N. Mendis & D. Roberts (2000) Spatial targeting of interventions against malaria. *Bull World Health Organ,* 78**,** 1401-1411.

Chaccour, C. & G. F. Killeen (2016) Mind the gap: residual malaria transmission, veterinary endectocides and livestock as targets for malaria vector control. *Malar J,* 15.

Chaccour, C. J., K. Ngha'bi, G. Abizanda, A. I. Barrio, A. Aldaz, F. Okumu, et al. (2018) Targeting cattle for malaria elimination: marked reduction of Anopheles arabiensis survival for over six months using a slow-release ivermectin implant formulation. *Parasites & Vectors,* 11.

Chacky, F., M. Runge, S. F. Rumisha, P. Machafuko, P. Chaki, J. J. Massaga, et al. (2018) Nationwide school malaria parasitaemia survey in public primary schools, the United Republic of Tanzania. *Malar J,* 17**,** 452.

Chanda, E. (2015) Malaria Vector Surveillance and Insecticide Resistance Monitoring and Management. *Malaria Control & Elimination,* 4.

Choi, L., J. Pryce & P. Garner (2019) Indoor residual spraying for preventing malaria in communities using insecticide‐treated nets. *Cochrane Database of Systematic Reviews*.

Coatney, R. (1976) Relapse in malaria-an enigma. *J Parasitol,* 62**,** 3-9.

Coetzee, M., M. Craig & D. Le Sueur (2000) Distribution of African malaria mosquitoes belonging to the Anopheles gambiae complex. *Parasitology Today,* 16**,** 74-77.

Coetzee, M. & L. L. Koekemoer (2013) Molecular systematics and insecticide resistance in the major African malaria vector Anopheles funestus. *Annu Rev Entomol,* 58**,** 393-412.

Cohen, J. & I. Saran (2018) The impact of packaging and messaging on adherence to malaria treatment: Evidence from a randomized controlled trial in Uganda. *J Dev Econ,* 134**,** 68-95.

Conner, R. O., Y. Dieye, M. Hainsworth, A. Tall, B. Cissé, F. Faye, et al. (2020) Mass testing and treatment for malaria followed by weekly fever screening, testing and treatment in Northern Senegal: feasibility, cost and impact. *Malaria Journal,* 19**,** 252.

Curtis, C., C. Maxwell, M. Lemnge, W. Kilama, R. W. Steketee & W. A. Hawley (2003) Scaling-up coverage with insecticide-treated nets against malaria in Africa: who should pay? *Lancet Infect Dis.,* 3.

Dar Es Salaam City Council. 2004. City Profile for Dar Es Salaam, United Republic of Tanzania. Dar es Salaam City Council With advice from Cities and Health Programme, WHO Centre for Development, Kobe, Japan, .

De Castro, M. C., Y. Yamagata, D. Mtasiwa, M. Tanner, J. Utzinger, J. Keiser, et al. (2004) Integrated urban malaria control: a case study in Dar es Salaam, Tanzania. *Am J Trop Med Hyg* 71**,** 103-117.

Derua, Y. A., M. Alifrangis, K. M. Hosea, D. W. Meyrowitsch, S. M. Magesa, E. M. Pedersen, et al. (2012) Change in composition of the *Anopheles gambiae* complex and its possible implications for the transmission of malaria and lymphatic filariasis in north-eastern Tanzania. *Malar J,* 11**,** 188.

Deutsch-Feldman, M., H. Hamapumbu, J. Lubinda, M. Musonda, B. Katowa, K. M. Searle, et al. (2018) Efficiency of a Malaria Reactive Test-and-Treat Program in Southern Zambia: A Prospective, Observational Study. *American Journal of Tropical Medicine and Hygiene,* 98**,** 1382-1388.

Diop, S., M. Ndiaye, M. Seck, B. Chevalier, R. Jambou, A. Sarr, et al. (2009) Prevention of transfusion transmitted malaria in endemic area. *Transfus Clin Biol,* 16**,** 454-9.

Dobson, M. J., M. Malowany & R. W. Snow (2000) Malaria control in East Africa: the Kampala Conference and the Pare-Taveta Scheme: a meeting of common and high ground. *Parassitologia,* 42**,** 149-166.

Draper, C. C., J. L. Lelijveld, Y. G. Matola & G. B. White (1972) Malaria in the Pare area of Tanzania. IV. Malaria in the human population 11 years after the suspension of residual insecticide spraying, with special reference to the serological findings. *Trans R Soc Trop Med Hyg,* 66**,** 905-12.

Durnez, L. & M. Coosemans (2013) Residual Transmission of Malaria: An Old Issue for New Approaches. *Anopheles Mosquitoes - New Insights into Malaria Vectors***,** 671-704.

Duvail, S., A. Mwakalinga, A. Eijkelenburg, O. Hamerlynck, K. Kindinda & A. Majule (2014) Jointly thinking the post-dam future: exchange of local and scientific knowledge on the lakes of the Lower Rufiji, Tanzania. *Hydrol Sci J. Taylor & Francis,* 59**,** 713-730.

Eisele, T. P., D. A. Larsen, N. Walker, R. E. Cibulskis, J. O. Yukich & C. M. Zikusooka (2012) Estimates of child deaths prevented from malaria prevention scale-up in Africa 2001–2010. *Malar J.,* 11.

Emami, S. N., L. C. Ranford-Cartwright & H. M. Ferguson (2017) The transmission potential of malaria-infected mosquitoes (An. gambiae-Keele, An. arabiensis-Ifakara) is altered by the vertebrate blood type they consume during parasite development. *Sci Rep,* 7.

Farnert, A., V. Yman, M. V. Homann, G. Wandell, L. Mhoja, M. Johansson, et al. (2014) Epidemiology of malaria in a village in the Rufiji River Delta, Tanzania: declining transmission over 25 years revealed by different parasitological metrics. *Malar J,* 13**,** 459.

Feachem, R. G. A., I. Chen, O. Akbari, A. Bertozzi-Villa, S. Bhatt, F. Binka, et al. (2019) Malaria eradication within a generation: ambitious, achievable, and necessary. *Lancet,* 394**,** 1056-1112.

Feachem, R. G. A., A. A. Phillips, G. A. Targett & R. W. Snow (2010) Call to action: priorities for malaria elimination. *Lancet,* 376**,** 1517-1521.

Feng, J., L. Zhang, F. Huang, J.-H. Yin, H. Tu, Z.-G. Xia, et al. (2018) Ready for malaria elimination: zero indigenous case reported in the People's republic of China. *Malar J,* 17**,** 315.

Filmer, D. & L. H. Pritchett (2001) Estimating wealth effects without expenditure data - Or tears: An application to educational enrollments in states of India. *Demography,* 38**,** 115-132.

Finda, M. F., A. J. Limwagu, H. S. Ngowo, N. S. Matowo, J. K. Swai, E. Kaindoa, et al. (2018) Dramatic decreases of malaria transmission intensities in Ifakara, south-eastern Tanzania since early 2000s. *Malar J,* 17**,** 362.

Finda, M. F., I. R. Moshi, A. Monroe, A. J. Limwagu, A. P. Nyoni, J. K. Swai, et al. (2019) Linking human behaviours and malaria vector biting risk in south-eastern Tanzania. *Plos One,* 14.

Franco, A. O., M. G. M. Gomes, M. Rowland, P. G. Coleman & C. R. Davies (2014) Controlling malaria using livestock-based interventions: a one health approach. *PloS One,* 9**,** e101699.

Galactionova, K., T. A. Smith, D. Savigny & M. A. Penny (2017) State of inequality in malaria intervention coverage in sub-Saharan African countries. *BMC Med,* 15.

Gallup, J. L. & J. D. Sachs (2001) The economic burden of malaria. *Am J Trop Med Hyg,* 64**,** 85-96.

Gantz, V. M., N. Jasinskiene, O. Tatarenkova, A. Fazekas, V. M. Macias, E. Bier, et al. (2015) Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito *Anopheles stephensi*. *Proc Natl Acad Sci USA,* 112**,** E6736-E6743.

Geissbühler, Y., P. Chaki, B. Emidi, N. J. Govella, R. Shirima, V. Mayagaya, et al. (2007) Interdependence of domestic malaria prevention measures and mosquito-human interactions in urban Dar es Salaam, Tanzania. *Malar J,* 6**,** 126.

Geissbühler, Y., K. Kannady, P. P. Chaki, B. Emidi, N. J. Govella, V. Mayagaya, et al. (2009) Microbial larvicide application by a large-scale, community-based program reduces malaria infection prevalence in urban Dar es Salaam, Tanzania. *PloS One,* 4**,** e5107.

Giglioli G (1951) Nation-wide malaria eradication projects in the Americas. III. Eradication of *Anopheles darlingi* from the inhabited areas of British Guiana by DDT residual spraying. *J Natl Malar Soc,* 10**,** 142-161.

Gilles, H. (1988) Anopheline mosquitos: vector behaviour and bionomics. Malaria principles and practice malariology. *London: Churchill Livingstone*.

Gilles, H. M. (1989) Malaria - an Overview. *Journal of Infection,* 18**,** 11-23.

Gilles, H. M. & D. A. Warrell. 2002. *Essential malariology*. Arnold.

Gillies, M. & M. Coetzee (1987) A supplement to the Anophelinae of Africa south of the Sahara (Afrotropical region). *S. Afr. Inst. M.Res*.

Gillies, M. & B. De Mellion (1968) The Anophelinae of Africa South of the Sahara (Ethiopian zoogeographical region). *Publications of the South African Institute for Medical Research,* 54**,** 1–343.

Gillies, M. & A. Smith (1960) The effect of a residual house-spraying campaign in East Africa on species balance in the *Anopheles funestus* group. The replacement of *A. funestus* Giles by *A. rivulorum* Leeson. *Bull Entomol Res,* 51**,** 243-252.

Gillies, M. T. & T. J. Wilkes (1965) A study of the age-composition of populations of *Anopheles gambiae* Giles and *A. funestus* Giles in North-Eastern Tanzania. *Bull Entomol Res,* 56**,** 237-262.

Gonçalves, B. P., C. Y. Huang, R. Morrison, S. Holte, E. Kabyemela & D. R. Prevots (2014) Parasite burden and severity of malaria in Tanzanian children. *N Engl J Med,* 370.

Govella, N. J., P. P. Chaki & G. F. Killeen (2013) Entomological surveillance of behavioural resilience and resistance in residual malaria vector populations. *Malar J,* 12**,** 124.

Govella, N. J. & H. Ferguson (2012a) Why use of interventions targeting outdoor biting mosquitoes will be necessary to achieve malaria elimination. *Frontiers in Physiology,* 3.

--- (2012b) Why Use of Interventions Targeting Outdoor Biting Mosquitoes will be Necessary to Achieve Malaria Elimination. *Front Physiol,* 3**,** 199.

Govella, N. J., J. D. Moore & G. F. Killeen (2010) An exposure-free tool for monitoring adult malaria mosquito populations. *Am J Trop Med Hyg* 83**,** 596-600.

Greenwood, B. M., K. Bojang, C. J. Whitty & G. A. Targett (2005) Malaria. *Lancet,* 365**,** 1487-98.

Habicht, J. P., C. G. Victora & J. P. Vaughan (1999) Evaluation designs for adequacy, plausibility and probability of public health programme performance and impact. *Int J Epidemiol,* 28**,** 10-8.

Hanson, K., T. Marchant, R. Nathan, H. Mponda, C. Jones, J. Bruce, et al. (2009) Household ownership and use of insecticide treated nets among target groups after implementation of a national voucher programme in the United Republic of Tanzania: plausibility study using three annual cross sectional household surveys. *BMJ,* 339**,** b2434.

Hawley, W. A., P. A. Phillips-Howard, F. O. Kuile, D. J. Terlouw, J. M. Vulule & M. Ombok (2003) Community-wide effects of permethrin-treated bednets on child mortality and malaria morbidity in western Kenya. *Am J Trop Med Hyg,* 68.

Hay, S. I., D. L. Smith & R. W. Snow (2008) Measuring malaria endemicity from intense to interrupted transmission. *Lancet Infect Dis,* 8**,** 369-378.

Hemingway, J. (2018) Resistance: A problem without an easy solution. *Pesticide Biochemistry and Physiology,* 151**,** 73-75.

Hernan, M. A., B. Brumback & J. M. Robins (2000) Marginal structural models to estimate the causal effect of zidovudine on the survival of HIV-positive men. *Epidemiology,* 11**,** 561-70.

Hiwat, H., S. Mitro, A. Samjhawan, P. Sardjoe, T. Soekhoe & W. Takken (2012) Collapse of *Anopheles darlingi* populations in Suriname after introduction of insecticide-treated nets (ITNs); malaria down to near elimination level. *Am J Trop Med Hyg* 86**,** 649-55.

Imbahale, S. S., J. M. Lopez, J. Brew, K. Paaijmansz, C. Rist & C. Chaccour (2019) Mapping the potential use of endectocide-treated cattle to reduce malaria transmission. *Sci Rep,* 9.

Ishengoma, D. S., B. P. Mmbando, M. D. Segeja, M. Alifrangis, M. M. Lemnge & I. C. Bygbjerg (2013) Declining burden of malaria over two decades in a rural community of Muheza district, north-eastern Tanzania. *Malar J,* 12**,** 338.

Kabula, B., P. Tungu, R. Malima, M. Rowland, J. Minja, R. Wililo, et al. (2014) Distribution and spread of pyrethroid and DDT resistance among the Anopheles gambiae complex in Tanzania. *Med Vet Entomol,* 28**,** 244-52.

Kaindoa, E., N. Matowo, H. Ngowo, G. Mkandawile, A. Mmbando, M. Finda, et al. (2017) Interventions that effectively target *Anopheles funestus* mosquitoes could significantly improve control of persistent malaria transmission in south–eastern Tanzania. *PLoS One,* 12**,** e0177807.

Kaindoa, E. W., G. Mkandawile, G. Ligamba, L. A. Kelly-Hope & F. O. Okumu (2016) Correlations between household occupancy and malaria vector biting risk in rural Tanzanian villages: implications for high-resolution spatial targeting of control interventions. *Malar J,* 15**,** 199.

Kaindoa, E. W., H. S. Ngowo, A. J. Limwagu, M. Tchouakui, E. Hape, S. Abbasi, et al. (2019) Swarms of the malaria vector Anopheles funestus in Tanzania. *Malar J,* 18**,** 29.

Kakwani, N., A. Wagstaff & E. Van Doorslaer (1997) Socioeconomic inequalities in health: Measurement, computation, and statistical inference. *Journal of Econometrics,* 77**,** 87-103.

Kamau, A., P. Mogeni, E. A. Okiro, R. W. Snow & P. Bejon (2020) A systematic review of changing malaria disease burden in sub-Saharan Africa since 2000: comparing model predictions and empirical observations. *Bmc Medicine,* 18.

Kelly, G. C., M. Tanner, A. Vallely & A. Clements (2012) Malaria elimination: moving forward with spatial decision support systems. *Trends Parasitol,* 28**,** 297-304.

Kern, S. E., A. B. Tiono, M. Makanga, A. D. Gbadoé, Z. Premji, O. Gaye, et al. (2011) Community screening and treatment of asymptomatic carriers of Plasmodium falciparum with artemether-lumefantrine to reduce malaria disease burden: a modelling and simulation analysis. *Malaria Journal,* 10**,** 210.

Khatib, R., J. Skarbinski, J. D. Njau, C. A. Goodman, B. F. Elling & E. Kahigwa (2012) Routine delivery of artemisinin-based combination treatment at fixed health facilities reduces malaria prevalence in Tanzania: an observational study. *Malar J.,* 11.

Khatib, R. A., P. P. Chaki, D. Q. Wang, Y. P. Mlacha, M. G. Mihayo, T. Gavana, et al. (2018) Epidemiological characterization of malaria in rural southern Tanzania following China-Tanzania pilot joint malaria control baseline survey. *Malar J,* 17**,** 292.

Khatib, R. A., G. F. Killeen, S. M. Abdulla, E. Kahigwa, P. D. Mcelroy & R. P. Gerrets (2008) Markets, voucher subsidies and free nets combine to achieve high bed net coverage in rural Tanzania. *Malar J.,* 7.

Khatib, R. A., M. Selemani, G. Abdalla, I. Masanja, M. Amuri & M. Njozi (2013) Access to artemisinin-based anti-malaria treatment and its related factors in rural Tanzania Dar es Salaam 2012. *Malar J.,* 12.

Kigadye, E. S., G. Nkwengulila, S. M. Magesa & S. Abdulla (2011) Spatial variability in the density, distribution and vectorial capacity of anopheline species in Rufiji district, south-eastern Tanzania. *Tanzan. J. Health Res,* 13**,** 112-8.

Kilama, W. (1994) Proceedings of the 11th Annual Joint Scientific Conference with a Seminar on Malaria Control Research.

Killeen, G., A. Tami, J. Kihonda, F. Okumu, M. Kotas, H. Grundmann, et al. (2007a) Cost-sharing strategies combining targeted public subsidies with private-sector delivery achieve high bednet coverage and reduced malaria transmission in Kilombero Valley, southern Tanzania. *BMC Infect Dis,* 7**,** 121.

Killeen Gerry F (2014) Characterizing, controlling and eliminating residual malaria transmission. *Malar J,* 13**,** 330.

Killeen, G. F. (2014) Characterizing, controlling and eliminating residual malaria transmission. *Malar J,* 13**,** 330.

--- (2020) Control of malaria vectors and management of insecticide resistance through universal coverage with next-generation insecticide-treated nets. *Lancet,* 395**,** 1394-1400.

Killeen, G. F., P. P. Chaki, T. E. Reed, C. L. Moyes & N. J. Govella. 2018. Entomological Surveillance as a Cornerstone of Malaria Elimination: A Critical Appraisal. In *Towards Malaria Elimination - A Leap Forward,* eds. Sylvie Manguin & V. Dev, 403-29. IntechOpen.

Killeen, G. F., N. J. Govella, D. W. Lwetoijera & F. O. Okumu (2016) Most outdoor malaria transmission by behaviourally-resistant Anopheles arabiensis is mediated by mosquitoes that have previously been inside houses. *Malar J.,* 15.

Killeen, G. F., N. J. Govella, Y. P. Mlacha & P. P. Chaki (2019) Suppression of malaria vector densities and human infection prevalence associated with scale-up of mosquito-proofed housing in Dar es Salaam, Tanzania: re-analysis of an observational series of parasitological and entomological surveys. *Lancet Planet Health,* 3**,** e132-e143.

Killeen, G. F., J. Kihonda, E. Lyimo, F. R. Oketch, M. E. Kotas, E. Mathenge, et al. (2006) Quantifying behavioural interactions between humans and mosquitoes: evaluating the

protective efficacy of insecticidal nets against malaria transmission in rural Tanzania. *BMC Infect. Dis,* 6**,** 161.

Killeen, G. F., S. S. Kiware, F. O. Okumu, M. E. Sinka, C. L. Moyes, N. C. Massey, et al. (2017a) Going beyond personal protection against mosquito bites to eliminate malaria transmission: population suppression of malaria vectors that exploit both human and animal blood. *Bmj Global Health,* 2.

Killeen, G. F., J. M. Marshall, S. S. Kiware, A. B. South, L. S. Tusting, P. P. Chaki, et al. (2017b) Measuring, manipulating and exploiting behaviours of adult mosquitoes to optimise malaria vector control impact. *BMJ Glob. Health,* 2**,** e000212.

Killeen, G. F., F. E. Mckenzie, B. D. Foy, C. Bøgh & J. C. Beier (2001) The availability of potential hosts as a determinant of feeding behaviours and malaria transmission by African mosquito populations. *Trans R Soc Trop Med Hyg,* 95**,** 469-476.

Killeen, G. F. & H. Ranson (2018) Insecticide-resistant malaria vectors must be tackled. *Lancet,* 391**,** 1551-1552.

Killeen, G. F. & T. A. Smith (2007) Exploring the contributions of bed nets, cattle, insecticides and excitorepellency to malaria control: a deterministic model of mosquito host-seeking behaviour and mortality. *Trans R Soc Trop Med Hyg,* 101**,** 867-880.

Killeen, G. F., T. A. Smith, H. M. Ferguson, S. Abdulla, H. Mshinda & C. Lengeler (2007b) Preventing childhood malaria in Africa by protecting adults from mosquitoes with insecticide-treated nets. *PLoS Med,* 4.

Killeen, G. F., A. Tatarsky, A. Diabate, C. J. Chaccour, J. M. Marshall, F. O. Okumu, et al. (2017c) Developing an expanded vector control toolbox for malaria elimination. *BMJ Glob. Health,* 2**,** e000211.

Kipyab, P. C., B. M. Khaemba, J. M. Mwangangi & C. M. Mbogo (2013) The bionomics of Anopheles merus (Diptera: Culicidae) along the Kenyan coast. *Parasit Vectors,* 6**,** 37.

Kisinza, W. N., T. E. Nkya, B. Kabula, H. J. Overgaard, D. J. Massue, Z. Mageni, et al. (2017) Multiple insecticide resistance in Anopheles gambiae from Tanzania: a major concern for malaria vector control. *Malar J,* 16**,** 439.

Kiszewski, A., A. Mellinger, A. Spielman, P. Malaney, S. E. Sachs & J. Sachs (2004) A global index representing the stability of malaria transmission. *Trans R Soc Trop Med Hyg,* 70**,** 486-498.

Kitau, J., R. M. Oxborough, P. K. Tungu, J. Matowo, R. C. Malima, S. M. Magesa, et al. (2012) Species shifts in the *Anopheles gambiae* complex: do LLINs successfully control *Anopheles arabiensis*? *PloS One,* 7**,** e31481.

Kitchen, A. D. & P. L. Chiodini (2006) Malaria and blood transfusion. *Vox Sang,* 90**,** 77-84.

Kiware, S. S., N. Chitnis, G. J. Devine, S. J. Moore, S. Majambere & G. F. Killeen (2012) Biologically meaningful coverage indicators for eliminating malaria transmission. *Biol Lett,* 8**,** 874-7.

Kiware, S. S., N. Chitnis, A. Tatarsky, S. Wu, H. M. S. Castellanos, R. Gosling, et al. (2017) Attacking the mosquito on multiple fronts: Insights from the Vector Control Optimization Model (VCOM) for malaria elimination. *PloS One,* 12**,** e0187680.

Kiware, S. S., T. L. Russell, Z. J. Mtema, A. D. Malishee, P. Chaki, D. Lwetoijera, et al. (2016) A generic schema and data collection forms applicable to diverse entomological studies of mosquitoes. *Source Code Biol Med,* 11**,** 4.

Koekemoer, L. L., L. Kamau, R. H. Hunt & M. Coetzee (2002) A cocktail polymerase chain reaction assay to identify members of the Anopheles funestus (Diptera: Culicidae) group. *Am J Trop Med Hyg,* 66**,** 804-11.

Kreppel, K. S., M. Viana, B. J. Main, P. C. D. Johnson, N. J. Govella, Y. Lee, et al. (2020) Emergence of behavioural avoidance strategies of malaria vectors in areas of high LLIN coverage in Tanzania. *Sci Rep,* 10**,** 14527.

Kruk, M. E., A. D. Gage, C. Arsenault, K. Jordan, H. H. Leslie, S. Roder-Dewan, et al. (2018) High-quality health systems in the Sustainable Development Goals era: time for a revolution. *Lancet Glob Health,* 6**,** e1196-e1252.

Lalji, S., J. M. Ngondi, N. G. Thawer, A. Tembo, R. Mandike, A. Mohamed, et al. (2016) School Distribution as Keep-Up Strategy to Maintain Universal Coverage of Long-Lasting Insecticidal Nets: Implementation and Results of a Program in Southern Tanzania. *Glob J Health Sci* 4**,** 251-263.

Landier, J., D. M. Parker, A. M. Thu, V. I. Carrara, K. M. Lwin, C. A. Bonnington, et al. (2016) The role of early detection and treatment in malaria elimination. *Malaria Journal,* 15**,** 363.

Landier, J., D. M. Parker, A. M. Thu, K. M. Lwin, G. Delmas, F. H. Nosten, et al. (2018) Effect of generalised access to early diagnosis and treatment and targeted mass drug administration on *Plasmodium falciparum* malaria in Eastern Myanmar: an observational study of a regional elimination programme. *Lancet,* 391**,** 1916-1926.

Larsen, D. A., A. Bennett, K. Silumbe, B. Hamainza, J. O. Yukich, J. Keating, et al. (2015) Population-wide malaria testing and treatment with rapid diagnostic tests and artemether-lumefantrine in southern Zambia: a community randomized step-wedge control trial design. *Am J Trop Med Hyg,* 92**,** 913-921.

Lefèvre, T., L.-C. Gouagna, K. R. Dabiré, E. Elguero, D. Fontenille, F. Renaud, et al. (2009) Beyond nature and nurture: phenotypic plasticity in blood-feeding behavior of *Anopheles gambiae ss* when humans are not readily accessible. *Am J Trop Med Hyg,* 81**,** 1023-1029.

Lengeler, C. (2004) Insecticide-treated bed nets and curtains for preventing malaria. *Cochrane Database Syst Rev***,** CD000363.

Lindsay, S. W., J. H. Adiamah, J. E. Miller, R. J. Pleass & J. R. M. Armstrong (1993) Variation in Attractiveness of Human-Subjects to Malaria Mosquitos (Diptera, Culicidae) in the Gambia. *J. Med. Entomol,* 30**,** 368-373.

Livadas, G. (1953) Is it necessary to continue indefinitely DDT residual spraying Programmes? Relevant Observations made in Greece. *Rivista di Parassitologia,* 14.

Livadas, G. A. & G. Georgopoulos (1953) Development of resistance to DDT by Anopheles sacharovi in Greece. *Bull World Health Organ,* 8**,** 497-511.

Lobo, N. F., B. St Laurent, C. H. Sikaala, B. Hamainza, J. Chanda, D. Chinula, et al. (2015) Unexpected diversity of *Anopheles* species in Eastern Zambia: implications for evaluating vector behavior and interventions using molecular tools. *Sci Rep,* 5.

Loha, E., T. M. Lunde & B. Lindtjørn (2012) Effect of bednets and indoor residual spraying on spatio-temporal clustering of malaria in a village in south Ethiopia: a longitudinal study. *PLoS One,* 7**,** e47354.

Lourenço, C., A. J. Tatem, P. M. Atkinson, J. M. Cohen, D. Pindolia, D. Bhavnani, et al. (2019) Strengthening surveillance systems for malaria elimination: a global landscaping of system performance, 2015–2017. *Malaria Journal,* 18**,** 315.

Lwetoijera, D. W., C. Harris, S. S. Kiware, S. Dongus, G. J. Devine, P. J. Mccall, et al. (2014) Increasing role of *Anopheles funestus* and *Anopheles arabiensis* in malaria transmission in the Kilombero Valley, Tanzania. *Malar J,* 13**,** 331.

Lyimo, I. N. & H. M. Ferguson (2009) Ecological and evolutionary determinants of host species choice in mosquito vectors. *Trends Parasitol,* 25**,** 189-96.

Lynn, M. & B. Bossak (2017) Analysis of a secular trend in malaria incidence: Venezuela, 1959–2015. *J Glob Epidemiol Environ Health.*, 2017.

Macdonald, G. 1957. *The epidemiology and control of malaria*.

Maghendji-Nzondo, S., L.-C. Kouna, G. Mourembou, L. Boundenga, R.-K. Imboumy-Limoukou, P.-B. Matsiegui, et al. (2016) Malaria in urban, semi-urban and rural areas of southern of Gabon: comparison of the Pfmdr 1 and Pfcrt genotypes from symptomatic children. *Malaria Journal,* 15**,** 420.

Mahande, A., F. Mosha, J. Mahande & E. Kweka (2007) Feeding and resting behaviour of malaria vector, *Anopheles arabiensis* with reference to zooprophylaxis. *Malar J,* 6**,** 100.

Maher, B. (2008) Malaria: the end of the beginning. *Nature,* 451**,** 1042-6.

Maheu-Giroux, M. & M. C. Castro (2013) Impact of Community-Based Larviciding on the Prevalence of Malaria Infection in Dar es Salaam, Tanzania. *PLoS One,* 8**,** e71638.

Main, B. J., Y. Lee, H. M. Ferguson, K. S. Kreppel, A. Kihonda, N. J. Govella, et al. (2016) The Genetic Basis of Host Preference and Resting Behavior in the Major African Malaria Vector, Anopheles arabiensis. *PLoS Genet,* 12**,** e1006303.

Malera Consultative Group on Modeling (2011) A research agenda for malaria eradication: modeling. *PLoS Med,* 8**,** e1000403.

Malera Consultative Group on Monitoring Evaluation Surveillance (2011) A research agenda for malaria eradication: monitoring, evaluation, and surveillance. *PLoS Med,* 8**,** e1000400.

Marquardt, W. C., R. S. Demaree & R. B. Grieve. 2000. *Parasitology and vector biology*. Orlando: Harcourt Brace & Company.

Massebo, F., M. Balkew, T. Gebre-Michael & B. Lindtjorn (2015) Zoophagic behaviour of anopheline mosquitoes in southwest Ethiopia: opportunity for malaria vector control. *Parasit Vectors,* 8**,** 645.

Matiya, D. J., A. B. Philbert, W. Kidima & J. J. Matowo (2019) Dynamics and monitoring of insecticide resistance in malaria vectors across mainland Tanzania from 1997 to 2017: a systematic review. *Malar J,* 18**,** 102.

Matowo, N. S., S. Abbasi, G. Munhenga, M. Tanner, S. A. Mapua, D. Oullo, et al. (2019) Fine-scale spatial and temporal variations in insecticide resistance in Culex pipiens complex mosquitoes in rural south-eastern Tanzania. *Parasit Vectors,* 12**,** 413.

Matowo, N. S., G. Munhenga, M. Tanner, M. Coetzee, W. F. Feringa, H. S. Ngowo, et al. (2017) Fine-scale spatial and temporal heterogeneities in insecticide resistance profiles of the malaria vector, Anopheles arabiensis in rural south-eastern Tanzania. *Wellcome Open Res,* 2**,** 96.

Mayagaya, V. S., G. Nkwengulila, I. N. Lyimo, J. Kihonda, H. Mtambala, H. Ngonyani, et al. (2015) The impact of livestock on the abundance, resting behaviour and sporozoite rate of malaria vectors in southern Tanzania. *Malar J,* 14**,** 17.

Mboera, L. E., V. M. Bwana, S. F. Rumisha, G. Stanley, P. K. Tungu & R. C. Malima (2015) Spatial abundance and human biting rate of Anopheles arabiensis and Anopheles funestus in savannah and rice agro-ecosystems of Central Tanzania. *Geospat Health,* 10**,** 322.

Mboera, L. E., E. A. Makundi & A. Y. Kitua (2007) Uncertainty in malaria control in Tanzania: crossroads and challenges for future interventions. *Am J Trop Med Hyg,* 77**,** 112-8.

Mendis, C., J. Jacobsen, A. Gamage‐Mendis, E. Bule, M. Dgedge, R. Thompson, et al. (2000) *Anopheles arabiensis* and *An. funestus* are equally important vectors of malaria in Matola coastal suburb of Maputo, southern Mozambique. *Med Vet Entomol,* 14**,** 171-180.

Meza, F. C., K. S. Kreppel, D. F. Maliti, A. T. Mlwale, N. Mirzai, G. F. Killeen, et al. (2019) Mosquito electrocuting traps for directly measuring biting rates and host-preferences of *Anopheles arabiensi*s and *Anopheles funestus* outdoors. *Malar J,* 18**,** 83.

Miller, L. H., M. F. Good & G. Milon (1994) Malaria pathogenesis. *Science,* 264**,** 1878-1883.

Ministry of Health. 2002. National Medium Term Malaria Strategic Plan (2002–2007). United Republic of Tanzania: Ministry of Health, Dar es Salaam.

Ministry of Health and Social Welfare. 2006. National Guidelines for Diagnosis and Treatment of Malaria. . 105 pages.

Ministry of Health and Social Welfare. 2014. National Malaria Strategic Plan 2014–2020. Dar es Salaam, Tanzania: NATIONAL MALARIA CONTROL PROGRAMME.

Ministry of Health, C. D., Gender, Elderly and Children (Mohcdgec) (Tanzania Mainland), . 2007. Tanzania Malaria Indicator Survey 2008. eds. Ministry of Health (Moh) (Zanzibar), National Bureau of Statistics (Nbs), Office of the Chief Government Statistician (Ocgs) & Icf. Dar es Salaam, Tanzania, and Rockville, USA.

Ministry of Health, C. D., Gender, Elderly Children,. 2016. Tanzania Demographic and Health Survey and Malaria Indicator Survey (TDHS-MIS) 2015-16. eds. O. O. T. C. G. S. National Bureau of Statistics & Icf. MoHCDGEC, MoH, NBS, OCGS, and ICF Dar es Salaam, Tanzania, and Rockville ….

Ministry of Health Community Development Gender Elderly and Children (Mohcdgec) [Tanzania-Mainland], & Icf. 2017. Malaria Indicator Survey 2017. In *Dar es Salaam, Tanzania, and Rockville, Maryland, USA.,* ed. M. Office of the Chief Government Statistician (Ocgs)Mohcdgec, Nbs, Ocgs, and Icf.

Mlacha, Y. P., P. P. Chaki, A. D. Malishee, V. M. Mwakalinga, N. J. Govella, A. J. Limwagu, et al. (2017) Fine scale mapping of malaria infection clusters by using routinely collected health facility data in urban Dar es Salaam, Tanzania. *Geospat Health,* 12**,** 494.

Mlacha, Y. P., D. Wang, P. P. Chaki, T. Gavana, Z. Zhou, M. G. Michael, et al. (2020) Effectiveness of the innovative 1,7-malaria reactive community-based testing and response (1, 7-mRCTR) approach on malaria burden reduction in Southeastern Tanzania. *Malar J,* 19**,** 292.

Monroe, A., D. Msaky, S. Kiware, B. B. Tarimo, S. Moore, K. Haji, et al. (2020) Patterns of human exposure to malaria vectors in Zanzibar and implications for malaria elimination efforts. *Malar J,* 19**,** 212.

Msellemu, D., H. I. Namango, V. M. Mwakalinga, A. J. Ntamatungiro, Y. Mlacha, Z. J. Mtema, et al. (2016) The epidemiology of residual *Plasmodium falciparum* malaria transmission and infection burden in an African city with high coverage of multiple vector control measures. *Malar J,* 15**,** 288.

Mueller, I., M. R. Galinski, J. K. Baird, J. M. Carlton, D. K. Kochar, P. L. Alonso, et al. (2009) Key gaps in the knowledge of Plasmodium vivax, a neglected human malaria parasite. *Lancet Infect Dis,* 9**,** 555-66.

Mukabana, W. R., W. Takken, R. Coe & B. G. Knols (2002) Host-specific cues cause differential attractiveness of Kenyan men to the African malaria vector *Anopheles gambiae*. *Malar J,* 1**,** 17.

Murray, C. J. L., L. C. Rosenfeld, S. S. Lim, K. G. Andrews, K. J. Foreman, D. Haring, et al. (2012) Global malaria mortality between 1980 and 2010: a systematic analysis. *Lancet,* 379**,** 413-431.

Mwakalinga, V. M., B. K. Sartorius, Y. P. Mlacha, D. F. Msellemu, A. J. Limwagu, Z. D. Mageni, et al. (2016) Spatially aggregated clusters and scattered smaller loci of elevated malaria

vector density and human infection prevalence in urban Dar es Salaam, Tanzania. *Malar J,* 15**,** 135.

Mwangangi, J. M., E. J. Muturi, S. M. Muriu, J. Nzovu, J. T. Midega & C. Mbogo (2013) The role of Anopheles arabiensis and Anopheles coustani in indoor and outdoor malaria transmission in Taveta District, Kenya. *Parasit Vectors,* 6**,** 114.

Najera, J. A., M. Gonzalez-Silva & P. L. Alonso (2011) Some lessons for the future from the global malaria eradication programme (1955-1969). *PLoS medicine,* 8**,** 84-90.

Namountougou, M., D. D. Soma, M. Kientega, M. Balboné, D. P. A. Kaboré, S. F. Drabo, et al. (2019) Insecticide resistance mechanisms in Anopheles gambiae complex populations from Burkina Faso, West Africa. *Acta Tropica,* 197**,** 105054.

National Bureau of Statistics (Nbs). 2013. Population and housing census 2012 Report: Population Distribution by Administrative Areas, United Republic of Tanzania., ed. Office of Chief Government Statistician (Ocgs). Dar es Salaam, : Ministry of Finance Dar es Salaam and President's Office, Finance, Economy and Development Planning Zanzibar.

National Bureau of Statistics. 2018. Tanzania Malaria Indicator Survey (TMIS) Key Indicators 2017. eds. M. O. H. Zanzibar, C. D. Ministry of Health, Gender, Elderly and Children, , N. B. O. S. N. D. E. Salaam, O. O. C. G. S. O. Zanzibar & M. U. The Dhs Program Rockville. National Bureau of Statistics (NBS) Dar es Salaam.

National Bureau of Statistics (Nbs/Tanzania). 2011. Tanzania Demographic and Health Survey 2010. ed. Icf Macro. Dar es Salaam,Tanzania: NBS/Tanzania and ICF Macro. .

National Malaria Control Programme. 2018. Supplementary Malaria Midterm Strategic Plan (2018-2020). 1-114. United Republic of Tanzania Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC).

National Malaria Control Programme , I. H. I. Who & K.-W. Trust. 2013. An epidemiological profile of malaria and its control in Mainland Tanzania. Report funded by Roll Back Malaria and Department for International ….

National Malaria Control Programme (Nmcp). 2012. Malaria Programme Performance Review Tanzania Mainland. ed. M. O. H. S. W. (Mohsw). United Republic of Tanzania: National Malaria Control Programme (NMCP).

Nkumama, I. N., W. P. O'meara & F. H. A. Osier (2017) Changes in Malaria Epidemiology in Africa and New Challenges for Elimination. *Trends Parasitol,* 33**,** 128-140.

Ochomo, E., N. M. Bayoh, L. Kamau, F. Atieli, J. Vulule, C. Ouma, et al. (2014) Pyrethroid susceptibility of malaria vectors in four Districts of western Kenya. *Parasit Vectors,* 7**,** 310.

Okumu, F. O., S. S. Kiware, S. J. Moore & G. F. Killeen (2013) Mathematical evaluation of community level impact of combining bed nets and indoor residual spraying upon malaria transmission in areas where the main vectors are Anopheles arabiensis mosquitoes. *Parasit Vectors.,* 6.

Okumu, F. O. & S. J. Moore (2011) Combining indoor residual spraying and insecticide-treated nets for malaria control in Africa: a review of possible outcomes and an outline of suggestions for the future. *Malar J,* 10**,** 208.

Opondo, K. O., D. Weetman, M. Jawara, M. Diatta, A. Fofana, F. Crombe, et al. (2016) Does insecticide resistance contribute to heterogeneities in malaria transmission in The Gambia? *Malar J,* 15**,** 166.

Ouedraogo, A., A. B. Tiono, A. Diarra, E. C. Bougouma, I. Nebie, A. T. Konate, et al. (2012) Transplacental Transmission of Plasmodium falciparum in a Highly Malaria Endemic Area of Burkina Faso. *J Trop Med,* 2012**,** 109705.

Paaijmans, K. P., S. Blanford, A. S. Bell, J. I. Blanford, A. F. Read & M. B. Thomas (2010) Influence of climate on malaria transmission depends on daily temperature variation. *Proc Natl Acad Sci U S A,* 107**,** 15135-9.

Padonou, G. G., G. Gbedjissi, A. Yadouleton, R. Azondekon, O. Razack, O. Oussou, et al. (2012) Decreased proportions of indoor feeding and endophily in *Anopheles gambiae s.l.* populations following the indoor residual spraying and insecticide-treated net interventions in Benin (West Africa). *Parasit Vectors,* 5**,** 262.

Pampana, E. (1969) A textbook of malaria eradication. *A textbook of malaria eradication. 2nd edition.*

Pluess, B., F. C. Tanser, C. Lengeler & B. L. Sharp (2010) Indoor residual spraying for preventing malaria. *Cochrane Database Syst Rev***,** CD006657.

Pock Tsy, J. M., J. B. Duchemin, L. Marrama, P. Rabarison, G. Le Goff, V. Rajaonarivelo, et al. (2003) Distribution of the species of the Anopheles gambiae complex and first evidence of Anopheles merus as a malaria vector in Madagascar. *Malar J,* 2**,** 33.

Port, G., P. Boreham & J. H. Bryan (1980) The relationship of host size to feeding by mosquitoes of the *Anopheles gambiae* Giles complex (Diptera: Culicidae). *Bull. Entomol. Res,* 70**,** 133-144.

President's Malaria Initiative. 2012. Malaria Operational Plan (MOP), TANZANIA, 2011 President's Malaria Initiative; .

Pryce, J., M. Richardson & C. Lengeler (2018) Insecticide-treated nets for preventing malaria. *Cochrane Database Syst Rev,* 11**,** CD000363.

Raman, J., N. Morris, J. Frean, B. Brooke, L. Blumberg, P. Kruger, et al. (2016) Reviewing South Africa's malaria elimination strategy (2012–2018): progress, challenges and priorities. *Malaria Journal,* 15**,** 438.

Ranson, H., R. N'guessan, J. Lines, N. Moiroux, Z. Nkuni & V. Corbel (2011) Pyrethroid resistance in African anopheline mosquitoes: what are the implications for malaria control? *Trends Parasitol,* 27**,** 91-98.

Reddy, M. R., H. J. Overgaard, S. Abaga, V. P. Reddy, A. Caccone, A. E. Kiszewski, et al. (2011) Outdoor host seeking behaviour of *Anopheles gambiae* mosquitoes following initiation of malaria vector control on Bioko Island, Equatorial Guinea. *Malar J,* 10**,** 184.

Roll Back Malaria. 2005. Roll Back Malaria Global Strategic Plan 2005-2015. 2010. Geneva: Roll Back Malaria Partnership Secretariat.

---. 2015. Action and investment to defeat malaria, 2016-2030. For a malaria free world.

Roll Back Malaria Monitoring and Evaluation Reference Group, World Health Organization, United Nations Children's Fund, Measure Dhs, A. Measure Evaluation & U. S. C. F. D. C. A. Prevention. 2005. Malaria Indicator Survey: Basic documentation for survey design and implementation. Calverton, Maryland.

Rose, N. H., M. Sylla, A. Badolo, J. Lutomiah, D. Ayala, O. B. Aribodor, et al. (2020) Climate and Urbanization Drive Mosquito Preference for Humans. *Curr Biol*.

Rumisha, S. F., L. E. Mboera, K. P. Senkoro, D. Gueye & P. K. Mmbuji (2007) Monitoring and evaluation of integrated disease surveillance and response in selected districts in Tanzania. *Tanzan Health Res Bull,* 9**,** 1-11.

Runge, M., R. W. Snow, F. Molteni, S. Thawer, A. Mohamed, R. Mandike, et al. (2020) Simulating the council-specific impact of anti-malaria interventions: A tool to support malaria strategic planning in Tanzania. *PLoS One,* 15**,** e0228469.

Russell, S. (2004) The economic burden of illness for households in developing countries: a review of studies focusing on malaria, tuberculosis, and human immunodeficiency virus/acquired immunodeficiency syndrome. *Am J Trop Med Hyg,* 71.

Russell, T. L., N. J. Govella, S. Azizi, C. J. Drakeley, S. P. Kachur & G. F. Killeen (2011) Increased proportions of outdoor feeding among residual malaria vector populations following increased use of insecticide-treated nets in rural Tanzania. *Malar J,* 10**,** 80.

Sachs, J. & P. Malaney (2002) The economic and social burden of malaria. *Nature,* 415**,** 680-685.

Schmidt, G. D. & L. S. Robert. 2000. *Foundations of parasitology*. The McGraw-Hill Companies.

Schwetz, J. & M. Peel (1934) Congenital malaria and placental infections amongst the negroes of Central Africa. *Trans R Soc Trop Med Hyg,* 28**,** 167-174.

Scott, J. A., W. G. Brogdon & F. H. Collins (1993) Identification of single specimens of the Anopheles gambiae complex by the polymerase chain reaction. *Am J Trop Med Hyg,* 49**,** 520-9.

Selemani, M., S. Mrema, A. Shamte, J. Shabani, M. J. Mahande, K. Yeates, et al. (2015) Spatial and space-time clustering of mortality due to malaria in rural Tanzania: evidence from Ifakara and Rufiji Health and Demographic Surveillance System sites. *Malar J,* 14**,** 369.

Shabani, J., A. M. Lutambi, V. Mwakalinga & H. Masanja (2010) Clustering of under-five mortality in Rufiji Health and Demographic Surveillance System in rural Tanzania. *Glob Health Action,* 3.

Sharp, B. L. & D. Le Sueur (1996) Malaria in South Africa - The past, the present and selected implications for the future. *S Afr Med J,* 86**,** 83-89.

Sherrard-Smith, E., J. E. Skarp, A. D. Beale, C. Fornadel, L. C. Norris, S. J. Moore, et al. (2019) Mosquito feeding behavior and how it influences residual malaria transmission across Africa. *P Natl Acad Sci USA,* 116**,** 15086-15095.

Sherrard-Smith, E., P. Winskill, A. Hamlet, C. Ngufor, R. N'guessan, M. W. Guelbeogo, et al. (2022) Optimising the deployment of vector control tools against malaria: a data-informed modelling study. *The Lancet Planetary Health,* 6**,** e100-e109.

Shretta, R., A. L. Avancena & A. Hatefi (2016) The economics of malaria control and elimination: a systematic review. *Malar J,* 15**,** 593.

Silumbe, K., T. P. Finn, T. Jennings, C. Sikombe, E. Chiyende, B. Hamainza, et al. (2020) Assessment of the Acceptability of Testing and Treatment during a Mass Drug Administration Trial for Malaria in Zambia Using Mixed Methods. *Am J Trop Med Hyg,* 103**,** 28-36.

Silumbe, K., J. O. Yukich, B. Hamainza, A. Bennett, D. Earle, M. Kamuliwo, et al. (2015) Costs and cost-effectiveness of a large-scale mass testing and treatment intervention for malaria in Southern Province, Zambia. *Malar J,* 14**,** 211.

Simon, C., K. Moakofhi, T. Mosweunyane, H. B. Jibril, B. Nkomo, M. Motlaleng, et al. (2013) Malaria control in Botswana, 2008-2012: the path towards elimination. *Malar J,* 12**,** 458.

Singh, B., L. Kim Sung, A. Matusop, A. Radhakrishnan, S. S. Shamsul, J. Cox-Singh, et al. (2004) A large focus of naturally acquired Plasmodium knowlesi infections in human beings. *Lancet,* 363**,** 1017-24.

Smith, A. (1962) Studies on Domestic Habits of *A. gambiae* that affect its Vulnerability to Insecticides. *East Afr Med J,* 39**,** 15-24.

Smith, D. L., K. E. Battle, S. I. Hay, C. M. Barker, T. W. Scott & F. E. Mckenzie (2012) Ross, Macdonald, and a Theory for the Dynamics and Control of Mosquito-Transmitted Pathogens. *PLOS Pathogens,* 8**,** e1002588.

Smith, D. L., T. A. Perkins, R. C. Reiner, Jr., C. M. Barker, T. Niu, L. F. Chaves, et al. (2014) Recasting the theory of mosquito-borne pathogen transmission dynamics and control. *Trans R Soc Trop Med Hyg,* 108**,** 185-97.

Snow, R. W., E. A. Okiro, P. W. Gething, R. Atun & S. I. Hay (2010) Equity and adequacy of international donor assistance for global malaria control: an analysis of populations at risk and external funding commitments. *Lancet,* 376.

Sougoufara, S., S. M. Diédhiou, S. Doucouré, N. Diagne, P. M. Sembène, M. Harry, et al. (2014) Biting by *Anopheles funestus* in broad daylight after use of long-lasting insecticidal nets: a new challenge to malaria elimination. *Malar J,* 13**,** 125.

Steketee, R. W. & C. C. Campbell (2010) Impact of national malaria control scale-up programmes in Africa: magnitude and attribution of effects. *Malar J,* 9**,** 299.

Stresman, G. H., J. C. Stevenson, C. Owaga, E. Marube, C. Anyango, C. Drakeley, et al. (2014) Validation of three geolocation strategies for health-facility attendees for research and public health surveillance in a rural setting in western Kenya. *Epidemiology and Infection,* 142**,** 1978-1989.

Sturrock, H. J., J. M. Cohen, P. Keil, A. J. Tatem, A. Le Menach, N. E. Ntshalintshali, et al. (2014) Fine-scale malaria risk mapping from routine aggregated case data. *Malar J,* 13**,** 421.

Sturrock, H. J., M. S. Hsiang, J. M. Cohen, D. L. Smith, B. Greenhouse, T. Bousema, et al. (2013a) Targeting asymptomatic malaria infections: active surveillance in control and elimination. *PLoS Med,* 10**,** e1001467.

Sturrock, H. J. W., J. M. Novotny, S. Kunene, S. Dlamini, Z. Zulu, J. M. Cohen, et al. (2013b) Reactive Case Detection for Malaria Elimination: Real-Life Experience from an Ongoing Program in Swaziland. *Plos One,* 8.

Taconet, P., A. Porciani, D. D. Soma, K. Mouline, F. Simard, A. A. Koffi, et al. (2021) Data-driven and interpretable machine-learning modeling to explore the fine-scale environmental determinants of malaria vectors biting rates in rural Burkina Faso. *Parasites & Vectors,* 14**,** 345.

Takken, W. & N. O. Verhulst (2013) Host preferences of blood-feeding mosquitoes. *Annu. Rev. Entomol,* 58**,** 433-453.

Tanner, M., B. Greenwood, C. J. Whitty, E. K. Ansah, R. N. Price, A. M. Dondorp, et al. (2015a) Malaria eradication and elimination: views on how to translate a vision into reality. *BMC Med,* 13**,** 167.

Tanner, M., B. Greenwood, C. J. M. Whitty, E. K. Ansah, R. N. Price, A. M. Dondorp, et al. (2015b) Malaria eradication and elimination: views on how to translate a vision into reality. *BMC Medicine,* 13**,** 167.

Tanzania Commission for Aids. 2013. Zanzibar AIDS Commission (ZAC), National Bureau of Statistics (NBS); Office of the Chief Government Statistician (OCGS); ICF International. Tanzania HIV/AIDS and malaria indicator survey 2011-12. TACAIDS, ZAC, NBS, OCGS, and ICF International Dar es Salaam.

Taylor, C., L. Florey & Y. Yé (2017) Increasing equity of insecticide-treated net ownership in sub-Saharan Africa from 2003 to 2014. *Bull World Health Organ,* 95.

Tediosi, F. & M. Penny (2016) Evidence for optimal allocation of malaria interventions in Africa. *Lancet Glob Health,* 4**,** e432-3.

Teklehaimanot, A. & P. Mejia (2008) Malaria and poverty. *Ann N Y Acad Sci,* 1136.

Temu, E. A., J. N. Minjas, M. Coetzee, R. H. Hunt & C. J. Shift (1998) The role of four anopheline species (Diptera: Culicidae) in malaria transmission in coastal Tanzania. *Trans R Soc Trop Med Hyg,* 92**,** 152-8.

Thawer, S. G., F. Chacky, M. Runge, E. Reaves, R. Mandike, S. Lazaro, et al. (2020) Sub-national stratification of malaria risk in mainland Tanzania: a simplified assembly of survey and routine data. *Malar J,* 19**,** 177.

The Ivermectin, R. (2020) A Roadmap for the Development of Ivermectin as a Complementary Malaria Vector Control Tool. *Am J Trop Med Hyg* 102**,** 3-24.

Tiono, A. B., A. Ouedraogo, B. Ogutu, A. Diarra, S. Coulibaly, A. Gansane, et al. (2013) A controlled, parallel, cluster-randomized trial of community-wide screening and treatment of asymptomatic carriers of Plasmodium falciparum in Burkina Faso. *Malar J,* 12**,** 79.

Tirados, I., C. Costantini, G. Gibson & S. J. Torr (2006) Blood‐feeding behaviour of the malarial mosquito *Anopheles arabiensis:* implications for vector control. *Med Vet Entomol,* 20**,** 425-437.

Torr, S. J., A. Della Torre, M. Calzetta, C. Costantini & G. A. Vale (2008) Towards a fuller understanding of mosquito behaviour: use of electrocuting grids to compare the odour-orientated responses of *Anopheles arabiensis* and *An. quadriannulatus* in the field. *Med Vet Entomol,* 22**,** 93-108.

Trigg, P. I. & A. V. Kondrachine (1998) Commentary: malaria control in the 1990s. *Bull World Health Organ,* 76**,** 11-6.

Tusting, L. S., T. Bousema, D. L. Smith & C. Drakeley (2014) Measuring changes in *Plasmodium falciparum* transmission: precision, accuracy and costs of metrics. *Adv Parasitol,* 84**,** 151-208.

Van Den Berg, H., H. S. Da Silva Bezerra, S. Al-Eryani, E. Chanda, B. N. Nagpal, T. B. Knox, et al. (2021) Recent trends in global insecticide use for disease vector control and potential implications for resistance management. *Scientific Reports,* 11**,** 23867.

Victora, C. G., A. J. Barros, H. Axelson, Z. A. Bhutta, M. Chopra & G. V. França (2012) How changes in coverage affect equity in maternal and child health interventions in 35 Countdown to 2015 countries: an analysis of national surveys. *Lancet,* 380.

Waite, J. L., S. Swain, P. A. Lynch, S. K. Sharma, M. A. Haque, J. Montgomery, et al. (2017) Increasing the potential for malaria elimination by targeting zoophilic vectors. *Sci Rep,* 7**,** 40551.

Walker, P. G. T., J. T. Griffin, N. M. Ferguson & A. C. Ghani (2016) Estimating the most efficient allocation of interventions to achieve reductions in Plasmodium falciparum malaria burden and transmission in Africa: a modelling study. *The Lancet Global Health,* 4**,** e474-e484.

Wang, D., P. Chaki, Y. Mlacha, T. Gavana, M. G. Michael, R. Khatibu, et al. (2019) Application of community-based and integrated strategy to reduce malaria disease burden in southern Tanzania: the study protocol of China-UK-Tanzania pilot project on malaria control. *Infect Dis Poverty,* 8**,** 4.

Wang, S. J., C. Lengeler, D. Mtasiwa, T. Mshana, L. Manane & G. Maro (2006) Rapid Urban Malaria Appraisal (RUMA) II: epidemiology of urban malaria in Dar es Salaam (Tanzania). *Malar J.,* 5.

Weiss, D. J., T. C. D. Lucas, M. Nguyen, A. K. Nandi, D. Bisanzio, K. E. Battle, et al. (2019) Mapping the global prevalence, incidence, and mortality of Plasmodium falciparum, 2000-17: a spatial and temporal modelling study. *Lancet,* 394**,** 322-331.

White, G., S. A. Magayuka & P. Boreham (1972) Comparative studies on sibling species of the *Anopheles gambiae* Giles complex (Dipt., Culicidae): bionomics and vectorial activity of species A and species B at Segera, Tanzania. *Bull. Entomol. Res,* 62**,** 295-317.

White Gb (1974) *Anopheles gambiae* complex and disease transmission in Africa. *Trans R Soc Trop Med Hyg,* 68**,** 278-298.

White, N. J., S. Pukrittayakamee, T. T. Hien, M. A. Faiz, O. A. Mokuolu & A. M. Dondorp (2014) Malaria. *Lancet,* 383**,** 723-35.
World Health Organization. 1993. *A global strategy for malaria control*. Geneva: World Health Organization.
World Health Organization. 1998. A global partnership. In *Roll Back Malaria*. Geneva: World Health Organization.
World Health Organization. 2006. Communicable disease surveillance and response systems: guide to monitoring and evaluating. Geneva: World Health Organization.
World Health Organization. 2012a. Community-based reduction of malaria transmission. Geneva.
World Health Organization. 2012b. Disease surveillance for malaria elimination: an operational manual. 64. Geneva 27, Switzerland: World Health Organization.
World Health Organization. 2012c. T3: Test. Treat. Track. Scaling up diagnostic testing, treatment and surveillance for malaria. .
World Health Organization. 2015a. Global Technical Strategy for Malaria 2016–2030. 35. Geneva: World Health Organization.
World Health Organization. 2015b. Health in 2015: from MDGs, millennium development goals to SDGs, sustainable development goals. Geneva: World Health Organization.
World Health Organization. 2015c. World malaria report 2014. Geneva: World Health Organization.
World Health Organization. 2016a. *World health statistics 2016: monitoring health for the SDGs sustainable development goals*. Geneva: World Health Organization.
World Health Organization. 2016b. World Malaria report 2016. Geneva: World Health Organisation.
World Health Organization. 2018. High burden to high impact: a targeted malaria response. Geneva: World Health Organization.
World Health Organization. 2019. World malaria report 2019. Geneva: World Health Organization.
World Health Organization. 2020a. Malaria eradication: benefits, future scenarios and feasibility. Geneva: World Health Organization.
World Health Organization. 2020b. World malaria report 2020: 20 years of global progress and challenges. Geneva: World Health Organization.
World Health Organization & UNICEF. 2017. Global vector control response 2017-2030.
Yman, V., G. Wandell, D. D. Mutemi, A. Miglar, M. Asghar, U. Hammar, et al. (2019) Persistent transmission of Plasmodium malariae and Plasmodium ovale species in an area of declining Plasmodium falciparum transmission in eastern Tanzania. *PLoS Negl Trop Dis,* 13**,** e0007414.
Yukich, J., L. Stuck, S. Scates, J. Wisniewski, F. Chacky, C. Festo, et al. (2020) Sustaining LLIN coverage with continuous distribution: the school net programme in Tanzania. *Malar J,* 19**,** 158.
Zhang, S., L. Zhang, J. Feng, J. Yin, X. Feng, Z. Xia, et al. 2018. Malaria elimination in the People's Republic of China: current progress, challenges, and prospects. In *Towards Malaria Elimination-A Leap Forward*. IntechOpen.
Zhou, S.-S., S.-S. Zhang, L. Zhang, A. E. Rietveld, A. R. Ramsay, R. Zachariah, et al. (2015a) China's 1-3-7 surveillance and response strategy for malaria elimination: Is case reporting, investigation and foci response happening according to plan? *Infect Dis Poverty,* 4**,** 55.
Zhou, S.-S., S.-S. Zhang, L. Zhang, A. E. C. Rietveld, A. R. Ramsay, R. Zachariah, et al. (2015b) China's 1-3-7 surveillance and response strategy for malaria elimination: Is case reporting,

investigation and foci response happening according to plan? *Infectious Diseases of Poverty,* 4**,** 55.

Zhou, S. S., S. S. Zhang, L. Zhang, A. E. Rietveld, A. R. Ramsay, R. Zachariah, et al. (2015c) China's 1-3-7 surveillance and response strategy for malaria elimination: Is case reporting, investigation and foci response happening according to plan? *Infect Dis Poverty,* 4**,** 55.

Zhou, X.-N., R. Bergquist & M. Tanner (2013) Elimination of tropical disease through surveillance and response. *Infect Dis Poverty,* 2**,** 1.

Carriculum vitae

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Profile

I am a medical entomologist specializing in the ecology and control of *Anopheles* mosquitoes. For the past eight years, my work has been dedicated to monitoring and evaluating malaria surveillance tools. As my knowledge of vector control deepened, I have added Geographical Information System skills, specifically, focusing on the disease control program. In this way, I hope to assist the global malaria control community to respond to the ever-shifting vector control environment to achieve malaria eradication in a timely and cost-effective manner.
https://scholar.google.com/citations?user=m1HAiYwAAAAJ&hl=en

Education

2017- Todate **PhD candidate**
The University of Basel, Swiss Tropical and Public Health, Basel-Switzerland
Department of Epidemiology and Public Health, Health Intervention Unit
PhD thesis- "Indentifying, characterizing and targeting the reservoir of malaria transmission in southern Tanzania"
Advisors: Prof. Marcel Tanner, Dr. Penelope Vounatsou and Dr. Prosper Chaki

2011-2012 **Masters of Science Biology and Control of Parasites and Disease Vectors**
The University of Liverpool, Liverpool School of Tropical Medicine (LSTM), United Kingdom.
Study emphases: Parasites Epidemiology and Control, Vector Population Biology and Control
Master's thesis: "Evaluating the use of anonymized routine health facility-based data as a resource to identify malaria infection clusters in urban Dar es Salaam".
Advisors: Dr. Stefan Dongus, Dr. Gerry Killen and Dr. Anja Terlouw

2004-2007 **Bachelor of Science in Wildlife Science and Conservation (Hons)**
University of Dar es Salaam, College of Natural and Applied Science, Tanzania
Study emphases: Wildlife science and conservation
Project title: Socio-economic impact of salt excavation in the Wami estuary to the local livelihood of Saadani National Park.

Formal short courses

- Using Geographic Information Systems (GIS/ArcGIS) in the disease control programme, offered by the University of Twente (Faculty of Geo-Information

Science and Earth Observation/ITC) and the Royal Tropical Institute (KIT), Netherlands, 23rd June- 4th July 2014.

- Statistics and use of the R software training; Sponsored by European Union (AvecNet project) and African Malaria Network Trust (AMANET), and delivered by Afrique One Research Consortium on Ecosystem and Population Health, 14-18 May 2012, Dar es Salaam, Tanzania

- Introduction to Geographic Information System (GIS/Quantum GIS); Sponsored by European Union (AvecNet project) and African Malaria Network Trust (AMANET) and delivered by Afrique One Research Consortium on Ecosystem and Population Health, 13-16 June 2011, Dar es Salaam, Tanzania.

Work Experience

Research scientist, Ifakara Health Institute, 2012-Present
Projects

1. China-Tanzania joint pilot project on malaria control: application of community-based and integrated strategy to reduce malaria burden in rural Tanzania
2. Entomological quality assurance: supporting country-wide entomological surveillance of malaria vectors in Tanzania
3. Is routinely collected health facility data adequate for identifying hot spots of malaria transmission that should be prioritized by national control programmes?
4. Field evaluation of an alpha-cypermethrin long-lasting insecticidal net (Veeralin LN) against natural populations of Anopheles arabiensis in experimental huts, Tanzania" to calibrate the Ifakara Semi Field Tunnel test
5. Spatial Repellent Multi Centre- Can a Transfluthrin Passive Spatial repellent prevent transmission of Plasmodium falciparum malaria? A cluster-randomized double-blind placebo-controlled trial in children under 5 in rural Tanzania.
6. Developing a home-based geo-information system to optimize local level interventions against malaria mosquitoes
7. Determining the effectiveness of water, sanitation and hygiene interventions to reduce health vulnerability to climate change in Tanzania

July 2009 to 2011: Research Officer, Ifakara Health Institute

- Supervising the AVECNET project, specifically on surveillance of the disease vector behaviors, trapping tools and its related disease transmission
- Coordinating and supervising the entomological baseline surveillance on the effect of Indoor Residual Spraying on the transmission of lymphatic filariasis (LF) in the LF endemic setting sponsored Liverpool School of Tropical Medicine (UK).
- Coordinating the evaluation of affordable scalable systems for entomological monitoring of transmission intensity and key vector behaviours sponsored by President's Malaria Initiatives (PMI).
- Coordinating and supervising the Monitoring and Evaluation tools to allow sustained elimination of malaria transmission in urban Dar es Salaam, Tanzania sponsored by Bill & Melinda Gates Foundation.
- Supervising species identification collected from field, preservation, data management,

- Supervising Quality Control on Monitoring Adult Mosquito surveillance and Mosquito
- Behavioural Studies in urban and rural study sites

Research Grants and Scholarship Awards

1. Swiss Embassy Excellence Scholarship September 2017.**PhD programme**
2. American Society of Tropical Medicine and Hygiene 2017 ASTMH Annual Meeting **Travel Award**,
3. 10th European Congress on Tropical Medicine and International Health (ECTMIH) 16 - 20 October 2017 Antwerp, Belgium. **Scholarship award for travel and accommodation**
4. World Health organization grants award, **Project Title**; Field evaluation of an alpha-cypermethrin long-lasting insecticidal net (Veeralin LN) against natural populations of *Anopheles arabiensis* in experimental huts, Tanzania. Role in the project: Co-investigator/Project leader, Contact duration: 6 months, **Support level: US $55,222**
5. Netherlands Fellowship Programme (NFP) award, **Type of award**: short course training **Project Title**: Using Geographic Information Systems (GIS) in disease control programmes KIT/ITC Enschede: **Course duration**: 15days (21st June- 5th July 2014), **Donor**: NFP, **Support Level**: 4,567EUR
6. Rising Stars in Global Health Award phase 5 Grant from Grand Challenges Canada™. Role in the project: Co-investigators, **Project title**: Developing a home-based geoinformation system to optimize local level interventions against malaria mosquitoes, Donor: Grand Challenges Canada™, Project duration: Jan 2013 to October 2015. Total value: 112,000 Canadian Dollars.
7. Wellcome Trust Masters Fellowship on Public Health and Tropical Medicine; Role in the project: Principal Investigator, **Project title**: "Is routinely collected health facility data adequate for identifying hot spots of malaria transmission that should be prioritized by national control programmes?" **Support** Level: £79,380, 2.6 years (September 2011–March 2014). Sponsors: Dr. Anja Terlouw, Liverpool School of Tropical, UK; Dr. Salim Abdulla, Ifakara Health Institute, Tanzania.

Scientific publications

1. Odufuwa OG, Ross A, **Mlacha YP**, Juma O, Mmbaga S, Msellemu D, Moore S: Household factors associated with access to insecticide-treated nets and house modification in Bagamoyo and Ulanga districts, Tanzania. *Malar J* 2020, 19:220.
2. Msellemu D, Gavana T, Ngonyani H, **Mlacha YP**, Chaki P, Moore SJ: Knowledge, attitudes and bite prevention practices and estimation of productivity of vector breeding sites using a Habitat Suitability Score (HSS) among households with confirmed dengue in the 2014 outbreak in Dar es Salaam, Tanzania. *PLoS Negl Trop Dis* 2020, 14:e0007278.
3. **Mlacha YP**, Wang D, Chaki PP, Gavana T, Zhou Z, Michael MG, Khatib R, Chila G, Msuya HM, Chaki E, et al: Effectiveness of the innovative 1,7-malaria reactive community-based testing and response (1, 7-mRCTR) approach on malaria burden reduction in Southeastern Tanzania. *Malar J* 2020, 19:292.
4. **Mlacha YP**, Chaki PP, Muhili A, Massue DJ, Tanner M, Majambere S, Killen GF, Govella NJ: Reduced human-biting preferences of the African malaria vectors Anopheles arabiensis and Anopheles gambiae in an urban context: controlled, competitive host-preference experiments in Tanzania. *Malar J* 2020, 19:418.

5. Brydegaard M, Jansson S, Malmqvist E, **Mlacha YP**, Gebru A, Okumu F, Killeen GF, Kirkeby C: Lidar reveals activity anomaly of malaria vectors during pan-African eclipse. *Sci Adv* 2020, 6:eaay5487.
6. Wang D, Chaki P, **Mlacha Y**, Gavana T, Michael MG, Khatibu R, Feng J, Zhou ZB, Lin KM, Xia S, et al: Application of community-based and integrated strategy to reduce malaria disease burden in southern Tanzania: the study protocol of China-UK-Tanzania pilot project on malaria control. *Infect Dis Poverty* 2019, 8:4.
7. Mhalu G, Hella J, Mhimbira F, Said K, Mosabi T, **Mlacha YP**, Schindler C, Gagneux S, Reither K, de Hoogh K, et al: Pathways and associated costs of care in patients with confirmed and presumptive tuberculosis in Tanzania: A cross-sectional study. *BMJ Open* 2019, 9:e025079.
8. Killeen GF, Govella NJ, **Mlacha YP**, Chaki PP: Suppression of malaria vector densities and human infection prevalence associated with scale-up of mosquito-proofed housing in Dar es Salaam, Tanzania: re-analysis of an observational series of parasitological and entomological surveys. *Lancet Planet Health* 2019, 3:e132-e143.
9. Killeen GF, Govella NJ, **Mlacha YP**, Chaki PP: Attribution of reductions in malaria prevalence in Dar es Salaam, Tanzania - Authors' reply. *Lancet Planet Health* 2019, 3:e247.
10. Sikalengo G, Hella J, Mhimbira F, Rutaihwa LK, Bani F, Ndege R, Sasamalo M, Kamwela L, Said K, Mhalu G, et al: Distinct clinical characteristics and helminth co-infections in adult tuberculosis patients from urban compared to rural Tanzania. *Infect Dis Poverty* 2018, 7:24.
11. Mwakalinga VM, Sartorius BK, Limwagu AJ, **Mlacha YP**, Msellemu DF, Chaki PP, Govella NJ, Coetzee M, Dongus S, Killeen GF: Topographic mapping of the interfaces between human and aquatic mosquito habitats to enable barrier targeting of interventions against malaria vectors. *Royal Society Open Science* 2018, 5:161055.
12. Moshi IR, Manderson L, Ngowo HS, **Mlacha YP**, Okumu FO, Mnyone LL: Outdoor malaria transmission risks and social life: a qualitative study in South-Eastern Tanzania. *Malar J* 2018, 17:397.
13. Khatib RA, Chaki PP, Wang DQ, **Mlacha YP**, Mihayo MG, Gavana T, Xiao N, Zhou XN, Abdullah S: Epidemiological characterization of malaria in rural southern Tanzania following China-Tanzania pilot joint malaria control baseline survey. *Malar J* 2018, 17:292.
14. Msellemu D, Shemdoe A, Makungu C, **Mlacha Y**, Kannady K, Dongus S, Killeen GF, Dillip A: The underlying reasons for very high levels of bed net use, and higher malaria infection prevalence among bed net users than non-users in the Tanzanian city of Dar es Salaam: a qualitative study. *Malar J* 2017, 16:423.
15. **Mlacha YP**, Chaki PP, Malishee AD, Mwakalinga VM, Govella NJ, Limwagu AJ, Paliga JM, Msellemu DF, Mageni ZD, Terlouw DJ, et al: Fine scale mapping of malaria infection clusters by using routinely collected health facility data in urban Dar es Salaam, Tanzania. *Geospat Health* 2017, 12:494.
16. Mwakalinga VM, Sartorius BK, **Mlacha YP**, Msellemu DF, Limwagu AJ, Mageni ZD, Paliga JM, Govella NJ, Coetzee M, Killeen GF: Spatially aggregated clusters and scattered smaller loci of elevated malaria vector density and human infection prevalence in urban Dar es Salaam, Tanzania. *Malar J* 2016, 15:135.
17. Msellemu D, Namango HI, Mwakalinga VM, Ntamatungiro AJ, **Mlacha Y**, Mtema ZJ, Kiware S, Lobo NF, Majambere S, Dongus S, et al: The epidemiology of residual

Plasmodium falciparum malaria transmission and infection burden in an African city with high coverage of multiple vector control measures. *Malar J* 2016, 15:288.
18. Majambere S, Massue DJ, **Mlacha Y**, Govella NJ, Magesa SM, Killeen GF: Advantages and limitations of commercially available electrocuting grids for studying mosquito behaviour. *Parasit Vectors* 2013, 6:53.
19. Chaki PP, **Mlacha Y**, Msellemu D, Muhili A, Malishee AD, Mtema ZJ, Kiware SS, Zhou Y, Lobo NF, Russell TL, et al: An affordable, quality-assured community-based system for high-resolution entomological surveillance of vector mosquitoes that reflects human malaria infection risk patterns. *Malar J* 2012, 11:172.

Conferences and workshop attended

1. United Nations World Data Forum, 15-18 January 2017 in Cape Town, South Africa.
2. Tanzania-South Africa Joint Technical Workshop on Technology, Innovation and Institution Development, 1st-2nd March 2017, Dar es Salaam, Tanzania.
3. Leadership Training and Performance Management organized by Ifakara Health Institute in collaboration with Royal Tropical Institute (KIT), Dar es Salaam, Tanzania, June 16-20.2016.
4. The Stakeholders meeting to review and update the current integrated malaria vector control strategy, held at Amabili-Mogolole sisters house, Morogoro, Tanzania, May 28-30,2015 organized by National Malaria Control Programme (NMCP).
5. National Institute of Medical Research (NIMR) 28th Annual Joint Scientific Conference, which was held at Julius Nyerere International Convention Centre, Dar Es Salaam, Tanzania, 22-24 April 2014, (Oral presentation).
6. Hydromal project progress and stakeholder Meeting workshop, the workshop involved several scientists from Ifakara Health Institute and Aberystwyth University, Morogoro-Tanzania, January 2014, (Oral presentation).
7. 6th Pan-African Malaria Conference held at the International Convention Centre, Durban, South Africa. Moving towards malaria elimination: Investing in Research and Control, Africa, 6-11 October 2013, (Poster presentation).
8. Use of climate information for malaria stratification (Early Warning Systems/Impact Assessment for Malaria Interventions). A Training Workshop and Stakeholder Meeting hosted by the Tanzania Meteorological Agency, Dar es Salaam, Tanzania-October 16-18, 2013.
9. Workshop on Basic Health Research Ethics (HRE), Sponsored by European Union and African Malaria Network Trust (AMANET), and European Union via AVECNET project, 25-29 July 2011, Dar es Salaam, Tanzania.