Closing the Malaria Prevention Gap

Measuring and Characterizing Human Behavioral Drivers of Persistent Malaria Transmission in Sub-Saharan Africa

Inauguraldissertation

zur

Erlangung der Würde eines Doktors der Philosophie

vorgelegt der

Philosophisch-Naturwissenschaftlichen Fakultät der

Universität Basel

von

April Monroe

von Baltimore, Maryland, USA

Basel, 2020

Genehmigt von der Philosophisch-Naturwissenschaftlichen Fakultät auf Antrag von PD Dr. Sarah Moore, Dr. Lena Lorenz, und Prof. Dr. Marcel Tanner.

Basel, 23.04.2019

Prof. Dr. Martin Spiess

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Acknowledgements

It is impossible to adequately express my gratitude for the opportunity to pursue my PhD at the Swiss Tropical and Public Health Institute or to the large network of people who supported me throughout the process. While it is impossible to properly thank everyone who contributed, I would like to take the opportunity to explicitly acknowledge people who had a transformative impact on this work.

First and foremost, I would like to thank my PhD committee. Sarah Moore – I can never thank you enough for agreeing to be my supervisor or for the exceptional support, thoughtful and constructive feedback, and invaluable mentorship you have provided throughout this process. I truly could not have imagined a better supervisor. I hope you know that your belief in me and my work has made a profound difference in my life. I am truly grateful to Marcel Tanner for agreeing to serve as my second supervisor and for taking the time to provide such invaluable support to students. I would also like to sincerely thank Lena Lorenz for so kindly agreeing to act as the External Expert for this thesis and for many interesting conversations on this topic early on.

To Fredros Okumu – what started as a chance meeting in Switzerland turned into a wonderful collaboration that has changed my life in many ways. Thank you for helping me find the courage and path to pursue my PhD and for all that you have taught me throughout the process. Most importantly, thank you for always reminding me that the work we do in global health is so much bigger than ourselves.

To my team at Johns Hopkins University – I am grateful to work with such an exceptional group of people. To Hannah Koenker – you set an amazing example of what is possible in this field. Thank you for your invaluable feedback on this work. To Andrea Brown – I am eternally grateful for your abundant compassion, unparalleled support, and sage advice, especially during difficult times. To Matt Lynch – for always taking the time to discuss new ideas and for providing input on many aspects of this work. To Steve Harvey – thank you for giving me the opportunity to work in northern Ghana years ago, for sparking my interest in this topic, and for your continued support and collaboration. And to Rebecca Shore, Danielle Piccinini, Sean Blaufuss, Bola Olapeju, Hunter Harig, Eric Filemyr, and Angela Acosta for discussing and providing useful feedback on many iterations of these concepts and figures.

This work was funded by the U.S. President's Malaria Initiative (PMI) under the VectorWorks project, and I am grateful for the input and support provided by PMI colleagues, especially George Greer in Tanzania and Sixte Zigirumugabe in Ghana.

To my colleagues at Ifakara Health Institute (IHI), Zanzibar Malaria Elimination Program (ZAMEP), and Noguchi Memorial Institute for Medical Research, especially to Samson Kiware, Dickson Msaky, Kimberly Mihayo, Brian Tarimo, and Lina Finda at IHI; Abdullah Ali, Faiza Abbas, and Khamis Haji at ZAMEP; and Collins Ahorlu at Noguchi – it has been a pleasure and an honor to work with you. I have learned so much and am truly grateful for the wonderful partnerships that have emerged. I look forward to many more opportunities for collaboration in the future.

To my friends in Baltimore and Basel, especially Emily Ricotta, Samantha Tsang, Apoorva Sharan, Nancy Matowo, and Isaac Lyatuu for making writing fun. Having good company and nice coffee made working on weekends infinitely more enjoyable.

To the communities and households that participated in this research – thank you for graciously welcoming us into your homes, for sharing your perspectives, and for the priceless information you shared with us. This work would not have been possible without you.

To my family – from the first time I traveled to East Africa over 12 years ago, you have encouraged me to pursue my interests and passion in global health to the fullest. Thank you for your love, encouragement, thoughtful questions, and willingness to visit me halfway around the world.

And finally, in memory of Casey Coes – I lost you shortly before beginning this PhD and you have been with me every single day. I have learned that it is possible to experience tremendous growth even during the most devastating times of our lives. Thank you for making me kinder in the way that I approach the world, more grateful for the things I have, and more focused on what is truly important in life.

Summary

Malaria, a parasitic disease that attacks red blood cells, is responsible for nearly half a million deaths, and 219 million cases each year. While endemic in many parts of the world, a disproportionate burden of malaria cases and deaths are borne by people living in sub-Saharan Africa. The global malaria community achieved significant progress in recent years with cases falling by 37% and deaths by 60% between 2000 and 2015. These gains have been driven by successful vector control interventions, namely insecticide-treated nets (ITNs) and indoor residual spraying (IRS), prompt testing and diagnosis, effective treatment with artemisinin-based combination therapy (ACT), intermittent preventive treatment in pregnancy (IPTp), and strong malaria surveillance systems. Despite these successes, progress is beginning to stall, with the number of cases and deaths remaining relatively unchanged between 2015 and 2017.

Malaria is transmitted by the female Anopheles mosquito and ongoing transmission is a direct result of the overlap between human and vector behavior, and intervention presence and use. An estimated two-thirds of the reduction in malaria burden over the past two decades is attributable to ITNs, which provide a physical barrier against mosquito bites and kill mosquitoes that come into contact with them. Distribution of ITNs through universal coverage campaigns and continuous distribution channels has led to a significant increase in access to this life-saving intervention across many endemic countries. Understanding how to optimize the impact of ITNs, as well as identifying and addressing the fundamental limits of their protection, will be critical to maintaining and accelerating gains in malaria control and elimination.

The aim of this thesis is to identify opportunities to improve malaria prevention in sub-Saharan Africa through optimization of ITN access and use of available nets, and to quantify and characterize prevention gaps that remain once high levels of access and use are

achieved. By identifying the source of prevention gaps, appropriate and specific programmatic solutions can be identified and implemented. This aim was achieved through a range of methodological approaches, including 1) secondary analysis of large-scale household survey data from ten countries in sub-Saharan Africa, 2) primary research utilizing quantitative and qualitative methods in two countries, 3) a review of the published literature, and 4) development of a standardized approach to measuring the malaria prevention gap. The results of this work are synthesized in six manuscripts contained in this thesis.

First, to better understand trends in ITN access and use, a multi-country analysis was carried out using national household survey data. The results showed that ITN use is typically higher in females compared to males, and that young children and women of reproductive age are prioritized when there are not enough ITNs in the household. Older children are the least likely to use an ITN in the context of insufficient supply. Perhaps the most important finding from this analysis is that age and gender differences in ITN use largely disappear when households have enough ITNs to cover all sleeping spaces.

While in many contexts, levels of use are high among those with access to an ITN, this is not the case in all settings. National survey data provide useful quantitative estimates of use by location and demographic group, however in-depth information on ITN use practices is needed in places where nets are not used when they are available (low use to access ratio). Ghana is a country where a large gap between access and use remains, despite significant increases in population access since 2010. To better understand barriers and facilitators to ITN use and opportunities to close the gap, a qualitative research study was designed and implemented utilizing focus group discussions and case studies. The study found that ITN use is not binary; participants frequently described situational and seasonal use patterns.

Among participants who did not use an ITN consistently, heat was the most frequently listed barrier. A combination of heat and lower perceived risk contributed to low reported ITN use during the dry season compared to the rainy season. Barriers to ITN use throughout the year included experiences with skin irritation even after airing the ITN; congestion, and lack of airflow in the sleeping space; the perception that ITNs provide limited value because of exposure to mosquito bites during early evening hours and nighttime activities and, in some cases, a lack of information on the connection between the use of ITNs and malaria prevention.

Having a traumatic experience getting malaria, or having a loved one fall ill from malaria, were the most powerful motivators for consistent ITN use. Growing up using an ITN, or developing a habit of ITN use, were also listed as facilitating factors. Regular users described the benefits of a good night's sleep and the value ITNs play in not being disturbed by mosquitoes and other insects throughout the night. They also discussed the economic benefit of prevention over treatment and not losing time for work or other productive activities. Participants reported that ITN use is possible outdoors, and that sleeping outdoors with an ITN is a viable option for overcoming the challenge of heat and ensuring a good night's sleep during the dry season. Opportunities for improving communication messages as well as structural approaches to enhance the usability of ITNs in challenging contexts were identified from this work.

While ensuring high levels of ITN access and use is essential, in many contexts, malaria can persist even once these targets have been achieved. A key challenge is the indoor orientation of current vector control measures such as ITNs. Increases in outdoor vector feeding and resting in settings where people spend significant time outside at night may allow vectors to avoid interventions and may consequently limit their effectiveness. Transmission that persists in the context of high coverage of ITNs or IRS, referred to as residual malaria transmission, represents a critical challenge for malaria elimination. To target residual malaria transmission, it is essential to better understand how human behavior intersects with vector behavior.

A review of published literature was carried out with the aim of synthesizing the current body of evidence on human behavior as it relates to transmission that can occur in the context of high vector control coverage, and existing methods for measuring and characterizing this human behavior. The review focused on human behavior in sub-Saharan Africa based on the disproportionate burden of malaria in these countries. Results of the review suggest there are broad night time human activity categories that may be similar across settings in sub-Saharan Africa, including household chores, entertainment, livelihood activities, and large-scale community events. The review also revealed that human-vector interaction indicators remain heavily under-utilized and inconsistently applied.

Improved approaches for measuring and characterizing human behavior and human-vector interaction were applied in a primary research study on the drivers of residual malaria transmission in Zanzibar. The work included layered entomological and human behavioral research and utilized quantitative and qualitative methods to measure and characterize human exposure to malaria vectors. The study revealed that while access to ITNs and use of ITNs during sleeping hours among the study population was generally high, less than half of total exposure to malaria vectors is prevented by current levels of ITN use. Gaps in protection were identified when participants were outdoors or away from home. Travel and migration emerged as a crucial issue and participants viewed seasonal workers as more likely to have a malaria infection and less likely to be connected to prevention and treatment services in Zanzibar. Some community leaders reported taking the initiative to link seasonal workers to the health care system and required malaria testing to work in their community.

In Zanzibar, and other pre-elimination settings, targeting interventions effectively is critical, and should be informed by a clear understanding of relevant human behavior. There is an opportunity to explore the use of supplemental vector control tools and accompanying social and behavior change interventions to help address these gaps. Migration and travel of malaria infected individuals from higher transmission settings into Zanzibar must also be addressed to reach elimination. Existing community structures provide potential mechanisms for addressing gaps in protection, as well as targeting higher risk groups such as travelers and seasonal workers.

Building on existing methods identified in the literature and lessons learned through primary research studies and global engagement, a harmonized approach to measuring gaps in malaria prevention was developed. This article included critical entomological and human behavioral data elements that need to be captured, methods for calculating relevant indicators for expressing human-vector interactions, and suggestions for best practices for collecting and analyzing this data. If collected and used consistently, this information can dramatically improve our understanding of how malaria transmission can persist in the context of core vector control interventions, how exposure patterns may change when additional vector control tools are introduced, and the potential and limitations of those tools.

A better understanding of human behavior, and how it intersects with vector behavior, will be essential for closing the malaria prevention gap. Targeting malaria transmission that persists across contexts in sub-Saharan Africa requires an understanding of the range of factors driving remaining transmission, including sub-optimal implementation quality for core vector control interventions, gaps in use among those with access, product effectiveness, as well as the fundamental limits of core vector control tools. To sustain and increase gains in malaria prevention in the context of limited resources, it is essential to ensure populations at risk of malaria have continuous access to effective vector control interventions, identify and address barriers to consistent use, maintain product effectiveness, and effectively measure and target remaining gaps in protection. Effective vector control tools can have an enormous impact on malaria cases and deaths. However, these opportunities to optimize malaria prevention must be coupled with sustainable solutions for economic development to ensure long-term success in the areas hardest hit by the disease.

List of abbreviations

ACT	artemisinin-based combination therapy
ANC	antenatal care
API	annual parasite incidence
aOR	adjusted odds ratio
CI	confidence interval
CSM	cerebrospinal meningitis
DDT	dichloro diphenyl trichloroethane
DHS	demographic and health survey
ELISA	enzyme-linked immunosorbent assays
EPI	expanded program on immunization
FGD	focus group discussion
GHS	Ghana Health Service
GPS	global positioning system
HLC	human landing catch
IDI	in-depth interview
IEBS	Ifakara entomology bioinformatics system
IPTp	intermittent preventative therapy in pregnancy
IRS	indoor residual spraying
ITN	insecticide-treated net
KII	key informant interview
MEP	Malaria Eradication Program
MERG	monitoring and evaluation reference group
MIS	malaria indicator survey

PCR	polymerase chain reaction
PMI	President's Malaria Initiative
RBM	Roll Back Malaria
RDT	rapid diagnostic test
WHO	World Health Organization
ZAMEP	Zanzibar Malaria Elimination Program

Chapter 1: Introduction

1.1 Malaria biology

Malaria kills a person nearly every minute, most often a child under the age of five. In 2017, malaria was responsible for an estimated 435,000 deaths and 219 million cases. Nearly half of the world's population lives at risk of the disease (WHO, 2018b). Symptoms of malaria include fever, headache, nausea, vomiting, and seizures. Severe malaria can lead to acute kidney failure, respiratory distress syndrome, coma, and death (White et al., 2014).

Malaria is a parasitic infection transmitted from one human to another by female *Anopheles* mosquitoes (White et al., 2014). Humans can be infected by several species of the *plasmodia* parasite: *Plasmodium falciparum, P. vivax, P malariae, and P. ovale,* and less commonly, *P. knowlesi.* Of these species, *P. falciparum and P. vivax* account for the majority of cases and *P. falciparum* is responsible for nearly all malaria-related deaths (WHO, 2018b, Warrell and Gilles, 2017, White et al., 2014).

The malaria parasite has a complex life-cycle. First, an infected mosquito injects sporozoites into a person's blood stream while taking a blood meal. Sporozoites move to the liver and multiply, creating merozoites which invade, and eventually burst, red blood cells. Some parasites develop into gametocytes, which can be picked up by an *Anopheles* mosquito during a blood meal. The gametocytes reproduce sexually in the mosquito's midgut and sporozoites then move into the salivary glands where they can be transmitted to a person during subsequent blood meals (White et al., 2014).

1.2 Historical context

Malaria once covered a broad swath of the globe, including many parts of Africa, Europe, Asia, and North and South America. The disease declined, and was eventually eliminated, in North America and Europe in the 19th and 20th centuries but persisted in tropical and sub-tropical regions of Africa, Asia, Latin America, and the Pacific (Packard, 2007). A number of factors likely contributed to this trend including stable malaria transmission in many parts of the tropics and the presence of efficient malaria vectors highly susceptible to malaria infection (Packard, 2007).

Social, political, and economic changes also impacted the trajectory of the disease. The introduction and advancement of agricultural practices, infrastructure development, changes in housing structure and quality, war, and expansion of industries such as mining, could impact the local vector ecology and human exposure to the disease (Packard, 2007). Likewise, population movements associated with these changes contributed to the spread of the disease across geographic locations.

Across settings, people living in poverty were more likely to live and work under conditions that exacerbated the impact of malaria. This included living in sub-standard housing, food insecurity, inadequate drainage and sanitation systems, insufficient access to treatment and other health services, living and working in conditions that increased exposure to malaria vectors, and displacement due to conflict (Packard, 2007).

1.3 Evolution of vector control for malaria prevention

Biomedical approaches directly targeting malaria vectors emerged at the end of the 19th century as the etiology of the disease became better understood. Prior to this time, reductions in malaria were largely associated with broader economic development, including advances in agricultural practices and improved housing, which limited human contact with malaria vectors (Packard, 2007).

In the early 20th century, malaria prevention focused largely on eliminating vector breeding sites either by draining them or using larvicides. During World War II, the urgency for developing new malaria control methods increased as soldiers fighting in malaria endemic areas suffered greatly from the mosquito-borne diseases (Packard, 2007). Methods previously used to reduce vector breeding sites were less effective due to the mobile nature of troops, making personal protection measures, such as long sleeves, repellents, and prophylaxis more useful. During this time, interest in chemical control measures heightened, while interest in broader areas of malaria research and control declined (Packard, 2007). In 1942, dichloro diphenyl trichloroethane (DDT), a potent new insecticide, was introduced. Following World War II, indoor residual spraying (IRS) with DDT was carried out in parts of Europe, Latin America, and India to reduce local vector populations. IRS worked by killing mosquitoes that rested on walls following a blood meal, and DDT's long residual life combined with high killing effect made it the insecticide of choice. Early successes led to a primary focus on DDT, and other pesticides, among control programs (Packard, 2007).

The Malaria Eradication Program (MEP) was launched in 1955, relying almost exclusively on IRS with DDT, and continued until 1969. The program achieved some success in eradicating malaria, largely in higher-resource countries that had existing sanitation systems, improved housing, strong heath systems, and the infrastructure to implement eradication strategies effectively. Eradication was not feasible in a large majority of tropical countries with eradication programs, and many of these countries experienced a severe resurgence of the disease following the MEP (Packard, 2007).

Challenges included difficulties in sustaining high levels of coverage and spray quality, a failure to sufficiently engage local communities to build acceptance for the intervention, and growing resistance of malaria vectors to DDT (Packard, 2007). Vector resistance to DDT was exacerbated by sub-optimal implementation quality, such as incomplete spray operations or use of diluted spray, as well as concurrent use of DDT for agriculture and vector control purposes. While additional insecticides were subsequently developed, they were more expensive than DDT, making effective large-scale deployment of IRS less feasible (Packard, 2007). The failure of the MEP to achieve its objectives led to subsequent declines in funding in the 1970s and 1980s, posing a significant challenge to malaria control efforts and contributing to resurgence of the disease in many parts of the world (Packard, 2007).

Funding levels began to rise again in the late 1990s and early 2000s, largely due to the establishment of new mechanisms for resource mobilization, coordination, and funding for malaria. The Roll Back Malaria (RBM) partnership, a multi-lateral program including the World Health Organization (WHO), United Nations Children's Fund, World Bank, and United Nations Development Program, was established in 1998, and played a key coordination role in the global response to malaria (RBM, 2017). The Global Fund to Fight AIDS, Tuberculosis, and Malaria was founded in 2002 and became a primary mechanism to raise, manage, and distribute funding from international donors (WHO, 2018b). The U.S. President's Malaria Initiative (PMI) was launched in 2005 and the United States government soon became the single largest international funder for malaria programs (WHO, 2018b). Initially focused on 15 high-burden countries in sub-Saharan Africa, PMI eventually expanded its reach to include work in 24 countries in sub-Saharan Africa and four programs in the Greater Mekong Sub-Region.

During this time, insecticide-treated nets (ITNs), which provide a physical barrier of protection and kill mosquitoes that come into contact with them, became a cornerstone of malaria control efforts. While untreated bed nets had been used in various forms for centuries, strong evidence of the public health impact of ITNs began to emerge in the 1980s from experimental huts trials (Darriet et al., 1984) and in the 1990s from individual and cluster randomized trials (Alonso et al., 1991, Binka et al., 1996, Habluetzel et al., 1997, Nevill et al., 1996). A systematic review found ITNs significantly reduced child mortality, malaria incidence, and parasite prevalence compared to untreated nets or no nets (Lengeler, 1998).

Initially targeted toward pregnant women and infants, in 2008 the WHO recommended universal coverage of ITNs for all people at risk of malaria (WHO, 2008b). Following this recommendation, funding for ITNs increased substantially, with the number of ITNs distributed in sub-Saharan Africa jumping from less than 6 million in 2004 to 145 million in 2010 and 175 million in 2017 (WHO, 2012b, WHO, 2018b). To achieve the goal of universal coverage, many countries began distributing ITNs at scale, largely through mass distribution campaigns, usually every three years, and to a lesser extent through continuous distribution channels such as antenatal and immunization clinics, schools, community-based channels, or the commercial sector (Stevens et al., 2005, Agha et al., 2007, Beiersmann et al., 2008, Müller et al., 2008, Yukich et al., 2009, Kolaczinski et al., 2010, Grabowsky et al., 2007, Hanson et al., 2009, Beer et al., 2010, Hightower et al., 2010, Terlouw et al., 2010, Thwing et al., 2008). As a result, the proportion of people living in endemic countries with access to an ITN increased from 33% in 2010 to 56% in 2015 and remained relatively unchanged between 2015 and 2017 (WHO, 2018b).

Today, ITNs and IRS are the two core vector control interventions recommended by WHO for widescale implementation among populations at risk of malaria (WHO, 2019). While ITNs have been distributed at scale in many countries, IRS is largely deployed in a targeted way, and was estimated to protect 3% of people at risk of malaria in 2017 (WHO, 2018b). Between 2000 and 2015, the global burden of malaria decreased significantly; annual cases fell by approximately 40% and annual deaths by 60% (WHO, 2016). ITNs alone were estimated to have contributed to 68% of the reduction in malaria infections during this time and combined, ITNs and IRS accounted for an estimated three-quarters of the decline (Bhatt et al., 2015a).

1.3 Residual malaria transmission

While ITNs and IRS have had a tremendous impact on public health, there are limitations to the protection they can provide. Residual malaria transmission, defined by the World Health Organization as, "persistence of parasite transmission even with good access to and usage of ITNs or well-implemented IRS, as well as in situations where ITN use or IRS are not practical," represents a critical challenge to malaria control and elimination efforts (malERA, 2011, Durnez and Coosemans, 2013b, Killeen, 2014, WHO, 2014).

The indoor orientation of these interventions presents a significant constraint as their effectiveness is limited against outdoor vector feeding at times when people are outdoors and active. This issue may be compounded by shifts in the behavior of Afrotropical vectors in response to vector control interventions across many settings (Durnez and Coosemans, 2013b, Govella and Ferguson, 2012a, Moiroux et al., 2012, Reddy et al., 2011, Wamae et al., 2015, Yohannes and Boelee, 2012). The dominant malaria vectors in Africa include *Anopheles gambiae sensu lato* (s.l.), which includes An. *gambiae sensu stricto*, *Anopheles coluzzii* and *Anopheles arabiensis*, and *Anopheles funestus sensu stricto* (s.s.) (Githeko et al., 1996, Moiroux et al., 2012, Sinka et al., 2010). *An. gambiae s.s.*, *An. coluzzii* and *An. funestus s.s.* are typically anthropophagic and feed and rest indoors (Durnez and Coosemans, 2013b), while *An. arabiensis'* behavior is more plastic, showing zoophagic and exophilic tendencies (Tirados et al., 2006b, Killeen et al., 2016). The differences in biting and resting behaviors affect the success of interventions like IRS and ITNs, as mosquitoes that feed and rest inside are more likely to encounter insecticide than those who feed and rest outside.

Further, in recent years shifts in vector behavior following introduction of malaria control interventions in certain locations have been observed (Moiroux et al., 2012, Govella and Ferguson, 2012a, Reddy et al., 2011, Yohannes and Boelee, 2012, Wamae et al., 2015, Gatton et al., 2013, Sinka et al., 2016). These changes can include species shifts, shifts toward early evening and early morning biting, toward outdoor resting and biting, and toward zoophily (Durnez and Coosemans, 2013b). While these shifts in vector behavior are a result of successful vector control (Rund et al., 2016), there is an urgent need to understand when and where people remain at risk for malaria transmission to effectively deploy appropriate interventions.

1.4 Human behavior and malaria prevention

An improved understanding of human behavior is essential to closing the malaria prevention gap. Investigations of human behavior can shed light on patterns of malaria exposure and factors that may increase or inhibit the operational effectiveness of current and future vector control interventions. The level of acceptance of malaria prevention interventions such as IRS, motivation to obtain an ITN from available distribution channels, decisions on if and how to use and maintain an ITN, and intra-household decision-making and prioritization of ITNs can all impact the protection provided by core vector control interventions (Lam et al., 2014, Packard, 2007, Eisele et al., 2011, Montgomery et al., 2010, Munguambe et al., 2011, Pulford et al., 2011, Loll et al., 2013, Mboma et al., 2018, Dillip et al., 2018).

Likewise, night time activity and sleeping patterns, sociocultural events, livelihood activities, and population movements can impact exposure to malaria vectors and highlight the limits to the protection provided by ITNs or IRS. An improved understanding of night time activity and sleeping patterns can inform effective targeting of supplemental interventions to specific places, groups, and activities where they are needed most. While significant attention has been given to measuring and monitoring vector behavior, as well as intervention coverage, a significant gap remains in our understanding of human behavior during times when malaria vectors are active, when and where human and vector behavior intersect, and how best to integrate this information toward programmatically meaningful recommendations.

Given the magnitude of ITN distribution globally and the level of contribution of ITNs to malaria prevention, this thesis focuses mainly on optimization of ITNs and understanding remaining gaps in personal protection. However, many issues raised are relevant for IRS programs. Likewise, it focuses specifically on issues in sub-Saharan Africa based on the disproportionate impact of malaria on the continent.

This thesis contributes to the evidence base through a range of methodological approaches, including secondary analysis of large-scale household survey data from ten countries in sub-Saharan Africa, primary research utilizing quantitative and qualitative methods in two countries, a review of the published literature, and development of a standardized approach to measuring gaps in personal protection. The results of this work are synthesized in six manuscripts presented here within.

1.5 Thesis aim and objectives

The aim of this thesis is to identify opportunities to improve malaria prevention in sub-Saharan Africa through optimization of ITN access and use, and to quantify and characterize prevention gaps that remain once high levels of access and use are achieved. Specific objectives contributing to this aim include:

1. Identify age and gender trends in ITN access and use across sub-Saharan Africa
2. Identify key barriers and facilitators to consistent ITN use in Ghana, where a large gap between ITN access and use remains
3. Document the current body of evidence on human behavioral determinants of residual malaria transmission in sub-Saharan Africa

4. Measure and characterize drivers of residual malaria transmission in Zanzibar, a pre-elimination context
5. Contribute to improved methods for measuring gaps in personal protection against malaria vectors

Chapter 2: Age and gender trends in insecticide-treated net use in sub-Saharan Africa: a multi-country analysis

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Published in
Malaria Journal 2018 **17**:423

https://doi.org/10.1186/s12936-018-2575-z

2.1 Abstract

Background

The degree to which insecticide-treated net (ITN) supply accounts for age and gender disparities in ITN use among household members is unknown. This study explores the role of household ITN supply in the variation in ITN use among household members in sub-Saharan Africa.

Methods

Data was from Malaria Indicator Surveys (MIS) or Demographic and Health Surveys (DHS) collected between 2011- 2016 from 29 countries in sub-Saharan Africa. The main outcome was ITN use the previous night. Other key variables included ITN supply (nets/household members), age and gender of household members. Analytical methods included logistic regressions and meta-regression.

Results

Across countries, the median (range) of the percentage of households with enough ITNs was 30.7% (8.5 to 62.0%). Crude analysis showed a sinusoidal pattern in ITN use across age groups of household members, peaking at 0-4 years and again around 30-40 years and dipping among people between 5-14 and 50+ years. This sinusoidal pattern was more pronounced in households with not enough ITNs compared to those with enough ITNs. ITN use tended to be higher in females than males in households with not enough ITNs while use was comparable among females and males in households with enough ITNs. After adjusting for wealth quintile, residence and region, among households with not enough ITNs in all countries, the odds of ITN use were consistently higher among children under 5 years and non-pregnant women 15-49 years. Meta-regressions showed that across all countries, the mean adjusted odds ratio (aOR) of ITN use among children under 5 years, pregnant and non-pregnant women aged 15-49 years and people 50 years and above was significantly higher than among men aged 15-49 years. Among these household members, the relationship was attenuated when there were enough ITNs in the household (dropping 0.26-0.59 points) after adjusting for geographical zone, household ITN supply, population ITN access, and ITN use:access ratio. There was no significant difference in mean aOR of ITN use among school-aged children compared to men aged 15-49 years, regardless of household ITN supply.

Conclusions

This study demonstrated that having enough ITNs in the household increases level of use and decreases existing disparities between age and gender groups. ITN distribution via mass campaigns and continuous distribution channels should be enhanced as needed to ensure that households have enough ITNs for all members, including men and school-aged children.

Keywords Insecticide-treated nets, use, household supply, age, gender, household members, sub-Saharan Africa

2.2 Background

According to the World Malaria Report, there were an estimated 216 million cases of malaria globally in 2016 while the estimated number of malaria deaths was 445,000 in 2016 (WHO, 2017e). Africa continues to carry a disproportionately higher share of the global malaria burden as 90% of malaria cases and deaths occur in this continent with 15 countries in sub-Saharan Africa accounting for 80% of the global malaria burden (WHO, 2017e). The World Health Organization (WHO) recommends the use of insecticide-treated nets (ITNs) as a key element of vector control by all individuals at risk of malaria, and distribution of free ITNs is a core intervention in national malaria control strategies of all sub-Saharan Africa countries (Sexton, 2011). In an effort to achieve universal coverage, i.e., universal access to and use of ITNs by populations at risk of malaria (WHO, 2017a), over 800 million nets have been delivered in sub-Saharan Africa between 2011 and 2016, mostly under universal coverage campaigns (WHO, 2017e). This investment has resulted in an increased proportion of Africans in malaria-endemic areas who slept under an ITN, from 2010 30%, to 2016 54% (WHO, 2017e). To meet the target of universal access, WHO recommends that one ITN be distributed for every two persons at risk of malaria (WHO, 2017e). To further improve ITN coverage in Africa, gaps in ITN access as well as ITN use need to be explored and addressed (van Eijk et al., 2011).

Recent studies have shown that the major driver of ITN use is access, as one cannot use an ITN unless there is one available for use (Eisele et al., 2009, Graves et al., 2011, Koenker and Kilian, 2014, Bhatt et al., 2015b). After ITN access has been addressed, individual level factors, including age and gender of household members, have also been associated with ITN use. Studies across Africa demonstrate that ITN use is typically higher among females compared to males (Garley et al., 2013). ITN use is also correlated with age (N Ng'ang'a et al., 2009) and has been shown to be higher in certain age groups, e.g., infants

(Larson et al., 2014a, Larson et al., 2014b) or children under 5 years of age (Fokam et al., 2017) compared to older children aged 5-14 years and adolescents and young adults aged 15-24 (Loha et al., 2013, Noor et al., 2009). The association of age with ITN use also seems to be moderated by gender, such that men, older children and teenagers were less likely to sleep under an ITN compared to women and children under five years old (Babalola et al., 2016). It is unclear whether certain household members are prioritized only because the number of nets in the household is not enough. Thus, the supply of nets in the household might be the reason for the age/gender disparities in ITN use.

This paper explores to what extent ITN supply (having enough nets for household members) accounts for age and gender disparities in ITN use among household members in sub-Saharan Africa. ITN use has been shown to increase dramatically in all age groups and gender following mass free distribution of ITN (Finlay et al., 2017, Loha et al., 2013) suggesting that certain household members are prioritized for ITN use when there are not enough ITNs in the household. The relationships between ITN supply, household members and ITN use are worth exploring to understand whether improving supply of ITNs in a household might reduce age and gender disparities in ITN use.

2.3 Methods

This study analyses secondary data from recent national surveys in sub-Saharan Africa.

Data from recent (conducted between 2011-2016) Malaria Indicator Surveys (MIS) or Demographic and Health Surveys (DHS) among countries in sub-Saharan Africa, were included in the analysis. Recent surveys were defined as those conducted between 2011 and 2016. The most recent publicly available MIS or DHS data from a total of 29 malaria endemic countries (Namibia was excluded given its limited malaria risk (WHO, 2017e)). were downloaded with permission from the DHS Program website, www.dhsprogram.com.

The countries were categorized into 3 geographical zones, Central, East and West Africa, based on the United Nations geoscheme for Africa. East Africa region included 10 countries (34.5%), Central Africa, 7 countries (24.1%) and West Africa, 12 countries (41.4%).

The main outcome of the study is use of an ITN the previous night and this was calculated for each *de facto* member of the household, i.e., all those present in the house the previous night, as recommended by WHO's Roll Back Malaria Monitoring and Evaluation Reference Group (MERG) (DHS, 2013b). A main predictor variable was household ITN supply and this was defined as the number of ITNs present in the household divided by the *de jure* household members and was further dichotomized into 'not enough' (ITN: person ratio of less than 0.5) *versus* 'enough' (ITN: person ratio of 0.5 or more equivalent to one ITN for every 2 people). The other main predictor variables of interest included gender (male *versus* female) and age (categorized in 5-10 year increments (0-4, 5-9, 10-14, 15-19, 20-29, 30-39, 40-49, 50-59, and 60+ years) of *de facto* household members. In addition, a composite variable called 'demographic group' variable was created based on age, gender and pregnancy status of the *de facto* household members. The following demographic groups were defined: children under 5 years old, school-aged children 5-14 years, women aged 15-49 years who were currently pregnant, women aged 15-49 years who were not currently pregnant, men aged 15-49 years (reference group) and adults aged 50 years or more.

Other socio-demographic variables included household wealth quintile based on the standard DHS wealth index determined by principal component analysis on household assets, residence (urban/rural), and region (sub-national administrative divisions for each country). Two contextual variables included in the analysis include population level ITN access and use given access (use:access ratio). The population ITN access indicator for each country was calculated according to MERG guidance by dividing the potential ITN users (number of ITNs in the household multiplied by 2) by the number of *de facto* members for each household, setting the result to 1 if there were more potential users than *de facto* members, and determining the overall sample mean of that fraction (Koenker and Kilian, 2014). To assess whether people who have ITNs actually use them, the ratio of population-level ITN use to population ITN access was calculated.

All analysis was limited to households with at least one ITN. First, plots of ITN use by age and gender of *de facto* household members, stratified by household ITN supply were constructed for each country separately. Then, multivariable logistic regressions were conducted for each country, stratified by household ITN supply, to explore differences in ITN use among demographic groups, controlling for household wealth quintile, residence and region. Next, to synthesize the findings across all countries, a meta-regression was conducted to explore the mean adjusted odds ratio (aOR) of ITN use across demographic groups across all 29 countries. Each country was stratified by household ITN supply for a total sample size of 58. Plots of the mean aOR and 95% confidence interval (CI) of ITN use among demographic groups stratified by ITN supply were constructed over all countries and also by the 3 geographic zones (Central, East and West Africa). The model included the following country-level covariates: geographical zone, household ITN supply, population ITN access and ITN use: access ratio. To account for different sample size of each country, the number of *de facto* populations in households with at least one ITN was used as a probability weight.

Data management and analysis was done using Stata version 14 (Stata, 2015) and Excel 2016. All country-level analyses used sample weights to adjust for DHS sample design and individual response rate (Rutstein and Rojas, 2006).

2.4 Results

Table 1 presents the proportion of households with enough ITNs and population-level ITN access and use:access ratio for each survey. Across countries, the median (range) of the percentage of households with enough ITNs was 30.7% (8.5-62.0%). The median (range) of the percentage of households with enough ITNs was 14.5% (8.5-24.3%) in Central; 38.4% (22.7-62.0%) in East Africa; and, 30.7% (9.3-56.7%) in West Africa. In only 3 countries did more than 50% of households own enough ITNs: Uganda (62.0%), Senegal (56.7%) and Ghana (50.3%). Similarly, the median (range) of the percentage of the *de facto* population with access to an ITN in their household was 26.9% (19.7-61.2%) in Central; 55.9% (37.2 - 78.8%) in East; and, 49.0% (25.3-75.7%) in West Africa. Overall, the proportion of the population that used an ITN the previous night was greater than 50% in only 8 countries (Madagascar, Rwanda, Uganda, Democratic Republic of Congo, Benin, Burkina Faso, Mali, Senegal). ITN use: access ratio varied widely across the countries from 0.23 in Zimbabwe to 1.15 in Congo-Brazzaville.

Figures 2.1-2.3 highlight country-level population ITN use stratified by ITN supply, age and gender in Central (Fig. 2.1), East (Fig. 2.2) and West (Fig. 2.3) Africa. In all countries, regardless of age and gender, ITN use was higher among people in households with enough ITNs compared to those in households with not enough ITNs. For people from households with not enough ITNs, ITN use showed a sinusoidal pattern, peaking at 0-4 years and again around 30-40 years and dipping among people between 5-14 and 50+ years. This sinusoidal pattern was less pronounced in households with enough ITNs. In households with not enough ITNs, ITN use was higher in females compared to males in many age groups. Among people living in households with enough ITNs, use was more comparable among males and females in all age groups.

Table 2.2 presents the aOR of ITN use the previous night among demographic groups (reference group: men 15-49 years) stratified by household ITN supply and controlling for household wealth index, household residence and region.

Among households with not enough ITNs, two demographic groups: children under 5 years and non-pregnant women had consistent significantly higher odds of ITN use compared to men aged 15-49 years in all countries. The median (range) aOR of ITN use among children under 5 years old in all 29 countries was 1.86 (1.22-3.81). Non-pregnant women in all 29 countries had a median (range) aOR of 1.76 (1.22-3.36). In addition, pregnant women in all 27 countries with available data had a median (range) aOR of 2.26 (1.48-4.27), although the aOR was not statistically significant in Zimbabwe, Ivory Coast, Madagascar, and Congo-Brazzaville. Children aged 5-14 years had a median (range) aOR of 0.94 (0.55-1.58); the aOR was significantly lower in 11 countries, significantly higher in 10 countries and not statistically significant in 8 out of 29 countries.

Among households with enough ITNs, the disparities in ITN use across demographic groups was attenuated. There was no demographic group with significantly higher odds of ITN use across all countries. The median (range) aOR of ITN use among children under 5 years old was 1.48 (0.93-2.80) although the aOR was not statistically significant in 8 and significantly higher in 21 of the 29 countries. Pregnant women had a median (range) aOR of ITN use of 1.29 (0.90-2.59). Similarly, the aOR was not statistically significant in eight countries and significantly higher in 21 countries of the 29 countries. Among pregnant women, the median (range) aOR of ITN use was 1.75 (0.46-4.36) although the aOR was significantly lower in Zimbabwe, not statistically significant in 14 countries and significantly higher in 12 of the 27 countries with available data. Children aged 5-14 years had a median (range) aOR of 0.98 (0.60-2.40), the aOR was significantly lower in 9 countries, significantly higher in 5 countries and not statistically significant in 15 countries.

Figure 2.4 presents results of the meta-regression of the aORs of ITN use among demographic groups, stratified by ITN supply across all 29 countries, and in addition, for each geographic zone. Overall, the mean aOR of ITN use was significantly higher among children under 5 years, pregnant and non-pregnant women aged 15-49 years and people 50 years and above compared to the reference group of men aged 15-49 years. Also, the differences in ITN use across demographic groups tended to be reduced when there were enough ITNs. In addition, for children under 5 years, pregnant and non-pregnant women aged 15-49 years and people 50 years and above, the aORs of ITN use were higher in households with enough ITNs compared to households with not enough ITNs. There was no significant difference in mean aOR of ITN use among school-aged children compared to men aged 15-49 years, regardless of household ITN supply. This trend was seen over all countries and across the 3 geographic zones. Of note, the variation in mean aOR of ITN use across household members was most pronounced in West compared to East or Central Africa.

Table 2.1 List of countries and key insecticide-treated net indicators

Country	Survey	Year	% of households with enough ITNs [1]	% of *de facto* population with ITN access	% of *de facto* population that used an ITN the previous night	Use : access ratio
Central Africa						
Angola	DHS	2015-16	10.9	19.7	17.6	0.89
Burundi	MIS	2012	23.9	46.0	48.6	1.06
Cameroon	DHS	2011	8.5	20.9	14.8	0.71
Chad	DHS	2014-15	40.8	61.2	33.3	0.54
Congo Brazzaville	DHS	2011-12	10.4	22.6	26.0	1.15
Democratic Republic of Congo	DHS	2013-14	24.3	46.5	50.2	1.08
Gabon	DHS	2012	14.5	26.9	26.7	0.99
East Africa						
Kenya	MIS	2015	40.1	52.5	47.6	0.91
Madagascar	MIS	2016	43.1	62.1	68.2	1.10
Malawi	DHS	2015-16	22.7	38.8	33.9	0.87
Mozambique	DHS	2015	38.4	53.8	45.4	0.84
Rwanda	DHS	2014-15	42.2	63.8	61.4	0.96
Tanzania	DHS	2015-16	37.2	55.9	49.0	0.88
Uganda	MIS	2014-15	62.0	78.8	68.6	0.87
Zambia	DHS	2013-14	25.0	65.0	56.9	0.88
Zimbabwe	DHS	2015	26.1	37.2	8.5	0.23
West Africa						
Benin	DHS	2011-12	43.3	64.0	62.6	0.98

Burkina Faso	MIS	2014	47.4	71.2	67.0	0.94
Cote D'Ivoire	DHS	2011	30.7	49.0	33.2	0.68
Gambia	DHS	2013	20.1	45.3	36.9	0.82
Ghana	MIS	2016	50.3	65.8	41.7	0.63
Guinea	DHS	2012	9.3	25.3	18.9	0.75
Liberia	MIS	2016	23.5	41.5	39.2	0.94
Mali	MIS	2015	37.6	69.5	63.8	0.92
Niger	DHS	2012	14.4	37.3	13.8	0.37
Nigeria	MIS	2015	34.4	54.7	37.3	0.68
Senegal	cDHS	2016	56.7	75.7	63.1	0.83
Sierra Leone	MIS	2016	14.6	37.1	38.6	1.04
Togo	DHS	2013-14	32.5	48.8	33.6	0.69

Abbreviations: DHS- Demographic Health Survey; ITN: Insecticide-treated nets; MIS: Malaria Indicator Survey. [1]a household supply of at least 0.5 net per person

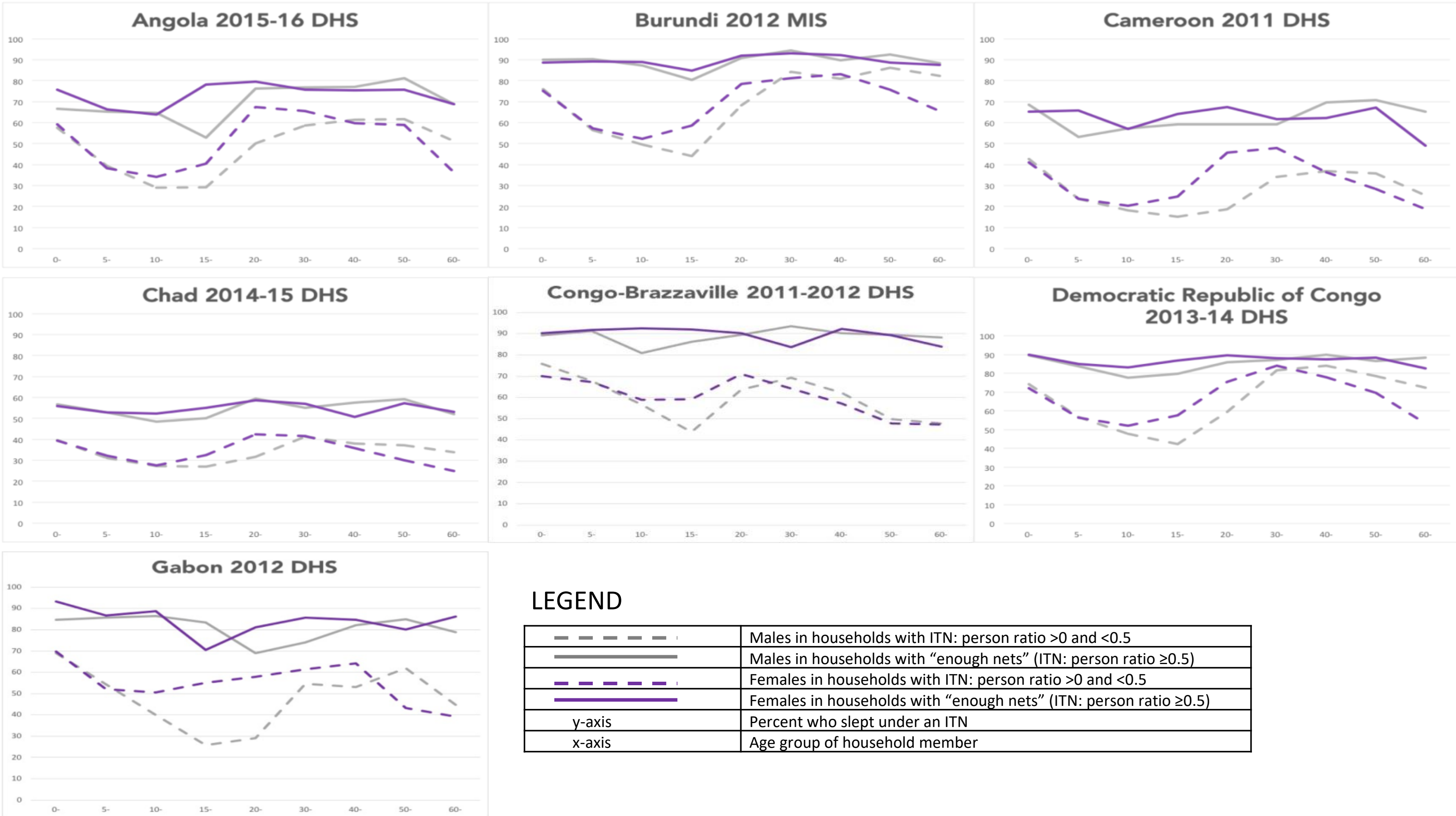

Figure 2.1 Insecticide-treated net use by insecticide-treated net supply, age and gender in Central Africa

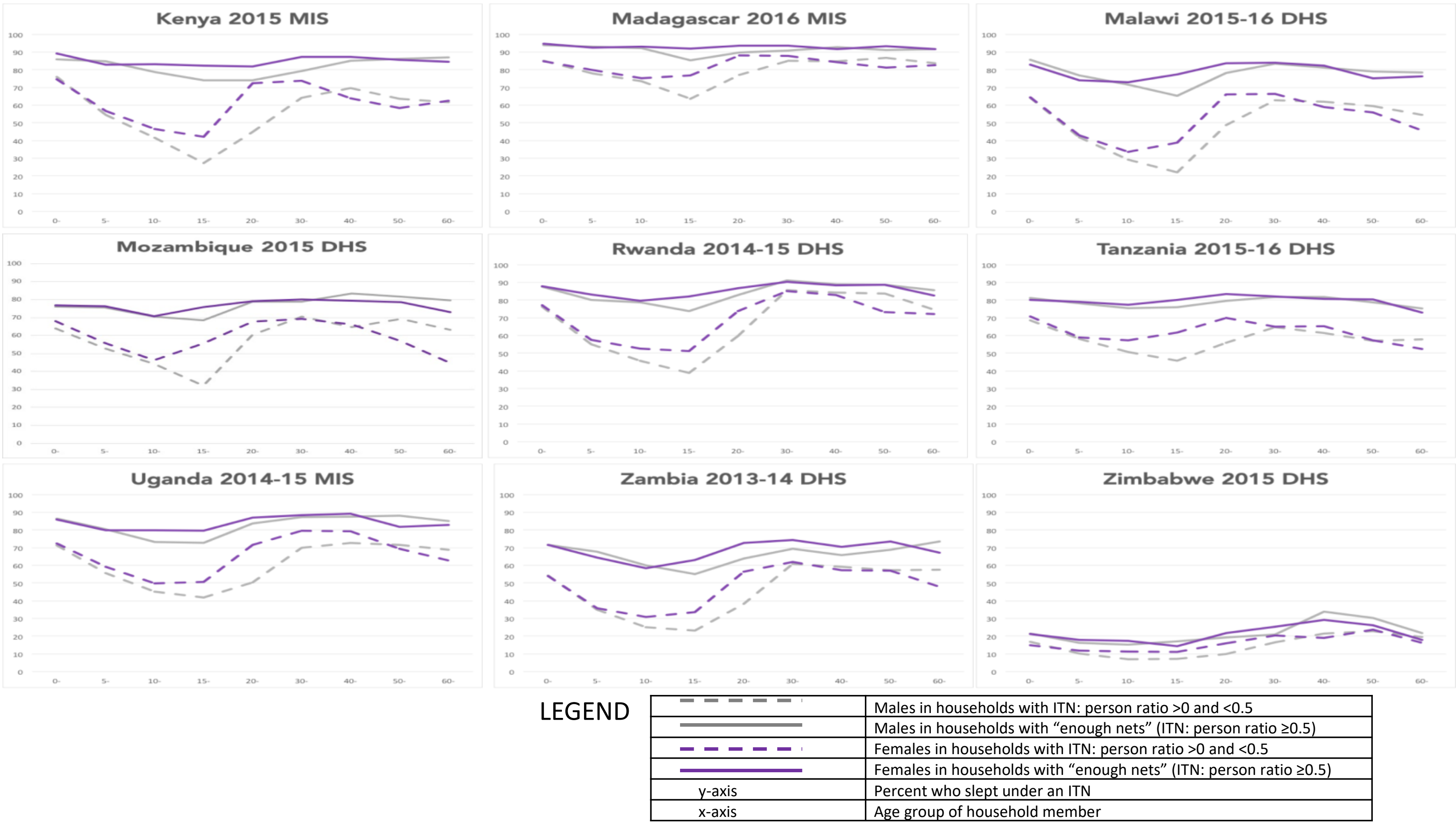

Figure 2.2 Insecticide-treated net use by insecticide-treated net supply, age and gender in East Africa

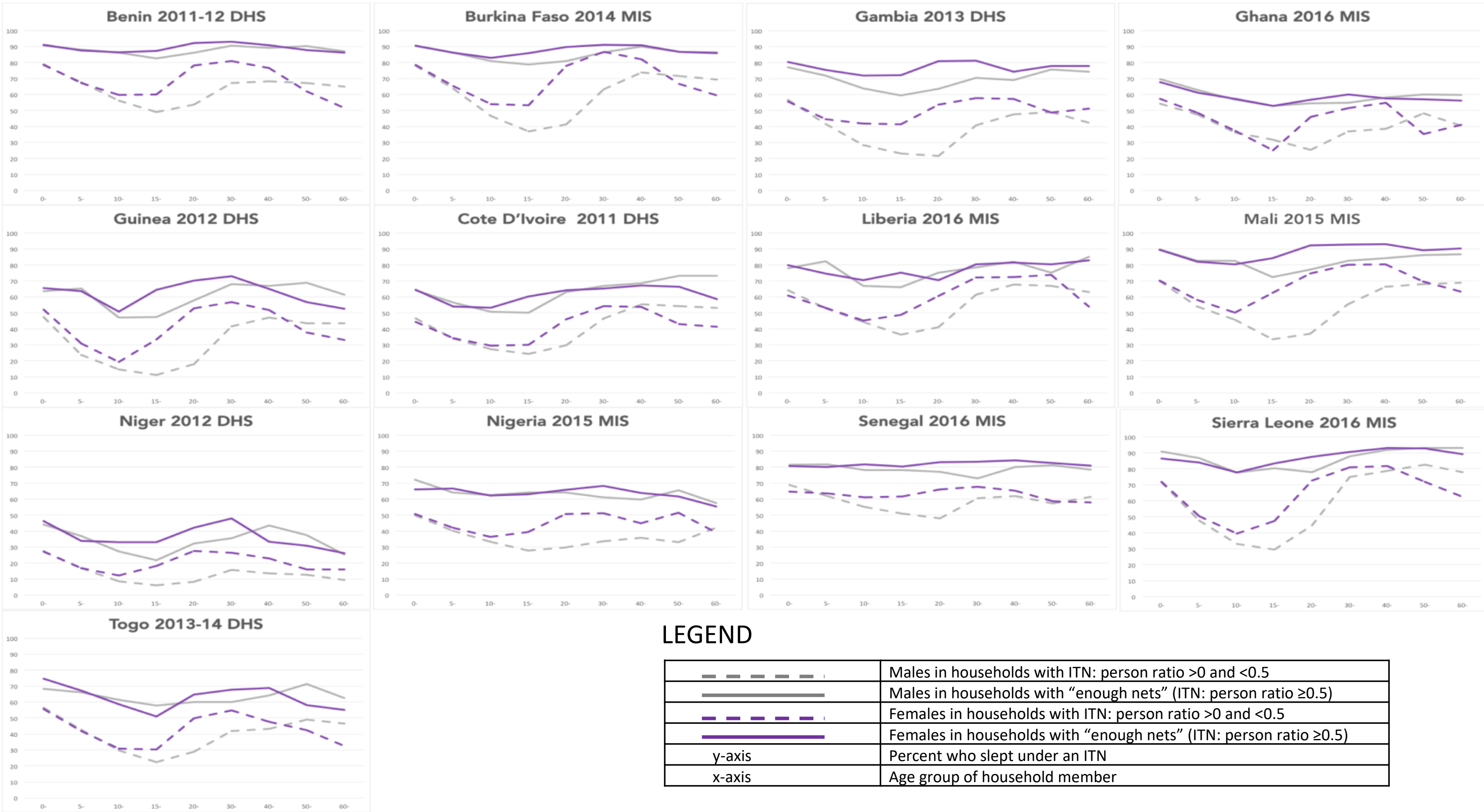

Figure 2.3 Insecticide-treated net use by insecticide-treated net supply, age and gender in West Africa

Table 2.2 Logistic regression of insecticide-treated net use among demographic groups (reference: men aged 15-49 years) stratified by insecticide-treated net supply, adjusted for wealth index, residence (urban/rural), and region

aOR[1] of ITN use among household members by household ITN supply

Country	Households with not enough ITNs (ref: male 15-49 years)					Households with enough ITNs (ref: male 15-49 years)				
			Female 15-49 years					Female 15-49 years		
	Children under 5 years	School-aged (5-14 years)	Not pregnant	Currently pregnant	50+ years	Children under 5 years	School-aged (5-14 years)	Not pregnant	Currently pregnant	50+ years
East Africa										
Madagascar	1.63*	0.93	1.76*	1.23	1.53*	1.82*	1.46*	1.41*	1.99*	1.21
Mozambique	1.48*	0.71*	1.48*	1.76*	1.12	0.99	0.80*	1.12	2.42*	1.12
Zimbabwe	1.22*	0.71*	1.33*	1.07	1.65*	0.97	0.73*	1.10	0.46*	1.08
Zambia	1.42*	0.56*	1.41*	1.48*	1.51*	1.37*	0.89	1.31*	2.03*	1.33*
Malawi	2.01*	0.66*	1.65*	1.51*	1.31*	1.73*	0.88*	1.43*	1.05	1.07
Rwanda	1.68*	0.58*	1.43*	3.55*	1.69*	1.48*	0.85*	1.29*	2.31*	1.38*
Tanzania	1.83*	1.02	1.60*	1.66*	1.08	1.21*	0.98	1.20*	1.08	0.98
Uganda	1.98*	0.85	1.80*	2.37*	1.70*	1.27*	0.76*	1.28*	1.61*	1.10
Kenya	3.2*	1.01	1.9*	3.57*	1.64*	2.04*	1.28*	1.59*	1.54	1.71*
Central Africa										
Angola	1.45*	0.57*	1.61*	2.26*	1.24	1.13	0.78*	1.41*	2.56*	1.23
Burundi	1.43*	0.55*	1.30*	2.64*	1.72*	1.08	1.07	1.13	2.74	1.14
Cameroon	2.34*	0.89	1.94*	2.89*	1.10	1.52*	0.98	1.21	0.76	0.98
Chad	1.56*	0.94	1.47*		1.08	1.22*	0.92	1.14*		1.14
Congo-Brazzaville	1.70*	1.1	1.22*	1.36	0.62*	0.93	0.90	0.90	1.50	0.77
DRC	1.45*	0.60*	1.57*	1.78*	1.26*	1.5*	0.79*	1.28*	1.70	1.13
Gabon	3.4*	1.49*	2.24*	2.28*	1.38*	2.8*	2.40*	1.45*	1.75	1.48
West Africa										
Benin	2.52*	1.20*	2.11*	4.27*	1.13*	1.54*	1.04	1.57*	2.00*	1.06

Burkina Faso	3.2*	1.22*	2.94*	4.24*	1.87*	1.82*	1.05	1.72*	1.97*	1.26*
Gambia	3.18*	1.58*	2.65*	3.21*	2.18*	2.25*	1.37*	1.89*	4.36*	1.94*
Ghana	2.60*	1.46*	1.80*	2.16*	1.35	1.82*	1.16	1.17	1.79*	1.01
Guinea	2.74*	0.77*	2.72*	3.45*	1.92*	1.49*	1.12	1.80*	1.37	1.38*
Cote D’Ivoire	1.27*	0.69*	1.47*	1.18	1.46*	0.94	0.60*	1.06	1.51*	1.00
Liberia	1.60*	0.94	1.72*	1.86*	1.72*	1.05	0.84	1.07	1.23	1.17
Mali	2.65*	1.24*	3.36*	3.66*	2.37*	2.20*	1.15	2.59*	2.65*	1.87*
Niger	3.81*	1.57*	3.18*	3.00*	1.43*	2.03*	1.09	1.52*	1.59	0.94
Nigeria	2.20*	1.30*	2.04*	2.72*	1.54*	1.28*	1.02	1.19*	1.25	0.99
Senegal	1.66*	1.20*	1.66*		1.19	1.47*	1.33*	1.52*		1.30*
Sierra Leone	1.86*	0.56*	1.90*	2.05*	2.03*	1.08	0.71*	1.37*	2.03	1.80*
Togo	2.56*	1.13*	1.84*	1.93*	1.39*	1.63*	1.13	1.17*	1.37	0.99

Abbreviations: aOR: adjusted odds ratio; ITN: insecticide-treated net.

[1] Adjusted for wealth index, residence (urban/rural), and region; * significant at p-value <0.05;

Data not available

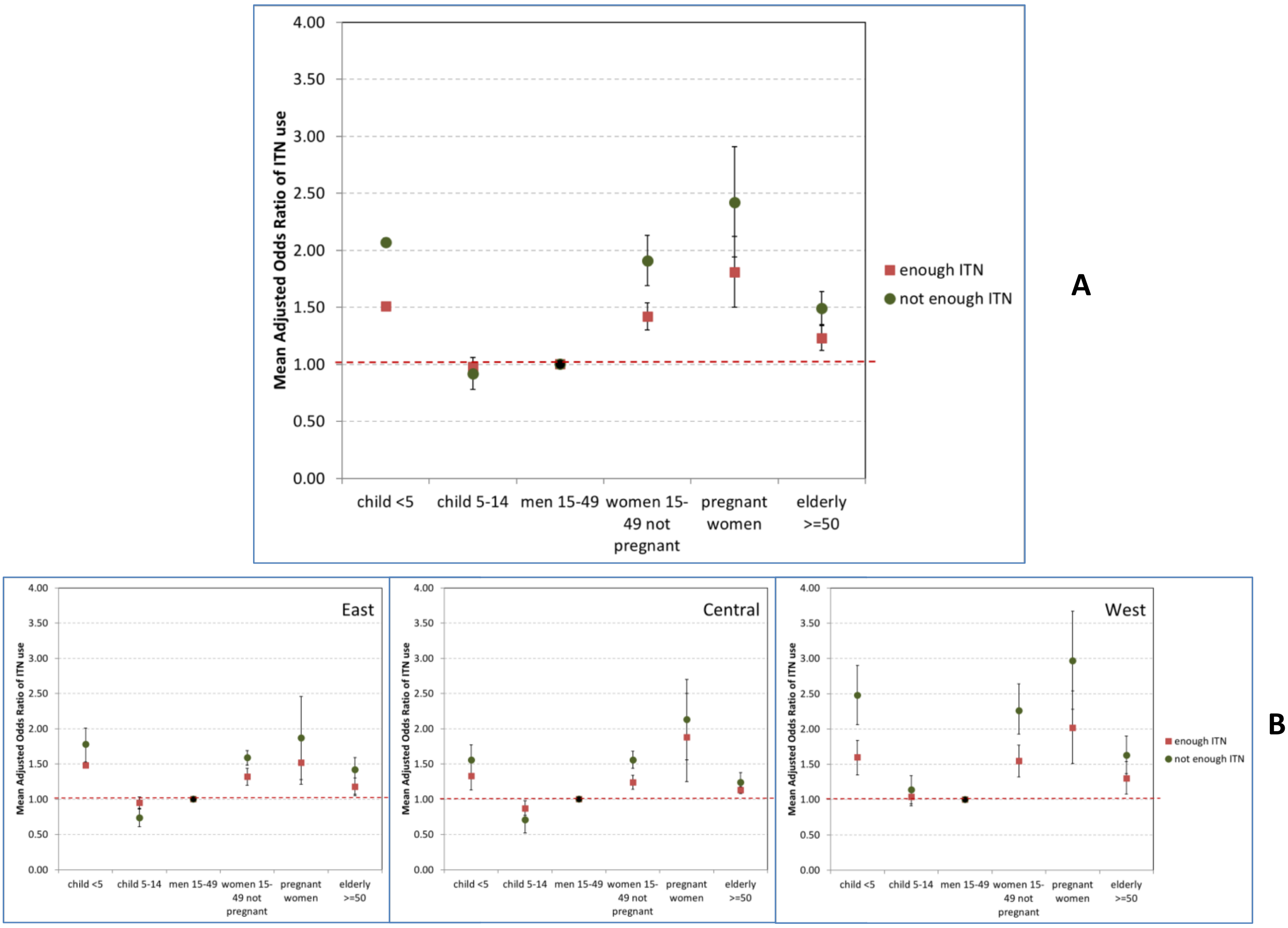

Figure 2.4 Mean adjusted odds ratios for insecticide-treated net use among demographic groups (reference group: men aged 15-49), by insecticide-treated net supply, overall (A) and by geographic region (B)

The meta-regression results in Table 2.3 highlight the influence of country-level ITN supply, population ITN access, ITN use:access ratio and geographic region on the mean aOR of ITN use for demographic groups across all 29 countries. The effect sizes shown in the Table represent the change in mean aOR per unit change of each covariate, holding others constant. Thus, the mean aOR is treated as a continuous variable in this analysis. For example, the mean aOR of ITN use among children under 5 years reduces by 0.59 points in households with not enough compared to enough ITN supply while each per cent increase in population ITN access has minimal effect on the mean aOR of ITN use. In general, the results confirm earlier findings, as the mean aORs of ITN use decreased (dropping by 0.26-0.59 points) among almost all demographic groups compared to men age 15-49 years when there are enough ITNs in the household compared to households with not enough ITNs. The only exception was the group children 5-14 years for whom the mean aOR did not change with household ITN supply. The level of population access to ITNs at the time of the survey (as shown in Table 1) did not have any impact on the mean aOR of ITN use among household members, again with the exception of children 5-14 years for whom the mean aOR increased by 0.06 for each 10% increase in population access. Changes in use-to-access ratio did not significantly contribute to differentials in the mean aOR of ITN use across demographic groups. As was suggested in Fig. 4, the mean aOR of ITN use for household members, except the 50 years and over, was significantly higher in West compared to the East Africa.

Table 2.3 Adjusted linear regression coefficients for mean adjusted odds ratios of insecticide-treated net use

Independent variable	Adjusted linear regression coefficients by demographic group[1]				
	Children under 5 years	School-aged (5-14 years)	Female 15-49 years		50+ years
			Not pregnant	Pregnant	
Household ITN supply enough *vs* not enough	-0.568*	0.524	-0.497*	-0.591*	-0.258*
Population access in %**	-0.0001	0.006*	-0.000	0.013	-0.005
Use : access ratio**	-0.195	-0.399	0.221	1.072	0.680
Central Africa *vs* East	-0.168	0.036	-0.040	0.389	-0.195
West Africa *vs* East	0.424*	0.231*	0.479*	0.779*	0.179
R squared	0.384	0.332	0.463	0.337	0.328

Abbreviations: ITN: insecticide-treated net
[1] Covariates included in the model: household ITN supply, population ITN access and geographic zone; * significant at p-value <0.05; ** variable shown in Table 1.

2.5 Discussion

This study demonstrated that regardless of setting and across a large number of countries, the groups most vulnerable to malaria are preferentially being covered, per WHO recommendations that pregnant women and infants in malaria-endemic areas use ITNs. It also suggests that ITNs are not hoarded by heads of households but used among household members, depending on household supply. The study showed that having enough ITNs in the household increases level of use and decreases existing disparities between age and gender groups. ITN use was consistently higher among people in households with enough compared to not enough nets. The role of ITN supply on use is important given the WHO target of 85% coverage of key malaria interventions, including ITN use by all people at risk of malaria, and the WHO recommendation of one ITN for every two people at risk of malaria (WHO, 2017e). Many countries struggle to meet this target among all households but have been able to achieve the target among households with enough ITNs. This suggests that people are typically willing to use ITNs but need to have enough ITNs to increase and sustain ITN use. Thus, increasing the household supply of ITNs improves use among members. These findings provide further evidence that the main barrier to ITN use is perhaps insufficient access and to a lesser degree unwillingness to use ITNs (Bhatt et al., 2015b, Eisele et al., 2009, Koenker and Kilian, 2014).

Our findings highlight existing disparities in ITN use among household members, corroborating previous research (Babalola et al., 2016, Fokam et al., 2017, Larson et al., 2014b, Loha et al., 2013, N Ng'ang'a et al., 2009). In most of sub-Saharan Africa, households rightfully prioritize children under 5 years as well as pregnant women, especially when there is not enough ITN supply. Children under 5 years and pregnant women of reproductive age may be more likely to sleep under an ITN because, in many settings, those children share sleeping spaces with their mothers or adolescent female siblings (Toé et al., 2009). It may also be due to the ITN interventions of the last few decades targeting pregnant women and children under 5 years old (Garley et al., 2013). While pregnant women and young children are biologically vulnerable to malaria, there are negative side effects with only prioritizing them for ITN use. Contraction of malaria by other household members still has unwelcome health, social and financial consequences for the family, hence the emphasis on universal coverage (Garley et al., 2013).

The role of ITN supply on disparities in ITN use among household members is a novel addition of this study to the existing literature. Pregnant women, children under 5 years old, women aged 15 to 49 years, and those over 50 years were still more likely to have used an ITN the previous night than men but having enough ITNs within the household reduced the gaps in ITN use across these groups. However, school-children aged 5-14 years were among the least prioritized in households, regardless of household ITN supply. Studies have found that school-aged children had the highest prevalence of malaria infection but were most likely to have asymptomatic infection, thus serving as an under recognized reservoir of malaria infection (Pullan et al., 2010, Walldorf et al., 2015). Protecting this age group with ITNs would reduce adverse health outcomes, such as anemia and mortality, and educational outcomes such as school absenteeism and lower cognitive function (Nankabirwa et al., 2014). In addition, protecting this age group with ITNs could protect the rest of the population from malaria transmission. As recommendations shift from covering vulnerable populations to universal coverage, there is a need to ensure that households have enough nets to eliminate disparities in ITN use among members. Mass distribution campaigns have been a major source of ITN supply in households, however, gaps in ITN coverage have been demonstrated between mass campaign cycles. Continuous distribution of ITNs through antenatal care, immunization services, communities, and schools has been recommended by WHO to complement mass campaigns and ensure universal coverage of ITNs, particularly antenatal care clinic and expanded programmes on vaccination distribution (WHO, 2017a). Continuous community-based (Zegers de Beyl et al., 2017, Kilian et al., 2017) and school-based ITN distribution (Zegers de Beyl et al., 2017, Stuck et al., 2017) has been shown to improve ITN ownership and access. However, although continuous antenatal care (ANC) and expanded programme on immunization (EPI) distribution systems targeting biologically vulnerable groups, such as children under 5 years and pregnant women, are supposed to be in place in almost every country, these are often low functioning, contributing to gaps in net access(Kilian et al., 2017). Efforts to improve the quality of existing distribution channels may involve ensuring complete household registration, enhancing data and communication campaigns to promote acceptability and uptake of distribution channels.

There are some limitations within this study. The analysis assumes that all ITNs included in the indicator of ITN supply in the household are all hung or usable. The study also uses slightly different denominators for the ITN indicators. Specifically, ITN supply is calculated from the *de jure* household members while ITN use is calculated from *de facto* members. This may be important in instances where the *de facto* and *de jure* members are markedly different. Seasonality of ITN use (Smithuis et al., 2013) is one of most important factors of ITN use but was not accounted for in this analysis. Research has shown seasonal variations in ITN use in sub-Saharan Africa, which may explain some of the differences in ITN use across countries as MIS and DHS surveys are usually conducted in different seasons. Typically, MIS is conducted during/at the end of rainy season while the DHS can be done any season. Given that ITN use is higher in the rainy season and immediately thereafter when malaria transmission is at a peak (Pinchoff et al., 2015, Thwing et al., 2008), ITN use is higher in MIS survey countries than in DHS countries. Also, the timing of the most recent ITN mass campaigns was not accounted for in the analysis. Mass campaigns that are closely followed by household surveys generally show higher levels of population ITN access, which in turn makes high levels of ITN use feasible (Finlay et al., 2017, Loha et al., 2013). In addition, the data analysed are cross-sectional in nature and thus do not permit causal inferences.

Finally, the study found some differences in ITN use among household members across the geographic zones explored. However due to the country eligibility criteria, not all countries within the three geographic regions are explored. Thus, regional differences in ITN use should be interpreted with caution. Also, malaria control research and programmatic efforts are also needed to understand the specific country level contextual factors that may explain trends in ITN access and use. For example, Zimbabwe has low levels of ITN use even among people in households with enough ITNs, and this may be related to national level indoor residual spraying interventions, resulting in a lower net use culture (Mabaso et al., 2004).

2.6 Conclusions

This study explored the role of ITN supply on ITN use among household members. The findings suggest that having enough ITNs in the household increases level of use and decreases existing disparities between age and gender groups. School-aged children were also consistently the least prioritized, regardless of a household’s ITN supply. ITN distribution via mass campaigns, ANC and EPI, school and community channels should be enhanced as needed in order to ensure that households have enough ITNs for all members, including men and school-aged children.

2.7 Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data and material: The datasets analyzed during the current study are available from the DHS Program web site, www.dhsprogram.com.

Competing interests: The authors have the following interests: Co-author Albert Kilian is employed by Tropical Health LLP.

Funding: This study was made possible by the generous support of the American people through the United States Agency for International Development (USAID) under the terms of USAID/JHU Cooperative Agreement No: AID-OAA-A-14-00057 for the VectorWorks Project. The contents are the responsibility of the authors and do not necessarily reflect the views of USAID or the United States Government. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Authors' contributions: HK conceived the study. AA, AK, **AM**, BO, EF, HH, HK, IC, RS, and SB managed the datasets and analyzed the data. BO and IC drafted the paper with revisions from AA, AK, HK, ML, EF, HH, **AM,** SB, and RS.

Acknowledgements: The authors are grateful to Lilia Gerberg, Lia Florey, and Anna Bowen for their comments on earlier drafts.

Chapter 3: Understanding the gap between access and use: a qualitative study on barriers and facilitators to insecticide-treated net use in Ghana

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Published in
Malaria Journal 2019 **18**:417

https://malariajournal.biomedcentral.com/articles/10.1186/s12936-019-3051-0

3.1 Abstract

Background

Mass and continuous distribution channels have significantly increased access to insecticide-treated nets (ITN) in Ghana since 2000. Despite these gains, a large gap remains between ITN access and use.

Methods

A qualitative research study was carried out to explore the individual and contextual factors influencing ITN use among those with access in three sites in Ghana. Eighteen focus group discussions, and free listing and ranking activities were carried out with 174 participants; seven of those participants were selected for in-depth case study. Focus group discussions and case study interviews were audio-recorded, transcribed verbatim, and analyzed thematically.

Results

ITN use, as described by study participants, was not binary; it varied throughout the night, across seasons, and over time. Heat was the most commonly cited barrier to consistent ITN use and contributed to low reported ITN use during the dry season. Barriers to ITN use throughout the year included skin irritation; lack of airflow in the sleeping space; and, in some cases, a lack of information on the connection between the use of ITNs and malaria prevention. Falling ill or losing a loved one to malaria was the most powerful motivator for consistent ITN use. Participants also discussed developing a habit of ITN use and the economic benefit of prevention over treatment as facilitating factors. Participants reported gender differences in ITN use, noting that men were more likely than women and children to stay outdoors late at night and more likely to sleep outdoors without an ITN.

Conclusion

The study results suggest the greatest gains in ITN use among those with access could be made by promoting consistent use throughout the year among occasional and seasonal users. Opportunities for improving communication messages, such as increasing the time ITNs are aired before first use, as well as structural approaches to enhance the usability of ITNs in challenging contexts, such as promoting solutions for outdoor ITN use, were identified from this work. The information from this study can be used to inform social and behavior change messaging and innovative approaches to closing the ITN use gap in Ghana.

Key Words Malaria, Ghana, insecticide-treated mosquito net, prevention

3.2 Background

Malaria remains a major public health problem in Ghana. In 2016, malaria accounted for 39% of outpatient attendance, 25% of all admissions and 4% of all deaths. Of those deaths, nearly half were among children less than 5 years old (2017a, GHS, 2017). The national malaria parasite prevalence in 2016 was 20%, ranging between 5% in the Greater Accra Region to 31% in the Eastern Region (GHS, 2017), an indication that Ghana remains within the control phase of the malaria control-elimination continuum (WHO, 2008a).

Insecticide-treated nets (ITNs) are a major intervention of global malaria control initiatives. This is based on overwhelming evidence showing significant reductions in malaria-related morbidity and mortality as a result of ITN use (Lengeler, 1998, Gamble et al., 2007). These studies stimulated efforts to increase ITN ownership in many malaria-endemic countries, driven largely by donor-funded ITN distribution programs (Baume and Marin, 2008, Gerstl et al., 2010, Hanson et al., 2009, Noor et al., 2007). Though access to ITNs has increased substantially in affected countries and rates of use have also improved, some countries continue to have below target use among those with access to ITNs, and seasonal variability in ITN use practices (Afolabi et al., 2009, Eisele et al., 2009, Korenromp et al., 2003).

Since 2000, Ghana has made significant progress toward increasing ITN access through mass and continuous distribution channels (GHS, 2015, GHS, 2011). Despite these gains, ITN use remains sub-optimal in some settings. National household surveys provide useful information on the levels of use given access and the differences in these levels across groups in Ghana. A secondary analysis of the 2011 Multiple Indicator Cluster Survey, 2014 Ghana Demographic and Health Survey (DHS), and 2016 Malaria Indicator Survey (MIS) data looked at net use given access across region, sex, age, and wealth quintile. Overall, 63% of Ghanaians with access to an ITN in their household reported using one; however, significant variation was observed across geographic zones and rural/urban settings. In many central areas of Ghana, between 60% and 80% of those with access to an ITN reported using it, compared to 20% to 40% along the coast, with a particularly low use to access ratio in and between the urban areas of Accra and Takoradi. The analysis revealed that ITN use among children under five years was highest compared to the general population, while ITN use was lowest among males aged 15 to 49 years. When controlling for other factors, household supply of ITNs, wealth quintile, and residence were the most important factors associated with ITN use (Koenker et al., 2018).

While national surveys provide useful quantitative estimates of ITN use trends in Ghana, and differences across groups, they do not offer insights into the key factors driving use and non-use of available ITNs. To fill this gap, a qualitative research study was carried out to provide in-depth information on barriers and facilitators to ITN use among those with access.

3.3 Methods

Study sites

Data were collected in March 2018, concurrently across three study sites. The 10 administrative regions of Ghana were divided into zones, based on the three ecological areas (the Coastal savannah ecological zone included the Volta, Greater Accra, Central and Western Regions; the Forest ecological zone included the Eastern, Ashanti, and Brong-Ahafo Regions; the Savannah ecological zone included the Upper East, Upper West, and the Northern Regions). One region was selected from each of three ecological zones based on a low ITN use-access ratio calculated from the 2016 MIS. A district was purposively selected from each of the three regions in consultation with the Ghana National Malaria Control Program. Gomoa West District in the Central Region (Coastal Savanna zone), Fanteakwa District in the Eastern Region (Forest zone) and Savelugu District in the Northern Region

(Northern Savanna zone) were selected (Figure 1). The selected districts were viewed as generally representative of their respective regions. In each district, an urban community, the district capital, and a rural community were selected for data collection.

Data Collection

Community Entry

Prior to initiation of data collection, regional, district and health facility officials of the Ghana Health Service (GHS) in the selected study sites were informed about the study objectives, methods, and timeline. Upon arrival in the community, the study team met the GHS officials who facilitated meetings with the local leaders. After gaining the support of the community leaders, the team, assisted by community-based volunteers and an officer of the district health management team, recruited study participants. Participants were selected based on the following categorizations: community leaders, health workers employed at the local health clinic, caretakers of children under-five, male community members ages 18–49, female community members ages 18–49, and male and female community members ages 50 or older. To be included in the study, all participants had to own at least one ITN in their household.

Questionnaire

Prior to focus group discussions, all participants filled out a brief questionnaire with information on age, sex, number of ITNs in their household, number of household members, and self-reported level of ITN use. Level of use was categorized as regular user, defined as using an ITN every night throughout the year; occasional user, defined as using an ITN some nights throughout the year; seasonal user, defined as using an ITN during rainy season only; and non-user, defined as someone who never uses an ITN.

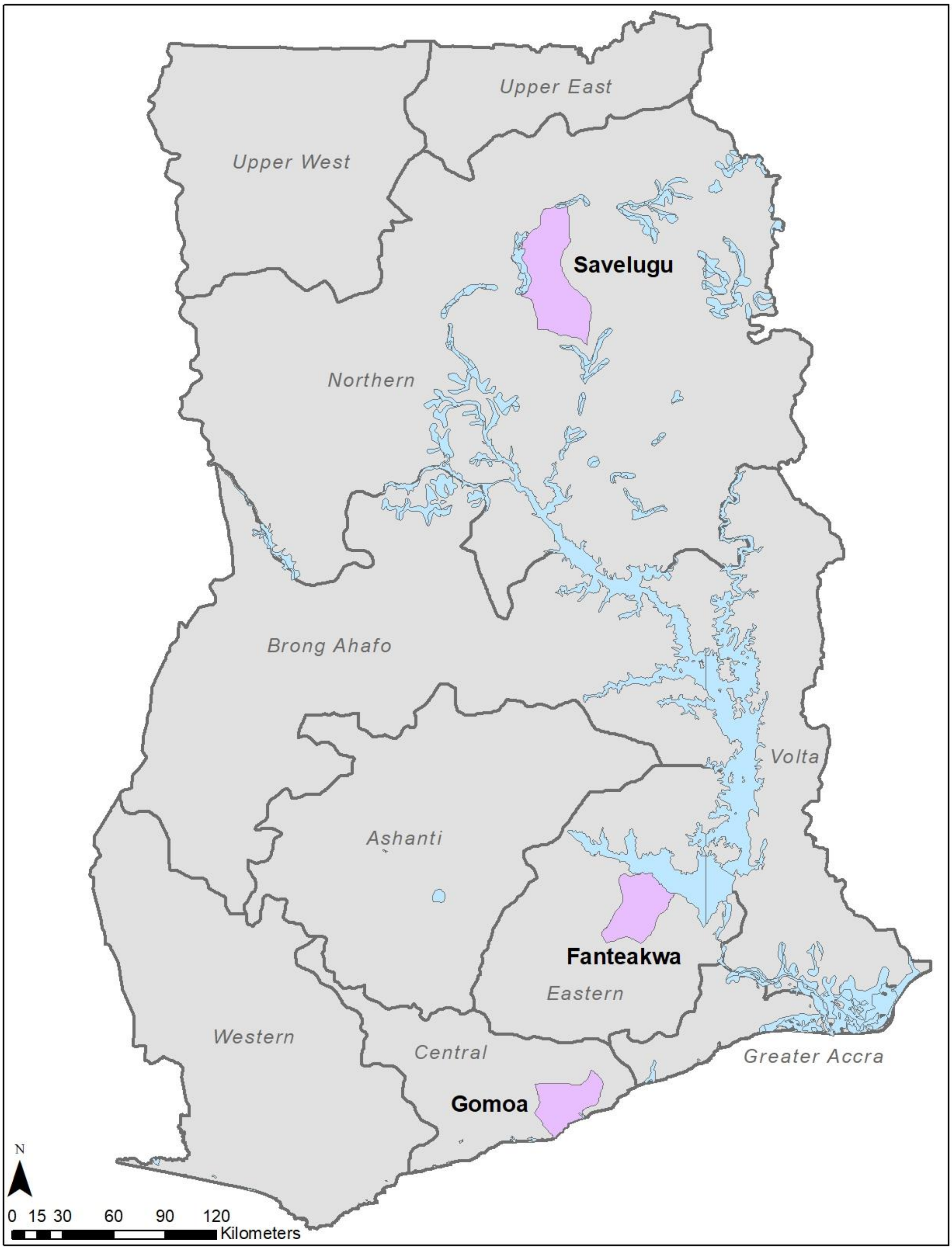

Figure 3.1 Map of Ghana showing study districts

Focus group discussions

Focus group discussion (FGD) was the primary data collection technique and was used to explore individual and contextual factors influencing ITN use among those with access to ITNs. Free listing and ranking activities were incorporated into the FGD, where at the end of each discussion, participants were asked to list all the motivators and barriers to ITN use in their households and in the community-at-large. After the listing, they were asked to rank them individually. At the end of the individual ranking, participants were brought together to discuss their most important motivators and barriers and arrive at a group consensus.

Trained and experienced FGD moderators led the sessions in the local languages; health worker FGDs were conducted in English. A moderator, note taker, and supervisor facilitated each FGD. The moderator followed a semi-structured discussion guide, developed around key themes of interest. Each FGD lasted approximately 90 to 150 minutes. The discussions were audio-recorded and transcribed verbatim into English on an on-going basis. Following each day's work, the study teams debriefed within and across sites to identify emerging themes and ensure data quality across the three sites. Supervisors reviewed all English translations and provided continuous feedback to the data collection teams.

Case Studies

To complement data from FGDs, a subset of FGD participants were selected for in-home case studies in each zone. Cases were selected to represent a range of ITN use practices. Participants were interviewed to build on information obtained from FGD sessions. Observations were done on the general sleeping arrangements; availability, location, and physical condition of ITNs. Field notes were taken using a semi-structured template and the interviews were audio-recorded. Audio recordings were transcribed verbatim on an ongoing basis.

Data Analysis

Data were analyzed using an iterative process, beginning during data collection through daily debriefings and review of data and emergent themes. NVivo 12 (QSR International), a qualitative data analysis software program for coding, storage, indexing, and retrieval, was used to thematically analyze the FGD and case study transcripts (Boyatzis, 1998).Visualizations were generated for the most common barriers and facilitators to ITN use by inputting content from the free-listing and ranking activity into Word Art, a free, online word cloud creator.

Access to ITNs was calculated using the approach put forward by Kilian *et al.* and endorsed by the Roll Back Malaria Monitoring and Evaluation Reference Group (DHS, 2013a, Kilian et al., 2013). To calculate the potential ITN users, study team members multiplied the number of ITNs in each of the participant's household by two. If the number of potential users was larger than the number of household members, the number of household members was used. To calculate access, potential ITN users were divided by the total number of people in study participants' households.

Ethical Approval

The study was reviewed by the Johns Hopkins University Institutional Review Board and met the criteria for exemption (IRB No. 8437). The study was reviewed and approved by the Noguchi Memorial Institute for Medical Research (IRB No.1276) and the Ghana Health Service Ethics Review Committee (GHS-ERC: 007/02/18). All participants provided written informed consent prior to participation.

3.4 Results

A total of 18 focus group discussions were carried out, six in each study site, with 174 total participants. The characteristics of participants are presented in Table 3.1. Participants were roughly evenly split between male (43%) and female (57%) and urban (53%) and rural (47%) communities in the selected districts.

Table 3.1 Focus Group Discussion Participant Characteristics

	Central # of groups (participants)	Eastern # of groups (participants)	Northern # of groups (participants)	Total
Health workers	1 (8)	1 (10)	1 (9)	3 (27)
Community leaders	1 (9)	1 (12)	1 (9)	3 (30)
Males ages 18 to 49	1 (10)	1 (12)	1 (10)	3 (32)
Females ages 18 to 49	1 (8)	1 (12)	1 (10)	3 (30)
Caretakers of children >5	1 (9)	1 (8)	1 (10)	3 (27)
Adults > 49	1 (10)	1 (9)	1 (9)	3 (28)
	6 (54)	6 (63)	6 (57)	18 (174)

Findings from the pre-FGD questionnaire showed that in total there were 1,490 people living in participants' households. Overall, 65% of the population within study households had access to an ITN, assuming one ITN protects two people. Access was similar across sites, with slightly higher access among study households in the Central Region (72%) compared to participants from the Northern (63%) and Eastern Regions (65%) respectively.

FGD participants represented a range of use practices. Approximately 32% reported being regular users, 23% reported being seasonal users, 43% reported being occasional users, and only 2% reported being non-users in the pre-FGD survey and FGDs revealed nuances beyond these categories. Seven cases were identified from FGD participants across the three sites. Selected cases represented a spectrum of ITN use profiles –consistent user, seasonal user, and non-user.

Table 3.2 Background Characteristics of Cases

Case ID	**Region**	**Age**	**Sex**	**Type of Case**
CS1	Central	33	Female	Consistent user

CS2	Central	42	Male	Non-user
CS3	Eastern	38	Female	Consistent user
CS4	Eastern	54	Male	Non-user
CS5	Northern	37	Male	Consistent user
CS6	Northern	28	Female	Seasonal user
CS7	Northern	63	Male	Non-user

Barriers to consistent ITN use

Heat and discomfort under the ITN were ranked as top barriers to consistent use across sites, while lack of malaria knowledge and lack of motivation to hang and use the ITN were reported from the Central and Northern Regions. The top ranked barriers to ITN use across sites and FGD categories are included in Table 3.3 and Figure 3.2.

Table 3.3 Top ranked reasons for inconsistent use of ITNs from free listing and ranking activity

	Central Region	Eastern Region	Northern Region
Community leaders	Heat Rashes Lack of education	Heat Chemical is too strong and causes reaction The net is short	Heat Reaction to the insecticide Itching
Under-five caretakers	Heat Do not see the need because of mosquito sprays, coils, fan, etc. Laziness to hang the ITN	Heat Reaction to the insecticide Difficulty in hanging the net	Heat Reaction to the insecticide/ itching Lack of education
Participants > 49 years	Heat Discomfort ITN material is too hard	Heat Discomfort Reaction to the insecticide	Lack of education Laziness
Health workers	Burning sensation (upon contact) Difficulty in hanging the ITN Heat Lack of education	Heat Reaction to the insecticide Itching	Misconceptions about ITNs Texture and shape of the ITN No access to the ITN by women and children (husband seized the ITN)
Male 18–49 years	Insecticide is too strong Lack of education Inability to hang the ITN	Heat Insecticide is too strong People just don’t like the ITN	Stubbornness Heat Itching/reaction to insecticide
Female 18–49 years	Heat Disruption of sexual activity Burning sensation	Heat Can’t breathe while under the ITN Skin rashes	Heat Laziness Procrastination

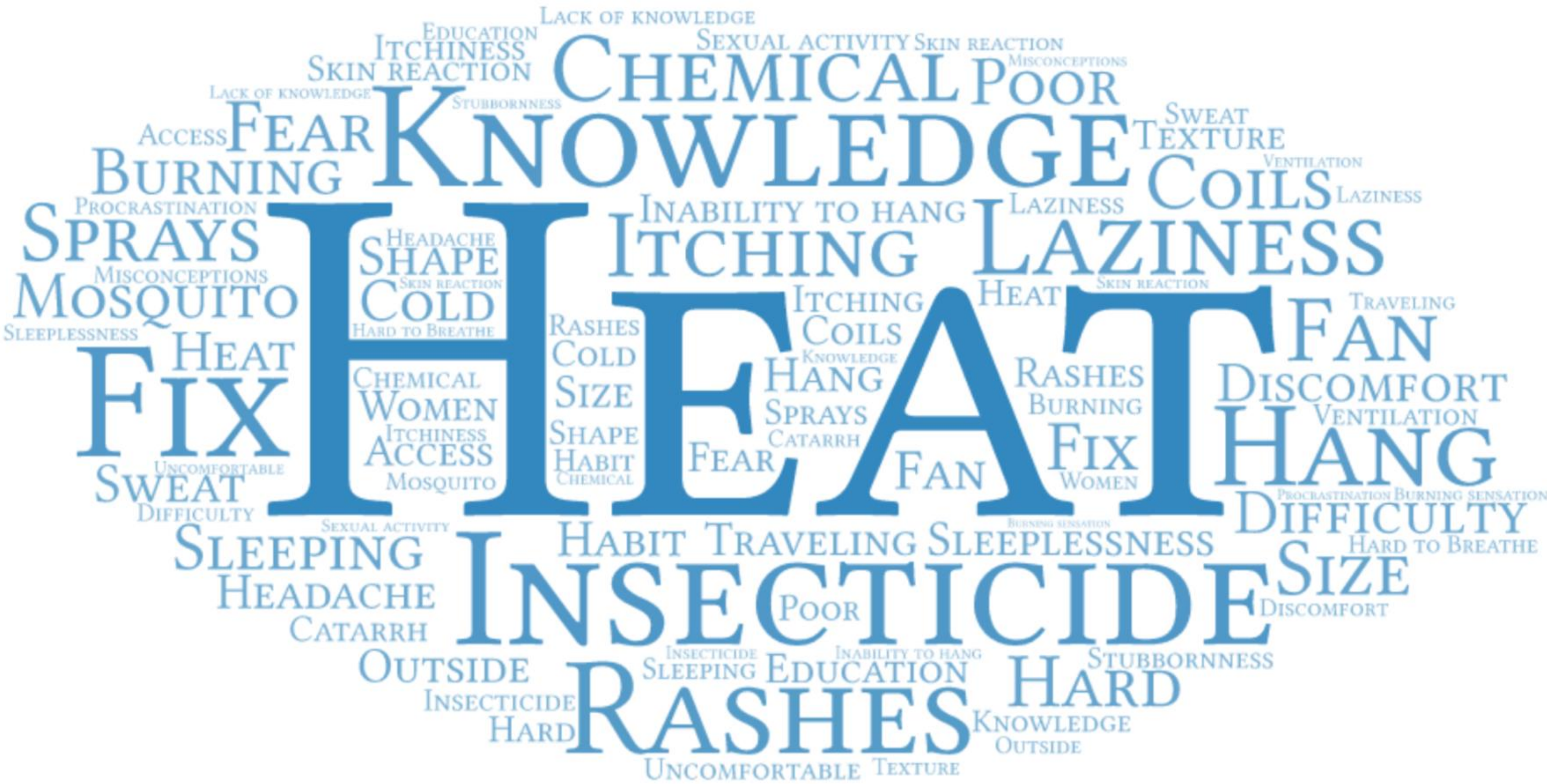

Figure 3.2 Visual representation (word cloud) of most common barriers to consistent ITN use

Participants across sites reported a number of physical reactions to the insecticide in the ITNs, even after reportedly airing the ITN as instructed during distribution and in some cases, after washing the net. A community leader from the Central Region explained, *"The chemical they used in the net is quite strong. When you sleep in it some people, and even me for instance, I experience a burning sensation so out of frustration I will move out of the net."*

A smaller number of participants discussed challenges associated with the design of the ITN. A male community member from the Northern Region described the challenge of hanging a rectangular net compared to a conical net, *"The round type (conical) is easy to fix and remove but it is distributed in small quantities (distributed less frequently). The four ropes type (rectangular) is difficult to tie, especially when you are tired and in a hurry to sleep."*

The inconvenience in getting in and out of the ITN in the night was also discussed as a barrier to use. Some participants indicated that sleeping under the net restricted their movement and made it difficult for them to get in and out of bed in the night and this was vividly captured in the narrative below:

> *"Once they fix the net and find entering the net uncomfortable, they will not sleep in it again because it did not serve the purpose…In the night, if they want to go and urinate and the net ties them up and they have to remove it, go out and come back to fix it, they feel like they are in prison and will not sleep under it."*
>
> (Female community leader, Eastern Region, FGD)

The material used in making ITNs was discussed and it emerged that participants have noticed a difference in the materials used in making the ITNs they had received at different time-points. A female community member from Northern Region explained, *"The* *reason why we are complaining of heat is because the recent one (net) they gave us is made of rubber (likely referring to polyethylene). That one produces a lot of heat, so we do not even tie it for the kids. If you try using it, you will end up roasting yourself."*

Some people who received the ITN described as being made of "hard" or "nylon" material, reported using them to make curtains and window screening to prevent mosquitoes from entering their rooms and these positions were represented in the narratives below:

> *"The one I had following the distribution, frankly speaking, I didn't sleep in it because it was hard. So I used it for my windows. I fixed them at the back of my windows and even my trap door (a door made of plywood at the lower half and netting material at the top half, usually fixed with a spring that makes it shut automatically), that's what I used. I have used it as a net for all my windows so that mosquitoes do not enter my room."*
>
> (Female community leader, Central Region, FGD).

Room size or crowdedness was not commonly cited as a key barrier to ITN use, although some participants explained that the smaller the room the more difficult it was to hang an ITN, especially hanging more than one rectangular net.

Facilitators to consistent ITN use

Across all study sites, malaria prevention, mosquito bites, saving money, and remaining healthy ranked highest among reasons why people with access to an ITN use it. The top ranked facilitators from the free listing and ranking activity are included in Table 3.4 and displayed visually in Figure 3.3

Table 3.4 Top ranked facilitators to ITN use from free listing and ranking activity

Type of Participants	Central Region	Eastern Region	Northern Region
Community leaders	To prevent malaria To prevent mosquito bites To avoid hospital bills/cost	To prevent malaria Educated about (the purpose of) ITNs To prevent mosquito bites	To protect against malaria To save money from hospital bills and to be healthy to work To protect against other insects, such as ants, flies, and rodents
Caretakers of children under five years	To prevent malaria To have a sound sleep To prevent mosquito bites	To prevent malaria To prevent convulsion in children To prevent miscarriage or malaria in pregnancy	To protect against malaria To protect against mosquito bites To remain healthy
Participants > 49 years	To prevent malaria To prevent mosquito bite To have a sound sleep	To protect ourselves To prevent malaria To prevent sickness and death	To prevent malaria To protect against mosquito bites To protect against other illnesses
Health workers	To be healthy To avoid economic cost of health care To prevent mosquito bites	To prevent malaria To protect from mosquito bites To prevent rodents entering the room	To prevent mosquito bites To protect against other insects To save family money
Male 18–49 years	To prevent malaria To prevent mosquito bites To avoid spending money at the hospital	To prevent malaria To prevent insect bites To prevent sickness	To prevent malaria To prevent high expenditure at the hospital To prevent mosquito bites
Female 18–49 years	To prevent mosquito bites To prevent malaria To stay healthy	To prevent malaria To prevent black flies To prevent other sickness	To prevent malaria To prevent mosquito bites To protect against other insects, wild geckos, and cockroaches

Figure 3.3 Visual representation (word cloud) of most common motivators to consistent ITN use

While many participants described malaria prevention as a motivating factor, serious first-hand experiences had the most profound impact on ITN use. A female caretaker of a child under five shared how she became a regular ITN user:

> *"…I had a baby girl, but we were not sleeping in the mosquito net and she had malaria. She looked very pale…so, we rushed her to the clinic… When we arrived there, she was dead, my baby girl was dead. Since that time, we have slept in the mosquito net every day. Even when it is hot, we sleep in it."*
>
> (Female caretaker of a child under five, Central Region, FGD)

Some participants drew on their personal experiences, or the experiences of their family and friends, as motivators for consistent use of an ITN. In a case study interview, a man from the Northern Region revealed how he almost died from malaria after he refused to use an ITN. Following that experience, he became a regular user. He explained, *"I had in the past refused to use the net because of the heat, itching, and other complaints I had heard about. However, I was attacked by malaria and had to be hospitalized for a week and almost died. After being discharged from the hospital, I decided to use the net regularly.*"

While preventing serious illness and death from malaria was of paramount concern, the positive financial impact of preventing malaria was also frequently mentioned. Participants often noted that ITN use was a way to save money and ensure they were able to work. A female community member from Easter Region explained, *"I have come to understand that if I do not allow my child to sleep in the net he will get malaria. When he gets malaria I too will not sleep and our finances will also come down."*

Beyond malaria prevention and saving money, a good night's sleep and preventing nuisance biting was frequently cited across the study sites. Many participants noted that the buzzing sound coupled with bites from mosquitoes and other insects made it difficult for them to sleep soundly. A male community member from Northern Region explained, *"My motivation for using the net is to prevent mosquito bites and malaria. I also use it to protect myself from the noise the mosquito makes, anytime I hear that noise I am not able to sleep again. So, the net gives me sound sleep."* Another female participant from Central Region echoed this sentiment during a case study interview, saying, "*Oh, the mosquito net, it's not only mosquitoes that it drives away from the room but also spiders, cockroaches, and other small insects in the room. When any insect gets into contact with it, then it dies."*

Seasonality

Participants frequently reported higher ITN use during the rainy season compared to the dry season due to higher perceived risk of malaria, higher density of mosquitoes, and the relative comfort that sleeping under an ITN in cool weather provides. A female community member from Eastern Region described, "*When the rainy season comes and you sleep in the net, it is really comfortable, and the air too circulates, so when the heat starts to come, then we reject it because…when you sleep in it you will sweat.*"

Participants reported that different factors influence malaria risk across seasons. Participants noted that the risk of malaria is higher during the rainy season; however changes in sleeping patterns, including higher frequency of outdoor sleeping and lower levels of ITN use during the dry season contribute to ongoing transmission in the dry season. A caretaker of a child under five from Northern Region explained the risk during the two seasons this way, *"Truly malaria affects us twice in a year. During the rainy season, when we have more mosquitoes, and during the time the place is hot because many people will sleep outside because of the heat, exposing them to mosquito bites."* Temperature differences between urban and rural dwellings were highlighted by a male community member in the Eastern Region. He explained:

"Err! The heat we are talking about when you are in town, maybe your room has an air conditioner and fan. But, when you come to the villages it is not so, we don't all have money. So, for the room itself, the sun always shines on the roofing sheets, which makes the room hot in the night. When you enter into the room, it is like you are in a coffin. So, you come out to sleep outside for fresh air until it becomes cool before you go to the room to sleep."

(Male community member, Eastern Region, FGD)

In the Northern Region of Ghana, participants revealed that they sleep outside because of the heat and the perception that sleeping outdoors prevents cerebrospinal meningitis (CSM). Hence, sleeping outside is very common during the dry season as described by this community member:

"Sometime back, when the heat was like this, they say that the heat is too much and that nobody should sleep in the room, because the heat gives us another condition called CSM. That we should sleep (outside) in the compound…and that we should fetch water and drink a lot of water during these hot seasons."

(Female community member, FGD, Northern Region)

Overcoming Known Barriers to ITN Use

Outdoor ITN Use

Outdoor ITN use was discussed across the three sites. Regular users indicated that they can use an ITN when they are sleeping outside their rooms, in the open-air compound. Participants described a number of local techniques for setting up ITNs outdoors including hanging the net over chairs, filling cans with sand or dirt to hold sticks for hanging the net or hanging the net over a clothes line. For instance, a case study participant from the Easter Region described her approach to using a net outdoors on her veranda this way, *"When it is hot inside, we sleep outside here on the veranda* and to prevent mosquito bites we bring the net outside and spread it over *four plastic chairs, when this is done, you can sleep until morning without feeling any heat. So for me, I like to sleep in the mosquito net."* (CS3)

A limited number of study participants indicated that it is possible for ITNs to be used when a person sleeps outside his/her compound, especially if their work requires that they sleep away from home. Some participants indicated they often use nets when they travel, although this was infrequently reported in this study. A female community leader from the Central Region explained, *"My fishermen brothers who go for fishing…some of them intentionally decide not to sleep in the net but some of them use their nets when sleeping outdoors."*

Developing a habit of ITN use

Some consistent ITN users noted that once they developed the habit of ITN use, it became easier to continue using it without difficulty. Developing the habit as a child made it easier to consistently use an ITN as an adult. A female case study participant from the Eastern Region described becoming accustomed to net use from a young age, explaining:

> *"The reason why I use the mosquito net is that, at first, we were living by the riverside, so when the mosquitoes bit us, we got sick, so they (the government) always brought us the mosquito net. So, when we moved to settle here, I realized sleeping under the mosquito net helps the body as well as the health because no insect will bite you."*

Education on ITN Use

Sustained health education emerged as an important factor for increasing ITN use and preventing malaria. The media, television, radio and the use of mobile community information vans and health workers were identified as the main sources of information on malaria in the community. A male case study participant from the Northern Region explained*, "Continuous education and constant reminders will ultimately bring the desired change we are all clamoring for. Some people are generally difficult and will require more education to change."*

The importance of images and photos to promote ITN usage was put forward by health workers in the Central Region. They believe that this will help the people to better understand the messages that they receive. The potential value of the use of images and photos was explained in the following narrative:

> *"I think we should try to put in images to show them… I was presenting and I got an image from the internet, the man had hung the net at the back…of the Toyota pickup truck… and was sleeping … I think when they see the images and all that… it will draw their attention to the fact that they are not the only person with this challenge (of using a net in difficult circumstances) …"*
>
> (Male health worker, Central Region, FGD)

Respondents stated that providing information on how to reduce heat within sleeping spaces could also help increase ITN use. This included addressing sources of heat in sleeping spaces, such as using bulbs that emit low heat, using light curtains, and moving curtains aside during the night to increase access to fresh air as this will reduce the heat associated with sleeping in the net.

Nighttime activities

Participants perceived gaps in protection before sleeping hours, as well as when away from home. A 61-year-old male community member from the Central Region explained:

> *"Sometimes, it is not only about you being in your room. Maybe in the evening by this time around 5:30 pm, if you are sitting outside getting some fresh air, even before you go and lie down in the net, the mosquitoes would have bitten you already. Maybe you are at home, eating outside in the evening. Before going to bed the mosquitoes would have bitten you already before you go and use the net. And this happens a lot during the rainy season."*
>
> (Male community member, Central Region, FGD).

Participants intimated that people of all ages sleep outside of their compounds during funeral rites (wake keeping), religious activities (crusades, conferences), and festivals. For some participants, their work requires that they sleep outside the home. Farming, fishing, and going on night duties were work-related reasons for sleeping away from home. These issues were raised across the study sites. A female community member from Central Region explained, *"Some of us go for funerals and have to do wake keeping, so we sleep outside the home; we are also engaged in fishing and so we have to go to work, and this will require sleeping outside. It is very common here because it is a fishing community."*

Additional malaria prevention methods

Community members employed several strategies to prevent malaria in addition to using ITNs. Participants indicated that they stay indoors in the night and use topical mosquito repellents, coils, aerosol sprays, and fans to protect against mosquito bites and malaria. In addition, at the individual level, people make "trap doors" with nets and use nets as screening material on the windows of their homes to prevent mosquitoes from entering the rooms. At the community-level, participants cited additional strategies used to prevent malaria in the community: clean-up events and clearing bushes around the community to reduce breeding sites for mosquitoes. Participants also identified local remedies to prevent mosquito bites, including the burning of gari (local food made of cassava), ground nut shells, bamboo leaves, orange peels, and other local leaves. The scents and smoke produced from burning these items is believed to ward off mosquitoes. These local remedies were reported across all the three study sites. A female caretaker of a child under five from the Central Region explained, *"If we are going to be outside till about 11 pm, we have to take orange peels, put them in a plate and add some fire and when the smoke disperses, the mosquitoes will not come near and bite us."*

Gender and age considerations

Differences were noted across age and sex related to perceived vulnerability, ITN use practices, nighttime activities, and sleeping patterns. Generally, participants stated that children and women go to bed earlier than men. Women and children were often perceived as having a greater risk of malaria and therefore more likely to sleep under an ITN. It was generally agreed among participants across the three study sites that men spent more time outdoors at night and were more likely to sleep outside of their compound. A female community member from the Northern Region explained, *"Men spend a lot of time in the night outside with friends, so they come to sleep late. We, mothers and children, go to bed earlier than them. So, they may be using the net around 12 midnight when they are ready to sleep."* A female case study participant, also from the Northern Region, echoed this sentiment explaining, "*So, in my opinion, a man can freely sleep outside but a woman cannot. She can only sleep in the compound."*

In the Northern Region, health workers noted a perception in some communities that ITN use was a sign of weakness for men. A female health worker from the Northern Region explained, *"They have this saying, 'dagban doo bi niŋda' (meaning a Dagomba man doesn't do that). So, like they are proud…He feels that he can take care of himself better than using a net because when he uses one, they will say he is just a weakling."*

Participants noted that the financial burden of sickness is borne mostly by men in the household, while women are the ones that send the sick child to hospitals and stay with them when they are hospitalized. Participants felt that women bear the highest burden of the child's ill health due to this caretaking role, which serves as a motivator for mothers to promote ITN use in the household. A caretaker of a child under five explained:

> *"When the children are sick, we (women) have to carry them to the hospital and the man provides the money. However, if you go to the hospital and the child is admitted, you the mother will have to stay in the hospital and take care of the child. So, for me, I use my net with the children even though their father does not care about the use of the net because when the children are sick, I suffer more."*
>
> (Female caretaker of a child under give, Northern Region, FGD)

3.5 Discussion

ITNs arguably remain the most effective tool available to prevent malaria; ensuring high levels of access to and use of ITNs is crucial to their success. Among the more than two dozen U.S. President's Malaria Initiative focus countries that completed DHS or MIS surveys in recent years, Ghana ranks close to the bottom in levels of use among those with access (Koenker et al., 2018). Understanding barriers and facilitators to use among those with access is critical for closing this gap.

Heat continues to be the most widely reported barrier associated with sleeping under an ITN and a dominant reason why people with access to an ITN choose not to use it at all, occasionally or seasonally. This finding is consistent with what was reported in a review of published literature which found discomfort, primarily associated with heat, was a primary barrier to ITN use (Pulford et al., 2011). Seasonal patterns of ITN use were documented in northern Ghana as early as the 1990s (Binka and Adongo, 1997, Binka et al., 1996). The seasonal use of ITNs is linked to perceived low mosquito density in the dry season. This perception is supported by entomological monitoring in Ghana which shows higher entomological inoculation rates during the rainy season (Coleman et al., 2017).

Adverse reactions to insecticide were frequently mentioned as inhibitors to ITN use. Changing messaging provided through mass and continuous distribution channels to encourage increased airing time (48 hours or longer) prior to first use has the potential to improve user experiences and promote consistent use.

The perceived effectiveness of ITNs in preventing malaria was commonly reported, however, some participants felt nets were more useful in preventing nuisance from mosquitoes, and other pests, for a good night's sleep. This was also reported in earlier studies where it has been indicated that the practical function of mosquito nets may differ from the intended function in some instances (Pulford et al., 2011, Binka and Adongo, 1997, Frey et al., 2006, Galvin et al., 2011, Klein et al., 1995, Koenker et al., 2013a). Examples of using ITNs for purposes other than sleeping under them were reported in a few instances. When the material of the ITN distributed was perceived as hard, the ITN was more likely to be used for other purposes. Examples of alternative use of ITNs has been documented elsewhere in the literature (Diema et al., 2017, Minakawa et al., 2008). A consensus statement put forward by the RBM Partnership to End Malaria classifies alternative use of ITNs in three categories including misuse, neutral repurposing, and beneficial repurposing (2018). Use of a *new* ITN for any alternative purpose is considered misuse, as is use of *any* ITN for fishing. However, use of an inactive ITN for purposes such as covering windows, which can provide some protection from malaria mosquitoes, is classified as beneficial repurposing. National Malaria Control Programs should consider these practices in development of SBCC messaging.

An important issue to address in ITN promotion is how to encourage ITN use among individuals who spend part or all of the night sleeping outdoors; this was one reason for 'partial' non-use reported in our study, and has been reported in earlier studies (Pulford et al., 2011, Eng et al., 2010, Frey et al., 2006, Gyapong et al., 1996). Having additional mosquito nets in the household that could be hung in the various sleeping areas, indoors and outdoors, may be helpful. Pulford *et al.*, (Pulford et al., 2011) argued that hanging mosquito nets outdoors may continue to be problematic given current mosquito net designs, which rely on external supporting structures, and proposed the development of 'outdoor' or 'standalone' mosquito nets that require no external supports yet remain portable and user friendly. Despite the challenge, a number of participants identified local solutions for using their current ITNs outdoors and ensuring a good night's sleep even during the dry season. Identifying and disseminating local solutions of outdoor ITN use should be considered. Providing visual representations of how to use an ITN outdoors, or in other challenging contexts, should also be explored.

ITN use must be promoted within the larger context of the malaria control and elimination agenda, bearing in mind that no single control tool will be enough to eliminate malaria. While ITNs are an essential tool for malaria prevention, they are designed to primarily protect people while sleeping. A number of studies across sub-Saharan Africa, including in Ghana, have identified activities that occur when malaria vectors are active but net use is not feasible (Monroe et al., 2015, Monroe et al., 2014). A review of the published literature identified common nighttime activity categories across different contexts in sub-Saharan Africa, including routine social and community events, as well as large scale social events and livelihood activities that can last throughout the night (Monroe et al., 2019b). To this end, personal protection measures, when proven effective, should be promoted among those who have to stay outdoors at night to work or perform other duties (Durnez and Coosemans, 2013b, Govella and Ferguson, 2012a, Killeen, 2014).

There are a number of limitations associated with this study. First, qualitative methods were selected to complement existing quantitative findings and provide a broader understanding of participants' experiences. The sample size was thus driven by the goal of theoretical saturation, not statistical significance, and must be interpreted accordingly. Further, while self-reported data was utilized to better understand participants' perspectives, there is the potential for social desirability bias, in which participants report what they perceive as the socially acceptable answer rather than their true behavior (Fisher, 1993, Lavrakas, 2008). However, a majority of participants reported that they were not consistent users, and spoke freely about the barriers to using ITNs, suggesting that social desirability bias did not influence the quality of study findings in a meaningful way.

3.6 Conclusions

ITN use, as described by study participants, was not binary (user versus nonuser); one's ITN use could vary throughout the night, across seasons, and over time. The study results suggest that the greatest gains in ITN use among those with access could be made by promoting consistent use throughout the year among occasional and seasonal users. Opportunities for improving communication messages as well as structural approaches to enhance the usability of ITNs in challenging contexts were identified from this work. Examples include positioning ITN use within the broader context of malaria prevention; increasing the salience of malaria risk; updating messaging to increase airing time before first using the ITN; highlighting the cost and time benefits of prevention over treatment as well as the benefits of a nuisance-free sleep; increasing knowledge of malaria transmission; and identifying and promoting solutions for using ITNs in outdoor or challenging environments.

The gender dimensions of ITN use suggest the need to focus on promoting ITN use for all family members and identifying messages and channels that will resonate with both males and females. The results of this study can help to inform social and behavior change messaging and innovative approaches to addressing the ITN use gap in Ghana.

3.7 Declarations

Ethics approval and consent to participate

The study was reviewed by the Johns Hopkins University Institutional Review Board and was determined to meet the criteria for exemption (IRB No. 8437). The study was reviewed and approved by the Noguchi Memorial Institute for Medical Research (IRB No.1276) and the Ghana Health Service Ethics Review Committee (GHS-ERC: 007/02/18). All participants provided written informed consent prior to participation.

Consent for publication

Availability of data and materials

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

Competing interests

The authors have declared that they have no competing interests.

Funding

This work was made possible by the generous support of the American people through the United States Agency for International Development (USAID) and the President's Malaria Initiative (PMI) under the terms of USAID/JHU Cooperative Agreement No. AID-OAA-A-14-00057 (VectorWorks Project). The contents are the responsibility of the authors and do not necessarily reflect the views of USAID or the United States Government.

Authors' contributions

CA designed the case studies and free listing and ranking activity, contributed to study protocol development, supervised data collection, led data analysis, and drafted sections of the manuscript. PA, SBS, EK, and PTT contributed to data collection and analysis and provided input on the manuscript. HK, DP, and BO contributed to the study design and provided input on the manuscript. SS contributed to data collection supervision and provided input on the manuscript. **AM** was responsible for overall study design, developed focus group discussion guides and study protocol, supervised data collection across sites, contributed to analysis and interpretation of study findings, drafted sections of the manuscript, and managed revisions to the manuscript. All authors reviewed and approved the final version of the manuscript.

Acknowledgements

The authors would like to thank study participants, community leaders, the Ghana National Malaria Control Program, and data collection teams for contributing to the success of this study. They would also like to thank Richard Kpabitey for contributing to data collection supervision; Jon Eric Tongren for providing input on the study concept and manuscript; Kwane Ankobea for providing input on the study concept; and Susan Henderson, Avery Avrakotos, and Matthew Lynch for providing feedback on the manuscript.

Chapter 4: Measuring and characterizing night time human behavior as it relates to residual malaria transmission in sub-Saharan Africa: a review of the published literature

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Published in
Malaria Journal 2019 **18**:6

https://doi.org/10.1186/s12936-019-2638-9

4.1 Abstract

Background

Malaria cases and deaths decreased dramatically in recent years, largely due to effective vector control interventions. Persistence of transmission after good coverage has been achieved with high-quality vector control interventions, namely insecticide-treated nets or indoor residual spraying, poses a significant challenge to malaria elimination efforts. To understand when and where remaining transmission is occurring, it is necessary to look at vector and human behavior, and where they overlap. To date, a review of human behavior related to residual malaria transmission has not been conducted.

Methods

Studies were identified through PubMed and Google Scholar. Hand searches were conducted for all references cited in articles identified through the initial search. The review was limited to English language articles published between 2000 and 2017. Publications with primary data from a malaria endemic setting in sub-Saharan Africa and a description of night time human behaviors were included.

Results

Twenty-six publications were identified that met inclusion criteria. Study results fit into two broad categories: *when* and *where* people are exposed to malaria vectors and *what* people are doing at night that may increase their contact with malaria vectors. Among studies that quantified human-vector interaction, a majority of exposure occurred indoors during sleeping hours for unprotected individuals, with some variation across time, contexts, and vector species. Common night time activities across settings included household chores and entertainment during evening hours, as well as livelihood and large-scale socio-cultural events that can last throughout the night. Shifting sleeping patterns associated with travel, visitors, illness, farming practices, and outdoor sleeping, which can impact exposure and use of prevention measures, were described in some locations.

Conclusions

While the importance of understanding human-vector interaction is well-established, relatively few studies have included human behavior when measuring exposure to malaria vectors. Broader application of a standardized approach to measuring human-vector interaction could provide critical information on exposure across settings and over time. In-depth understanding of night time activities that occur during times when malaria vectors are active and barriers to prevention practices in different contexts should also be considered. This information is essential for targeting existing interventions and development and deployment of appropriate complementary prevention tools.

Keywords Malaria, residual transmission, outdoor transmission, review, sub-Saharan Africa, insecticide treated nets, human behavior, human-vector interaction, human-vector contact

4.2 Background

Substantial and sustained global efforts have led to a significant decrease in malaria burden over the last 15 years, with a 41% decrease in incidence rates and 62% decrease in mortality(Bhatt et al., 2015a, WHO, 2016). These efforts include large-scale distribution of insecticide-treated nets (ITNs), targeted indoor residual spraying (IRS), wider availability of affordable and effective artemisinin-based combination therapy (ACT), and intermittent preventive therapy during pregnancy (IPTp). An estimated 68% of the decrease in infections can be attributed to ITNs, making this the most effective malaria prevention tool currently available (Bhatt et al., 2015a, Hemingway, 2015). Combined, the core vector control interventions, ITNs and IRS, account for an estimated three quarters of clinical malaria cases averted (Bhatt et al., 2015a).

Despite the contribution of ITNs and IRS to vector control, malaria persists, with a disproportionate impact on sub-Saharan Africa. In 2016, sub-Saharan Africa accounted for 90% of all malaria cases and 91% of all malaria deaths (WHO, 2017d). Residual malaria transmission, defined by the World Health Organization as '*persistence of parasite transmission even with good access to and usage of ITNs or well-implemented IRS, as well as in situations where ITN use or IRS are not practical*', represents a critical challenge for malaria control and elimination efforts(malERA, 2011, Durnez and Coosemans, 2013b, Killeen, 2014, WHO, 2014).

As indoor-focused interventions, there are limitations to the protection ITNs and IRS can confer. This issue may be compounded by shifts in vector behavior and species composition in response to vector control interventions across settings(Moiroux et al., 2012, Govella and Ferguson, 2012a, Reddy et al., 2011, Yohannes and Boelee, 2012, Wamae et al., 2015, Durnez and Coosemans, 2013b). Significant research has been done to understand mosquito feeding and resting behavior. The dominant malaria vectors in Africa are *Anopheles* *gambiae sensu lato* (*s.l.*) (including *An. gambiae sensu stricto*, *Anopheles coluzzii* and *Anopheles arabiensis*) and *Anopheles funestus sensu stricto* (*s.s*.) (Githeko et al., 1996, Moiroux et al., 2012, Sinka et al., 2010). Typically, *An. gambiae* s.s., *An. coluzzii* and *An. funestus* s.s are anthropophagic and feed and rest indoors [4, 6], while *An. arabiensis'* behavior is more plastic, showing zoophagic and exophilic tendencies (Tirados et al., 2006a, Killeen et al., 2016). The differences in biting and resting behaviors affect the success of interventions like IRS and ITNs, as mosquitoes that feed and rest inside are more likely to encounter insecticide than those who feed and rest outside. In addition, in recent years shifts in vector behavior following introduction of malaria control interventions in certain locations have been observed (Moiroux et al., 2012, Govella and Ferguson, 2012a, Reddy et al., 2011, Yohannes and Boelee, 2012, Wamae et al., 2015, Gatton et al., 2013, Sinka et al., 2016). These changes can include species shifts, shifts toward early evening and early morning biting, toward outdoor resting and biting, and toward zoophily (Durnez and Coosemans, 2013b).

While these observed shifts are a result of successful vector control, there is an urgent need to understand when and where people remain at risk for malaria transmission to effectively target specific places, groups, and activities. This information is critical for guiding malaria control and elimination efforts. To understand when and where remaining transmission is occurring, it is necessary to look at both vector and human behavior, and specifically the times when they overlap. While significant attention has been given to vector behavior, to date a comprehensive review of night time human behavior has not been carried out. The aim of this review is to synthesize the current body of evidence on human behavior as it relates to transmission that can occur in the context of high vector control coverage, and existing methods for measuring and characterizing this human behavior. The review focuses on human behavior in sub-Saharan Africa based on the disproportionate burden of malaria in these countries.

4.3 Methods

A literature review of published research findings was carried out using electronic databases, specifically PubMed and Google Scholar. Search terms were developed and refined prior to beginning the review (Table 1). Articles were identified and screened if they included any combination of the search terms in the title, abstract, or the body of the article. Additional articles were identified through a hand search of all references in articles identified through the initial keyword search. The review was limited to English language articles published between January 1, 2000 and December 31, 2017.

Table 4.1 Search terms and resulting number of articles

Search terms Limits: Species-Human; Publication Dates: 01/01/2000-12/31/2017	Number of articles screened
Africa[MeSH Terms] AND human AND (behavior OR behavior) AND malaria	1361
Africa[MeSH Terms] AND "Human Activities" [MeSH Terms] AND malaria	732
outdoor OR outside OR residual AND malaria AND (behavior OR behavior)	307
malaria AND (outdoor OR residual) AND behavior	217
human AND "location" AND "malaria"	119
("human behavior" or “human behavior”) AND malaria	45
“human activities"[Mesh] and malaria and (outdoor OR residual)	23
anthropology OR anthropologic AND malaria exposure	17
outdoor AND human AND behavior AND night AND Africa	21
outdoor AND malaria AND ("human behavior" OR "human behavior")	6
Africa[MeSH Terms] AND “human exposure” AND malaria	35
Africa[MeSH Terms] AND "Human Activities" [MeSH Terms] AND night time	4
Africa[MeSH Terms] AND human AND (behavior OR behavior) AND night time	12

Studies were included in the review if they involved investigation of human behaviors in relation to malaria exposure. Specifically, studies needed to include a malaria endemic setting in sub-Saharan Africa and a description of human behaviors occurring during times when malaria transmission can occur, i.e. when malaria transmitting vectors are active. Behavior is defined by PubMed as, “the observable response of a man or animal to a situation,” and the term is used broadly in this review to encompass human activities, location, and sleeping patterns. This includes activities occurring within or nearby the home, within the community, or outside of the community. Abstracts for articles identified with the search terms were reviewed, and for those that met the above criteria, the full-text was evaluated and grouped by categories of human activities occurring during times when local malaria vectors are active, methods for capturing human behavior, and presence and type of entomology data collected alongside the human behavioral data. Articles that included mosquito biting rates without measuring human behavior and articles that described ITN use only were excluded.

4.4 Results

A total of twenty-six articles were identified that met inclusion criteria. These studies provided information on two key areas of interest: when (time of night) and where (indoors versus outdoors) people are exposed to malaria vectors and characterization of night time activities occurring during hours when malaria vectors are active.

Human exposure to malaria vectors

Ten studies integrated human behavioral and entomological data to provide a quantitative estimate of human-vector interaction occurring indoors and outdoors (Table 4.2).

Table 4.2 Studies quantifying human-vector interaction

(Reference)	Country	Human behavior methods	Human behavioral information collected	Entomological methods	Timing of entomology and human behavior data collection	Human exposure to malaria vectors
(Killeen et al., 2006)	Tanzania	Survey	Usual bed time and wake-up time	Indoor and outdoor HLC, 6:00pm-6:00am	Mosquito collections: 1997 and 2004 Survey: 2002-2004	Indoor exposure for non-user: 90% Indoor exposure during sleeping hours (9:00pm-5:00am): 80% Protective efficacy of an ITN: 70%
(Geissbuhler et al., 2007)	Tanzania	Survey and direct observation	Survey: Dinner location, location after dinner, usual bed time and wake-up time, use of prevention measures Direct observation: people outdoors for each hour of the night	Indoor and outdoor HLC, 6:00pm-7:00am	Mosquito collections: April-June 2006 Survey: carried out in same households; exact timing not specified	Indoor exposure for non-user (*An. gambiae s.l.)*: 79% Indoor exposure during sleeping hours for non-user (*An. gambiae s.l.)*: 74% Protective efficacy of an ITN (*An. gambiae s.s.*): 59% Protective efficacy of an ITN (*An. arabiensis*): 38%
(Russell et al., 2011)	Tanzania	Survey	Usual bed time Usual wake-up time	Indoor and outdoor HLC, 7:00pm-7:00am	Mosquito collections: 1997, 2004, and 2009 Survey: 2002-2004	Indoor exposure for non-user (1997 *An. gambiae s.l.*): 92% Indoor exposure for non-user (2004 *An. gambiae s.l.*): 99% Indoor exposure for non-user: (2009 *An. gambiae s.l.*): 79% Indoor exposure for non-user (1997 *An. funestus*): 93% Indoor exposure for non-user (2004 *An. funestus*): 73% Indoor exposure for non-user (2009 *An. funestus*): 45%

(Seyoum et al., 2012)	Zambia	Survey	Usual time indoors for the night, bed time, wake-up time, time to leave home in the morning, use of ITNs	Indoor and outdoor HLC,7:00pm-7:00am	Mosquito collections: September-October 2009, February-March 2010 Survey: April 2010	Indoor exposure for non-user (*An. funestus)*: 98% Indoor exposure for non-user (*An. quadriannulatus*): 97% Indoor exposure for ITN-user (*An. funestus*): 57% Indoor exposure for ITN-user (*An. quadriannulatus)*: 58%
(Huho et al., 2013b)	Burkina Faso Kenya Tanzania Zambia	Burkina Faso and Tanzania: Direct observation by field worker 6:00pm until all household members went to sleep and 4am-6am Kenya and Zambia: Malaria indicator survey	Observation: Household members awake, by hour Survey: To the nearest hour, time that each household member went indoors, to bed, woke up, and left the home	Indoor and outdoor HLC, start time ranged from 6:00pm to 8:00pm and end time ranged from 6:00am to 7:00am across sites	Tanzania and Burkina: 2001and 2004 Kenya and Zambia: 2009 and 2010 Exact timing of entomological and human behavioral data collection was not provided	Indoor exposure for non-user (*An. gambiae s.l.*): ranged from 87% to 97% across sites Indoor exposure for non-user (*An. funestus s.l.*): ranged from 62% to 97%
(Bayoh et al., 2014)	Kenya	Survey	ITN use, usual time indoors for the night, bed time, wake-up time, time to leave home in the morning	Indoor and outdoor HLC, 5:00pm-7:00am	Mosquito collections: June-July 2011 Survey: July-August 2011 Data compared to data from previous study carried out in 1989-1990	Indoor exposure for non-user: >90% in all years Indoor exposure for non-user during sleeping hours: ≥90% for all species except for *An. arabiensis* (97% in 1989/1990; 80% in 2009; 84% in 2011) Indoor exposure for ITN-user during sleeping hours: (64-77% in 1989-1990; 20-52% in 2009 and 2011)
(Moiroux et al., 2014)	Benin	Survey	Time each household member entered and exited the house the night before the survey and entered and exited the sleeping space	Indoor and outdoor HLC, 11:00pm-9:00am	Mosquito collections: April 2011 Survey: March 2013	Indoor exposure for non-user: 86% and 94% in the two study sites Protective efficacy of an ITN: 80% and 87% Indoor exposure for ITN-user: 55% and 31%

(Cooke et al., 2015)	Kenya	Survey completed by head of household on behalf of household members, using digital watch	Time household members entered and exited the house, time to sleep, and use of ITNs	CDC light-traps set next to occupied ITNs, emptied hourly Indoor traps 5:30pm-5:30am; outdoor traps 5:30pm-10:30pm only	Mosquito collections: June 2011-May 2012 Survey: June 2011-May 2012	Indoor exposure for non-user: 95% (31% before bed and 64% while asleep) Protective efficacy of an ITN:51%
(Bradley et al., 2015)	Equatorial Guinea-Bioko Island	Annual malaria indicator survey	Time household members entered the house the night before, any other time spent outside the house between 7:00 pm and 6:00 am, bed time	Indoor and outdoor HLC, 7:00pm-6:00am	Mosquito collections: January-October 2009-2013 Survey: 2013	Indoor exposure for non-user: 80%
(Kamau et al., 2018)	Kenya	Survey administered to head of household	Time each household member went to sleep and woke up	HLC and CDC light traps: 6:00pm-6:00am	Mosquito collections: July and August 2016 Survey: September and October 2016	Indoor exposure for non-user (children <5): 90%

Studies that integrated human and vector data used estimates of indoor and outdoor vector biting as well as the distribution of people indoors and outdoors for each hour of the night to produce a weighted estimate of exposure occurring indoors and outdoors. This analytical approach was used to quantify human-vector interaction by Killeen *et al.* in rural Tanzania (Killeen et al., 2006). In this study, human landing catches were used to assess nightly mosquito biting behavior before and after widespread coverage of ITNs. The proportion of time people spent indoors and outdoors was estimated based on self-reported survey questions on when household members went to bed and woke up in the morning. These data were combined with hourly indoor and outdoor biting rates to calculate the proportion of bites that occur indoors for unprotected individuals, the proportion of bites that occur during sleeping hours, and the "true protective efficacy of an ITN", defined as the overall reduction in nightly biting rate for an ITN user compared to a non-user.

Variations of this approach to measuring human-vector interaction were found in nine subsequent publications (Geissbuhler et al., 2007, Huho et al., 2013b, Bayoh et al., 2014, Moiroux et al., 2014, Cooke et al., 2015, Ototo et al., 2015, Bradley et al., 2015, Kamau et al., 2018, Seyoum et al., 2012, Russell et al., 2011). Mosquito biting behavior was measured in the majority of studies using human landing catches (HLC) indoors and outdoors on an hourly basis. Cooke *et al.* used CDC light traps and human baited ITNs (Cooke et al., 2015). All of the studies focused mosquito collections on the peri-domestic setting, which included inside of dwellings and in the outdoor space directly outside of the dwelling (Tuno et al., 2010). Mosquito collections were generally carried out indoors and outdoors, from dusk until dawn, with some variation in start and end times across study sites.

The human behavioral variables of interest and approach used to calculate indoor and outdoor components of human-vector interaction were similar across studies. Like the study by Killeen *et al.*, these studies included estimates of time spent indoors and outdoors throughout vector biting hours, however in some cases they used different methods to derive these estimates. For example, Cooke et al. provided digital watches to heads of household and had them fill out surveys on household members' night time behavior (Cooke et al., 2015). Geissbuhler *et al*. used self-reported survey data, validated by a smaller number of evening observations(Geissbuhler et al., 2007). Huho *et al.* looked at human-vector interaction across countries, using different methods for measuring human behavior in different locations (Huho et al., 2013b). This included direct observation of night time behavior from 6:00pm to bedtime and 4:00am to 6:00am in selected sites in Tanzania and Burkina Faso, and self-reported survey data from malaria indicator surveys in Zambia and Kenya. The two methods were not compared to one another. Bradley *et al.* also used data from questions included in a malaria indicator survey (Bradley et al., 2015). Other studies used self-reported survey data to gather similar information to Killeen *et al*. The exact list and phraseology of the questions was not included in all publications, but differences in content were identified. Some studies only asked about the time participants went to bed and woke up, while others included additional questions on time participants went inside the house and time they went outside in the morning to more closely approximate when people were outdoors, indoors and awake, and indoors and asleep.

The most common human-vector indicators presented in the studies reviewed included proportion of exposure to malaria vectors occurring indoors for an unprotected individual, exposure to malaria vectors occurring indoors during sleeping hours for an unprotected individual, exposure occurring indoors for an ITN user, and protective efficacy of an ITN. However, these indicators were not uniformly calculated and were not included across all studies integrating human and vector data.

Across settings, a majority of human exposure to malaria vectors for non-users of ITNs was found indoors, largely during sleeping hours. However, variation was observed across settings. In Western Kenya, Cooke *et al.* found that without the protection of an ITN over 90% of exposure occurred indoors, similar to estimates from Killeen *et al.* in the Kilombero Valley of Tanzania, Seyoum *et al*. in South-East Zambia, Bayoh *et al.* in western Kenya, Moiroux *et al*. in south Benin, and Huho *et al.* in six sites in rural Burkina Faso, Kenya, Zambia, and Tanzania (Cooke et al., 2015, Killeen et al., 2006, Bayoh et al., 2014, Moiroux et al., 2014, Seyoum et al., 2012, Huho et al., 2013b). However, Cooke *et al.* found that use of an ITN could prevent only about half of exposure to malaria vectors despite predominantly endophagic primary vectors, likely due to high levels of indoor exposure before sleeping hours (Cooke et al., 2015). Kamau *et al.* estimated the fraction of exposure occurring indoors and outdoors for children under five. Overall, the study estimated that 10% of exposure is happening outdoors, primarily during early evening hours between 6:00pm and 9:00pm(Kamau et al., 2018).

Results suggest shifts in both time and place (indoor/outdoor) of exposure across time. Russell *et al.* found significant changes in indoor human exposure to malaria vectors for both *An. gambiae s.l.* and *An. funestus* as ITN use increased (Russell et al., 2011). In 1997, over 90% of exposure occurred indoors for both vector species; by 2009 when ITN access and use had increased, indoor exposure dropped to 79% for *An. gambiae s.l.* and. 45% for *An. funestus* and a higher proportion of exposure outdoors during early evening hours was observed. The protective efficacy of an ITN varied from approximately 50% to over 80% in studies that reported on it, with even lower protective efficacy (38%) reported for specific vector species, namely *An. arabiensis*(Geissbuhler et al., 2007, Killeen et al., 2006, Moiroux et al., 2014, Cooke et al., 2015).

Association between night time location and malaria risk

Seven studies were identified that linked night time location with malaria risk. Four of the six studies specifically looked at whether time spent outdoors at night was associated with an increased risk of malaria infection. A case control study in South-West Kenya by Githinji *et al*. assessed micro-ecological and human behavioral factors associated with an increased risk of malaria infection. Human behavior was assessed through a standardized survey (Githinji et al., 2009). No detail on the content of the human behavioral survey questions was included in the methods section. Results showed participants who spent time outside at night were more likely to be infected with malaria. Spending time outside at night was binary and did not specify length of time or time of the night. The discussion section described '*experiences gathered during data collection period*' that showed community ceremonies such as funerals were commonly carried out at night, leading to an increased exposure to the risk of mosquito bites. However, no description was provided in the study methods about how night time activities were recorded nor was this information included in the results section.

In two studies, Bradley *et al.* investigated the association between time spent outdoors and malaria infection on Bioko Island, Equatorial Guinea. In a 2012 publication, Bradley analyzed data from an annual malaria indicator survey, which includes a question asking whether a child spent time outside between 10pm and 6am (Bradley et al., 2012). Children aged two to fourteen were tested for *Plasmodium falciparum* using rapid diagnostic tests (RDT). Only 4% of children were reported to spend time outside during this time and no significant difference in prevalence was observed for children who spent time outside verses those who did not. In a 2015 publication, Bradley *et al.* conducted a survey to measure the association between time spent outdoors and malaria infection as measured by RDT, in addition to measuring exposure to malaria vectors (Bradley et al., 2015). Malaria infection was not significantly higher in individuals who reported spending time outside between

7:00pm and 6:00am the previous night compared to those who did not, in both adults and children. Malaria infection in neither adults nor in children was associated with exposure to outdoor bites, even after adjusting for confounders.

Mwesigwa *et al.* assessed incidence of *Plasmodium falciparum* infection using a cohort study in The Gambia (Mwesigwa et al., 2017). The study included a household survey that asked about outdoor sleeping among household members. Outdoor sleeping varied by season and was associated with a significantly higher risk of malaria infection.

Hetzel *et al.* carried out a longitudinal study looking at time spent at *shamba* (farm houses) and incidence of fever in rural Tanzania (Hetzel et al., 2008). The study included a survey to record where household members spent time during the day and night and use of ITNs as well as a treatment-seeking questionnaire recording fever episodes and treatment-seeking behavior. During weeding and harvesting seasons a large proportion of household members spent days and nights at the farm houses. Fever incidence rates were lower in the *shamba* compared to the village, and 97% of participants reported using a mosquito net the night before. The discussion noted that since *shamba* houses are spread out there is little opportunity for socializing in the evening and, therefore, household members were likely to go to bed early; however, information on night time social activities and average bed times were not reflected in the study methods or results.

Using global positioning system (GPS) data loggers, Searle *et al.* assessed seasonal movement patterns in rural Southern Zambia(Searle et al., 2017). As part of the study, the team assessed time spent away from the household compound during peak biting hours, defined as 7:00pm to 6:00am for the primary local vector, *An. arabiensis*. On average, participants spent 5.6% of time away from the household compound during peak vector biting hours. Time spent in high or low risk areas, identified by a malaria risk map, depended on the level of risk for the area in which a participant's compound was located. Participants largely spent time in and close to their household compound, with less frequent longer distance movements. While the study assessed time away from the household compound during peak biting hours, the spatial resolution of the loggers was not sufficient to distinguish time spent indoors and outdoors specifically.

Ototo *et al.* included the percentage of the population outdoors during times of the night when the highest densities of blood fed vectors were collected in a study in Kenya (Ototo et al., 2015). Approximately half of the study population was outdoors in the evening between 6:00pm and 8:00pm and in the morning between 6:00am and 8:00am. In the highland sites, participants reporting going outdoors earlier in the morning compared to the lowland sites, between 4:00am and 6:00am, largely due to agricultural activities. The results show that no one slept outdoors, even in the hot months. While presented together, the data were not integrated to provide an estimate of exposure to malaria vectors.

Characterization of night time activities

A total of 10 studies included some description of night time activities occurring during times when local malaria vectors are active (Table 4.3). These studies identified activities taking place in the peri-domestic setting (inside and directly outside of the home), as well as away from home, throughout the night. This included routine household chores and entertainment occurring in the evening hours before bed, routine livelihood activities that lasted throughout the night such as security and fishing, and large-scale socio-cultural events, such as weddings and funerals which lasted throughout the night. Circumstances that could temporarily disrupt usual sleeping patterns were also described including travel, illness, and house guests, as well as seasonal changes to sleeping patterns associated with farming practices and outdoor sleeping.

Table 4.3 Studies including description of night time human activities

(Reference)	Location	Methods Used to Capture Night time Activities	Night time Activities Identified	Night time Activity Categories
(Alaii et al., 2003)	Kenya	Early morning (4:00am-6:00am) observation of ITN use Survey question on barriers to ITN use for children under 5	Funeral ceremonies Disruption of sleeping patterns due to visitors	Large-scale socio-cultural events travel/visitors
(Dunn et al., 2011)	Tanzania	In-depth interviews Focus group discussions Participatory methods	Spending night at farming plot Outdoor sleeping Socio-cultural events e.g. funerals Household chores (women) Drinking, watching television, and socializing (men)	Livelihood activities Large-scale socio-cultural events Routine household activities Entertainment
(Tuno et al., 2010)	Ghana	Survey	Outdoor sleeping	Outdoor sleeping
(Monroe et al., 2014)	Uganda	In-depth interviews Focus group discussions	Funerals, weddings, religious events, parties Socializing, visiting bars Overnight visits with friends/family Occupations such as police and fishing Outdoor sleeping Domestic disputes, insurgency, illness	Large-scale socio-cultural events Entertainment Travel/visitors Livelihood activities Outdoor sleeping Times of difficulty
(Dlamini et al., 2015)	Swaziland	In-depth interviews Focus group discussion Direct observation from morning to late evening	Soccer playing and socializing (adolescent boys) Drinking at local bars (men) Preparing meals and fetching water (women and adolescent girls)	Entertainment Routine household activities

(Ototo et al., 2015)	Kenya	Survey	Early morning farming practices	Livelihood activities
(Monroe et al., 2015)	Ghana	Direct observation (6:00pm-6:00am) In-depth interviews	Household chores Socializing Weddings, funerals Outdoor sleeping	Routine household chores Entertainment Large-scale socio-cultural events Outdoor sleeping
(Swai et al., 2016b)	Tanzania	Direct observation (6:00pm-7:00am) In-depth interviews Focus group discussions	Farming practices Relaxing and storytelling, playing Cooking, eating, fetching water and firewood	Livelihood activities Routine household activities
(Moshi et al., 2017)	Tanzania	In-depth interviews Focus group discussions	Cooking, eating, household chores Socializing, drinking at bars	Routine household activities Entertainment
(Masalu et al., 2017)	Tanzania	Focus group discussions	Farming, night guard, sex work Funerals, parties, and gatherings	Livelihood activities Large-scale socio-cultural events
(Makungu et al., 2017)	Tanzania	In-depth interviews Focus group discussions Photovoice methods	Household chores Watching television, drinking at bars Fishing, street vending Funeral ceremonies	Routine household activities Entertainment Livelihood activities Large-scale socio-cultural events

Methods used to document and characterize human behavior included in-depth interviews, focus group discussions, participatory methods (e.g. mapping, diagramming, and photovoice recordings), direct observation of night time events, and questionnaires. These studies often looked at specific night time activities, as well as the impact of these activities on use of malaria prevention tools.

The level of detail provided on night time activities and sleeping patterns varied widely across publications. In some studies, night time human behavior was the primary area of focus. For example, Dunn et al. explored shifting household sleeping patterns in response to livelihood practices and socio-cultural events, and how these could impact malaria exposure and prevention practices in rural Tanzania (Dunn et al., 2011). The study documented changes in daily and seasonal sleeping patterns associated with farming practices that could impact human-vector interaction either through differences in time spent indoors/outdoors or differences in use of ITNs. The study also identified risk behaviors during socio-cultural events, such as funeral ceremonies, that could also impact time spent outdoors and use of ITNs.

In a study by Monroe *et al*. in Uganda, spending time away from home at night emerged as an important theme for understanding potential malaria exposure and prevention practices(Monroe et al., 2014). Social events, livelihood activities, and times of "difficulty" were identified as circumstances in which people spend part or all of the night away from home. Social events included funerals, weddings, religious ceremonies, spending time at bars and discos, and visiting friends and family. Livelihood activities included professions such as police, security guards, soldiers, fishermen, and brick-makers who might stay outside all night as part of their job. Times of difficulty at the family and community level included domestic violence or disputes, and security issues. Social barriers inhibited net use away from home as people feared being perceived as rude or as showing off if they brought their nets to large or small-scale social events. Not having a place to hang the net, or not having enough nets at home to take one when staying away, were also barriers.

A study by Monroe *et al.* in northern Ghana included both in-depth characterization of night time activities and assessment of potential human-vector interaction. In addition to in-depth interviews with community members and health workers, and semi-structured observations of night time activities and sleeping patterns throughout the night, the study team observed when people were indoors or outdoors, under a net, and sleeping for each household member at half-hourly intervals throughout the night. Entomology data were not collected as part of the study, however biting times from entomological monitoring in nearby sites was discussed in relation to human activities and sleeping patterns throughout the night (Monroe et al., 2015). This study identified a range of routine household chores, social activities, and large-scale events that may impact exposure to malaria vectors and use of prevention tools. Large-scale socio-cultural events and outdoor sleeping were the most common reasons for people to be outside during peak vector biting hours in the middle of the night.

In other studies, night time activities were included to a smaller extent as part of a larger research study. Alaii *et al.* monitored ITN use through early morning observations following net distribution. A household survey included a question on reasons why children under 5 might not use a net. Among those that provided reasons, social reasons accounted for a third of responses and included disruption of sleeping arrangements, funerals, visitors, and illness. Entomological indices were calculated in control villages but were not integrated with the human behavioral data (Alaii et al., 2003).

Masalu *et al.* conducted a study to test transfluthrin-treated decorative baskets and wall decorations at bars and included a small number of focus groups to assess acceptability of the products(Masalu et al., 2017). Focus group discussion respondents noted common night time activities, including farming, night guarding, sex work, funerals, parties, and other gatherings as activities that could increase risk of exposure to malaria. Mosquito collections were carried out in bars but were not linked with human behavioral data.

Dlamini et al. used a combination of semi-structured interviews, focus group discussions, and observations to identify behaviors that might impact malaria control interventions. Group socialization outside late into the evening at soccer games, friends' houses, or drinking establishments was found to be the primary behavior keeping people from using ITNs during vector biting hours. These activities were most common among young men. Preparing meals and fetching water were identified as common activities for women and girls (Dlamini et al., 2015).

A study by Tuno *et al.* in Ghana included a survey to determine the frequency of outdoor sleeping in study sites as well as where and when participants slept outdoors. The findings from this component of the study were presented separately from the entomological component. A significant proportion of men (37% and 82%) and women (16% and 56%) reported sleeping outdoors for a portion of the night in the two sites.

Swai *et al.* looked at biting risk associated with migratory farming practices. In addition to looking at mosquito biting behavior, the frequency of night time human activities (cooking, eating, washing dishes, fetching water and firewood, and storytelling) was recorded through direct observation. These activities were frequently observed during the times when the highest biting rates were recorded for local vectors, between 6:00pm and 11:00pm. While human and vector data were collected and analysed together to describe where humans may be at risk, the data was not integrated to provide a quantitative estimate of indoor and outdoor exposure based on the distribution of humans and vectors throughout the night (Swai et al., 2016b).

As part of a qualitative study, Moshi *et al.* used in-depth interviews and focus group discussions to better understand community knowledge of malaria transmission. The study described time spent outdoors, primarily during the early evening hours. During this time household chores, such as cooking, and socializing were common. Sitting outdoors at bars was described as a common activity for males (Moshi et al., 2017). Likewise, Makungu *et al.* used focus group discussions, in-depth interviews, and photovoice methods to capture perceptions and practices around mosquito control. Participants described gaps in protection when they were outdoors, particularly during livelihood and leisure activities. Examples of activities that kept people outside at night included fishing, street vending, watching television, drinking at bars, and attending funeral ceremonies (Makungu et al., 2017).

While some differences were noted across settings, activity categories were largely consistent across studies, including activity timing, duration, frequency, and location (Table 4.4). Within the peri-domestic space, household members engaged in chores, socializing, and relaxing on a nightly basis. Likewise, entertainment activities and small business activities occurred within the community, away from the peri-domestic setting, on a nightly basis, most commonly for adolescent and adult males. Livelihood activities occurred nightly or seasonally and impacted a smaller segment of the study populations. Large-scale social events such as weddings, funerals, and religious events were common across settings and often involved males and females of all ages.

Table 4.4 Night time activity categories

Activity Category	Population	Frequency	Timing	Location
Routine household activities	Common across settings; involves a large segment of the population; household chores most common among adolescent and adult females	Daily	Evening and early morning	Indoors and outdoors within the peri-domestic space
Routine livelihood activities e.g. security	Common across settings; most common among adult males	Daily	All-night	Outdoors within the community or beyond
Seasonal livelihood activities e.g. farming	Varies by setting	Seasonal	Early morning and evening or in some cases staying at farm plots for days or weeks	Away from home
Large-scale socio-cultural events	Common across settings and involves a large segment of the population	Variable	All-night	Outdoors within the community or beyond
Entertainment e.g. bars, watching television	Common across settings; most common among adolescent and adult males	Daily	Evening and late night	Outdoors within the community
Travel/visiting	Varies by setting	Variable	All-night	Outside of the community; likely indoors
Outdoor sleeping	Varies by setting	Seasonal	Part or all of the night	Near the home, in open air spaces

4.5 Discussion

This review identified two categories of importance related to night time human behavior. The first relates to when (time of night) and where (indoors versus outdoors) people are exposed to malaria vectors. The second is *what* people are doing at night that may increase their contact with malaria vectors. This understanding of human behavior is crucial for targeting context-appropriate vector control interventions across settings.

While it was not possible to compare study results directly due to differences in study design and methods, the results of the studies in this review suggest a majority of exposure to malaria vectors continues to occur indoors during sleeping hours for unprotected individuals. This is true even in contexts where unweighted biting rates are higher outdoors than indoors. However, when looking at ITN users, roughly half of exposure occurred outdoors in some settings, signaling a gap in protection. One of the most relevant indicators for understanding residual malaria transmission is the protective efficacy of ITNs, defined as the proportion of human exposure to malaria vectors prevented by ITN use out of total exposure i.e. compared to a non-user. Protective efficacy, the overall reduction in nightly biting rate for an ITN user compared to a non-user, was as low as 50% in some settings, with even lower estimates of protection for primarily exophagic malaria vectors. The fraction of exposure occurring indoors during non-sleeping hours and outdoors can pose a threat to malaria control and elimination efforts (Govella and Ferguson, 2012a).

While the review focused on studies published between 2000 and 2017, the importance of considering both vector and human behavior was put forward as early as 1964. First referred to as “man-biting rate” in a World Health Organization Bulletin, Garrett-Jones described measurement of contact between humans and mosquito vectors, including examples of its use in Mexico and Zanzibar (Garrett-Jones, 1964). The “man-biting rate” comprised indoor and outdoor components of mosquito contact. Garrett-Jones highlighted the importance of considering not only mosquito biting rates, but also where humans stay during biting times. He explained that humans as well as mosquitoes must be studied, including their distribution throughout the night (Garrett-Jones, 1964). Nearly half a century later a commentary by Linblade emphasized that an understanding of human behavior is as important as vector behavior for understanding when and where malaria transmission occurs and that the presence of humans must be considered when calculating risk of infective bites (Lindblade, 2013).

Despite the importance of human behavior to understanding malaria transmission dynamics, relatively few studies were identified that included it. Further, differences in methodological approaches were identified across studies, limiting the comparisons that could be made. Moreover, estimates of exposure away from the peri-domestic setting are lacking. Analytical approaches measuring human-vector interaction should account for outdoor sleeping as well as segments of the population that may spend most or all of the night away from home. When possible, human and vector data should be collected close in time and location, and across time points, to reflect changes in vector and or human behavior across seasons and over time.

A standardized approach and further validation of the estimates provided by different methodologies for collecting human behavioral data will be important next steps. Once validated, a small set of survey questions with uniform phraseology would allow for comparison of human exposure to malaria vectors across settings and over time on a large scale, as well as the evaluation of vector control tools. At a minimum, the human behavioral component should include estimates of the proportion of the population indoors/outdoors throughout the night. This information can be integrated with indoor and outdoor biting rates to calculate a weighted estimate of human exposure to malaria vectors indoors and outdoors. Information on the proportion of the population under an ITN and sleeping during times when malaria vectors are active can provide higher-resolution information on exposure by accounting for ITN use. These data can be used to quantify human exposure to malaria vectors occurring indoors and outdoors, exposure prevented by current ITN use practices, potential gains that could be made through optimizing ITN use during sleeping hours, and exposure that can only be prevented by supplemental tools.

Beyond understanding when and where exposure is occurring, it is crucial to characterize night time activities and sleeping patterns that can put people at risk. The results of the review suggest there are broad night time human activity categories that may be similar across settings in sub-Saharan Africa, including household chores, entertainment, livelihood events, and large-scale community events. Occurrence of outdoor sleeping varied across settings and could be an important factor to consider in settings where the practice is common.

In the context of high access to and use of ITNs, it will become increasingly important to understand gaps in protection. Local information is needed to identify the relative importance of activity categories and target groups based on the entomological, human behavioral, and epidemiological context. The activity categories identified in this review provide a useful framework for informing context-specific research on the relative importance of these activities that can drive locally appropriate interventions.

There are a number of limitations associated with this review. It is possible that studies that would have met inclusion criteria were not identified in the review process. This review did not cover factors that could influence transmission dynamics such as large-scale population movements and internally displaced populations. While important topics to consider, they were outside the scope of this review. However, by not focusing on population movement in the review it is possible that relevant articles could have been missed. Nonetheless, a comprehensive and structured process was utilized. Additionally, inclusion and exclusion criteria and search strategy were determined *a priori*, thus limiting potential bias in article selection. Lack of standardization in methods across studies precluded meta-analysis and underscored the potential gains to be made from a standardized approach to future collection of these types of data.

4.6 Conclusions

Where possible, studies should include human behavioral research to better understand night time activities and sleeping patterns as they relate to malaria risk. Moving forward, entomological studies should include parallel human behavioral research. A standardized approach will enable tracking of human-vector interaction and gaps in protection provided by ITNs, and other vector control interventions, over time and across settings. This information is essential for strategic targeting of existing tools, effective social and behavior change interventions, and development and deployment of appropriate complementary prevention tools.

4.7 Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Competing interests

The authors have declared that they have no competing interests.

Funding

This work was made possible by the generous support of the American people through the United States Agency for International Development (USAID) and the President's Malaria Initiative (PMI) under the terms of USAID/JHU Cooperative Agreement No. AID-OAA-A-14-00057 (VectorWorks Project). The contents are the responsibility of the authors and do not necessarily reflect the views of USAID or the United States Government.

Authors' contributions

AM conceptualized and carried out the review, synthesized study results, drafted the manuscript, and managed the revision process. HK, ML, and SM provided significant feedback on the manuscript. ER contributed to conceptualization, carried out the review, and made substantial inputs to the manuscript. All authors read and approved the final manuscript.

Acknowledgements

The authors would like to thank Dr. Seth Irish and Dr. Christen Fornadel for providing feedback on the manuscript as well as Dr. Gerry Killeen for providing input on Table 2 Studies quantifying human-vector interaction,

Chapter 5: Patterns of human exposure to malaria vectors in Zanzibar and implications for malaria elimination efforts

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Published in
Malaria Journal 2020 **19**:212

https://doi.org/10.1186/s12936-020-03266-w

5.1 Abstract

Background

Zanzibar provides a good case study for malaria elimination. The islands have experienced a dramatic reduction in malaria burden since the introduction of effective vector control interventions and case management. Malaria prevalence has now been maintained below 1% for the past decade and the islands can feasibly aim for elimination.

Methods

To better understand factors that may contribute to remaining low-level malaria transmission in Zanzibar, layered human behavioral and entomological research was conducted between December 2016 and December 2017 in 135 randomly selected households across six administrative wards selected based on high annual parasite incidence and receipt of indoor residual spraying (IRS). The study included: 1) household surveys, 2) structured household observations of nighttime activity and sleeping patterns, and 3) paired indoor and outdoor mosquito collections. Entomological and human behavioral data were integrated to provide weighted estimates of exposure to vector bites, accounting for proportions of people indoors or outdoors, and protected by insecticide-treated nets (ITNs) each hour of the night.

Results

Overall, 92% of female *Anopheles* mosquitoes were caught in the rainy season compared to 8% in the dry season and 72% were caught outdoors compared to 28% indoors. For individual ITN users, ITNs prevented an estimated two-thirds (66%) of exposure to vector bites and nearly three quarters (73%) of residual exposure was estimated to occur outdoors. Based on observed levels of ITN use in the study sites, the population-wide mean personal protection provided by ITNs was 42%.

Discussion/Conclusions

This study identified gaps in malaria prevention in Zanzibar with results directly applicable for improving ongoing program activities. While overall biting risk was low, the most notable finding was that current levels of ITN use are estimated to prevent less than half of exposure to malaria vector bites. Variation in ITN use across sites and seasons suggests that additional gains could be made through targeted social and behavior change interventions in sites with low levels of ITN use, with additional focus on increasing net use in the rainy season when biting risk is higher. However, even for ITN users, gaps in protection remain, with a majority of exposure to vector bites occurring outdoors before going to sleep. Supplemental interventions targeting outdoor exposure to malaria vectors, and groups that may be at increased risk of exposure to malaria vectors, should be explored. Interventions such as larval source management, which can reduce both indoor and outdoor-biting vector populations, could also be considered.

Key Words Malaria, residual transmission, outdoor transmission, human behavior, Zanzibar, Tanzania, human-vector contact, human-vector interaction, exposure

5.2 Background

Zanzibar provides a good case study for malaria elimination. Despite historically high transmission, the islands experienced a dramatic decline in malaria cases and deaths following the introduction of artemisinin-based combination therapy (ACT) and effective vector control interventions, namely insecticide-treated nets (ITNs) and indoor residual spraying (IRS) (Björkman et al., 2019). Since 2008, low level transmission has been maintained with malaria prevalence below 1% (Björkman et al., 2019). Field evidence suggests remaining cases are geographically focused and coincident with areas with high vector abundance (Hardy et al., 2015a).

Zanzibar has operationally scaled up core vector control interventions in recent years. Universal coverage campaigns were implemented in 2012 and 2016 with the goal of providing one ITN for every two people. Beginning in 2014, continuous distribution of ITNs through community and health facility-based channels has helped to maintain high levels of access (PMI, 2019). IRS was introduced in 2007 with the goal of universal coverage, and in 2012, shifted from blanket spraying to targeted deployment in hot spots once a year before the start of the rainy season (Björkman et al., 2019).

In addition to optimizing the impact of core vector control interventions, it is increasingly important to understand factors that can contribute to persistent low-level malaria transmission once high coverage of these interventions has been achieved (Durnez and Coosemans, 2013b, Killeen, 2014). Challenges such as increased outdoor biting proportions in response to indoor insecticidal interventions, shifts in peak biting times to early-evening hours before most people are under their ITNs, and human activities outdoors when malaria vectors are active may attenuate the protection provided by ITNs or other indoor interventions (Durnez and Coosemans, 2013b, Govella and Ferguson, 2012a, Matowo et al., 2017, Reddy et al., 2011, Russell et al., 2011).

To better understand patterns of vector behavior, entomological monitoring is now carried out in ten sentinel sites in Zanzibar providing valuable data on vector species abundance and distribution as well as insecticide resistance (PMI, 2018). While entomological monitoring is critical, a more complete understanding of the protection provided by current vector control interventions requires an understanding of how vector behavior corresponds to human activity and sleeping patterns. This information can provide a clearer picture of when (time of night) and where (indoors or outdoors) people may be exposed to vector bites. As part of a larger study investigating potential drivers of persistent malaria transmission in Zanzibar, this article presents results from layered human behavioral and entomological data collection.

5.3 Methods

Study Area

This study took place in six *Shehia* (wards) on Unguja Island, the main island of Zanzibar, an archipelago located off the coast of mainland Tanzania (Figure 5.1). Sites were selected in partnership with the Zanzibar Malaria Elimination Program (ZAMEP) on the basis of high malaria incidence, defined as annual parasite incidence (API) of 5/1000 or higher, and receipt of IRS in 2016.

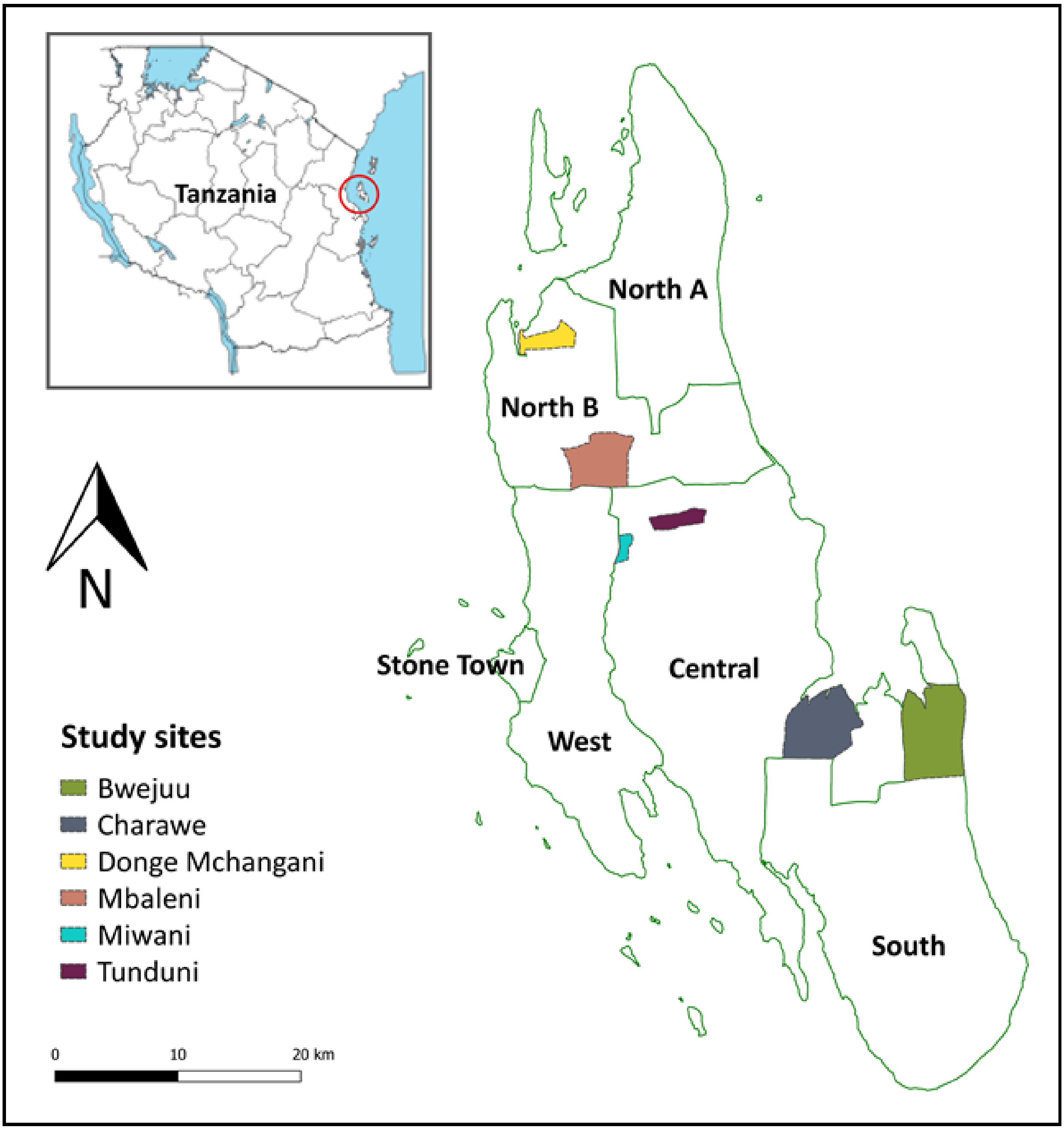

Figure 5.1. Map of study sites on Unguja Island, Zanzibar

Study Design

This study included household surveys, structured observations of nighttime human activity and sleeping patterns, and indoor and outdoor mosquito collections. In Zanzibar, there are generally two dry seasons occurring approximately from December through February and June through September. The rainy season, which is characterized by heavy downpours, generally occurs from March through May, with a peak in April. A less pronounced rainy season is also observed from October through November. Human behavioral data were collected in the dry season in December 2016 and rainy season from April through May 2017. Entomological data were collected across ten months between December 2016 and December 2017. Five months were classified as rainy season (March, April, May, October and November) and the remaining as dry season (January, February, August, September and December). The same households were used for human behavioral and entomological data collection and across data collection time points.

Sample Size

The sample size was generated to answer the primary research question of whether there was a difference in number of malaria vectors biting indoors compared to outdoors each night. The method developed by Cohen for power calculations in behavioral sciences was used (Cohen, 2013). Based on previous estimates from entomological monitoring, an average of 7 *Anopheles arabiensis* caught outdoors and 4 caught indoors was assumed, which translates to medium effect sizes. However, considering potential for heterogeneity in vector biting densities across households, sites, and seasons, effect sizes (measured as $R^2/1-R^2$) as low as 0.02-0.15 were assumed on a generalized linear model regressing mosquito counts as a function of position (indoors/outdoors as a fixed effect and day and location as random effects to account for heterogeneity in the data). The study was then designed to achieve 80% power at 95% confidence intervals, which returned a requirement for 200 nights of mosquito collection per site.

Based on previous research using direct observation of night time human behavior, it was determined that 20-25 households per site would be needed to capture variation in human behavior across households and sites (Monroe et al., 2015). Therefore, to achieve 200 nights of mosquito collection per site from the same households where human behavioral data was collected, eight nights of indoor and outdoor mosquito collection were carried out in each household. Collection nights were evenly distributed across seasons.

A random number generator was used to select 30 households for each of the six *shehia* (wards) using household listings provided by the *Sheha* (local leader) for each site. Of the 180 households selected, 143 were home, and therefore approached, during community entry. A total of 135 households consented to participate as follows: Bwejuu (n=20), Charawe (n=23), Donge Mchangani (n=24), Mbaleni (n=23), Miwani (n=25) and Tunduni (n = 20). Of the households approached, four households declined to participate, two household heads were not available to provide consent, and two indicated that they would be traveling throughout the data collection period.

Data Collection

Human Behavior

Study team members administered a survey to respective heads of household prior to beginning night-time observations. The survey included questions on household members, housing characteristics, and bed net ownership. For each person living in the household, information was collected on relationship to head of household, age, sex, and pregnancy status, if known. Net ownership and characteristics were recorded using a standard net roster (DHS, 2013a).

Study team members made structured observations half-hourly of each individual household members' activities and sleeping patterns from 6:00pm to 7:00am. This included a) whether each household member was indoors, outdoors, or away from home, b) whether each household member was awake or asleep and c) if sleeping, whether they were using an ITN.

Data from surveys and household observations were recorded electronically using tablets configured with programmed questionnaires and observation forms. These data collection tools were first translated into Swahili and then programmed using the open-source platform, Open Data Kit (ODK) (Hartung et al., 2010). Data collectors were trained on how to operate tablets, complete the forms, and upload the data. The data was uploaded daily to a secure server configured with Secure Socket Layer (SSL) with encryption. Appropriate logical constraints were implemented on every question to ensure data quality. In addition, for the household observations, time stamps were fixed to block entry of missed observations. Supervisors reviewed data for quality on a daily basis and provided feedback to the data collection team.

Vector Behavior

Indoor and outdoor mosquito collections were conducted hourly from 6:00pm to 7:00am in the selected households in each *shehia* using human-baited miniaturized double net traps (DN-mini) (Figure 5.2), an exposure-free method developed at Ifakara Health Institute (Limwagu et al., 2019). This trap was developed based on the design previously used by WHO (WHO, 1975) and modified by Tangena *et al* (Tangena et al., 2015). Observations of indoor and outdoor proportions and hourly biting patterns of Anopheles in Tanzania with DN-mini match those of the gold standard estimate of human exposure to mosquito bites the human landing catch (Limwagu et al., 2019). Mosquitoes were collected hourly using a mouth aspirator and put in a paper cup, with a separate cup labeled for each hour of collection. The collectors sampled mosquitoes for 45 minutes each hour and rested for 15 minutes. Collectors worked in two sets with each set doing collections indoors and outdoors for six to seven hours each night of collection.

Mosquitoes were sorted by taxa, sex, and physiological status (fed, unfed or gravid), and then stored individually or in batches for laboratory analysis. These samples were stored in microcentrifuge tubes containing cotton wool and silica gel, and were later analyzed by Polymerase Chain Reaction (PCR) to distinguish between members of *Anopheles gambiae* *sensu lato* (*s.l.*), and by enzyme-linked immunosorbent assays (ELISA) to determine proportions carrying *Plasmodium falciparum* sporozoites in their salivary glands (Beier et al., 1991). The field data and laboratory results were recorded electronically using tablets, linked, cleaned, and stored in a secure web-based database application, the Ifakara Entomology Bionformatics System (IEBS) (Kiware et al., 2016).

Figure 5.2. Photo of the miniaturized double net trap used to catch host-seeking mosquitoes. The miniaturized double net trap consists of an inner chamber, normally occupied by adult volunteer mosquito catchers. There is an outer netting cover, hanging 80cm from the ground, which traps host-seeking mosquitoes attempting to reach the volunteer inside. Host-seeking mosquitoes are trapped between the inner and outer netting compartments are collected by the volunteer through the multiple sleeves which open outwards from the inner compartment using a mouth aspirator.

Data Analysis

Human Behavior

Descriptive analysis of household survey data and observation data were completed using STATA 14 (Stata, 2015) and graphs were generated in Microsoft Excel (Excel, 2018). ITN access was calculated using the approach originally described by Kilian *et al* and recommended by the Roll Back Malaria Monitoring and Evaluation Reference Group (DHS, 2013a, Kilian et al., 2013). Potential ITN users were calculated by multiplying the number of ITNs in each household by two (assuming a maximum of two users per ITN). If the potential users exceeded the number of people in the household, the number of ITN users was set to the number of household members. ITN access was then calculated by dividing potential ITN users by the total number of study participants [18]. The use to access ratio (UAR) was calculated by dividing the proportion of the study population observed to be using an ITN by the proportion of study population with access to an ITN.

Vector behavior

Mosquito biting patterns were assessed based on hourly catches each night for dry and rainy seasons separately. Collection nights were evenly distributed across seasons. No mosquitoes were infected with *Plasmodium* and, therefore, no calculation was done for the sporozoite rate. The probability of a mosquito biting indoors or outdoors was estimated from a Generalized Linear Mixed Effects Regression (GLMER) with a Poisson distribution with a log link, using household ID and round of collection as random effects and location (in versus out) as a fixed effect. Analysis was done using R statistical package version 3.6.1(2019).

Human-vector interaction

Human exposure to malaria vectors was calculated based on data from household observations carried out in the peri-domestic setting and indoor and outdoor mosquito collections in the same households. Exposure patterns were calculated only for *An. gambiae s.l.* as densities of other *Anopheles* complexes were too low to explore patterns of exposure.

Analysis included calculation of the following indicators of human-vector interaction, described by Monroe *et al.(Monroe et al., 2020)*:

1. Percentage of vector bites occurring indoors for an unprotected individual ($\pi_{I,u}$) (Bayoh et al., 2014, Huho et al., 2013a, Killeen et al., 2006, Moiroux et al., 2014, Seyoum et al., 2012): This is an indicator of the maximum possible protection any indoor intervention could provide. Calculated as the sum of the measured indoor vector biting rates (B_I) for each one-hour time period (*t*) over a 24-hour period weighted by the estimated proportion of humans indoors (*I*) at that time, divided by total location weighted exposure (indoors and outdoors):

$$\pi_{I,u} = \frac{\sum_{t=1}^{24} B_{I,t}\, I_t}{\sum_{t=1}^{24} B_{I,t}\, I_t + B_{O,t} O_t}$$

2. Percentage of vector bites occurring while asleep indoors for an unprotected individual ($\pi_{S,u}$) (Bayoh et al., 2014, Huho et al., 2013a, Kamau et al., 2018, Killeen et al., 2006, Seyoum et al., 2012): Calculated as, the sum of the indoor vector biting rates (B_I) for each one-hour time period (*t*) over a 24-hour period weighted by the estimated proportion of humans sleeping (*S*) indoors at that time, divided by total location weighted exposure i.e. the sum of the indoor and outdoor biting rates respectively weighted by the proportions of humans indoors and outdoors at each time over the same 24-hour period :

$$\pi_{S,u} = \frac{\sum_{t=1}^{24} B_{I,t}\, S_t}{\sum_{t=1}^{24} B_{I,t}\, I_t + B_{O,t} O_t}$$

3. Percentage of all vector bites prevented by using an ITN (P_S^*)(Cooke et al., 2015, Geissbühler et al., 2007, Moiroux et al., 2014, Thomsen et al., 2016): Calculated as the product of the proportion of exposure occurring while asleep and the personal protection against bites (feeding inhibition) provided by an ITN while in use (*ρ*). ITNs were assumed to prevent 97% of vector bites when in use. This estimate for *ρ* was based on reference estimates from experimental hut trials of 7 brands of ITNs in Tanzania (Lorenz et al., 2019).

$$P_S^* = \rho\pi_{S,u} = \frac{\rho\sum_{t=1}^{24} B_{I,t}\, S_t}{\sum_{t=1}^{24} B_{I,t}\, I_t + B_{O,t} O_t}$$

4. Percentage of remaining exposure occurring indoors for a protected user of an ITN ($\pi_{I,p}$) (Killeen et al., 2006, Moiroux et al., 2014, Seyoum et al., 2012): Calculated by adjusting the estimate of $\pi_{I,u}$ to allow for the indoor personal protection provided by using an ITN:

$$\pi_{I,p} = \frac{(\sum_{t=1}^{24} B_{I,t}\, I_t) - \rho(\sum_{t=1}^{24} B_{I,t}\, S_t)}{(\sum_{t=1}^{24} B_{O,t} O_t + B_{I,t}\, I_t) - \rho(\sum_{t=1}^{24} B_{I,t}\, S_t)}$$

5. Population-wide mean personal protection against biting exposure provided by community-level coverage of humans (*C*) with ITNs ($P_{S,C}^*$): Calculated as the product of the coverage of the human population with ITNs, estimated as the proportion of humans using an ITN at each hour during the night and the overall personal protection provided by an ITN while it is in use, and accounting for the attenuating effects of exposure occurring when the user is active outside the net.

$$P_{S,C}^* = \frac{\rho \sum_{t=1}^{24} B_{I,t}\, C_t}{\sum_{t=1}^{24} B_{I,t}\, I_t + B_{O,t} O_t} = \rho\, \pi_{S,p} C$$

Ethical Approval

This study received ethical approval from the Johns Hopkins Bloomberg School of Public Health (IRB# 7390), Ifakara Health Institute (IHI/IRB/No: 035 - 2016), and the Zanzibar Medical Research and Ethics Committee (Protocol #: ZAMREC/0005/OCT/016). Only consenting mosquito collection volunteers participated. Volunteers received appropriate training and were provided with medical supervision, chemoprophylaxis, and access to diagnosis and treatment on a regular basis. Heads of household provided separate written consent for household observations and mosquito collection respectively. Community entry activities were conducted prior to beginning data collection. This included a one-day information session for *Sheha* (local leaders) and assistant *Sheha* in the selected sites and district-level representatives. During site visits study team members explained the purpose of the study to community members and obtained informed consent from selected heads of household.

5.4 Results

Results are grouped by human behavior, vector behavior, and human-vector interaction. Specific result areas include demographic characteristics of household members, nighttime location and sleeping patterns of household members, levels of ITN access and use, indoor and outdoor vector biting patterns and species composition, and finally patterns of human exposure to malaria vectors as a function of human and vector data.

Demographic characteristics

A total of 699 people was observed across 135 households. The same households were observed once each during the dry and rainy seasons. Participants were roughly evenly split by sex; additional detail on the participant demographic characteristics is provided in Table 5.1.

Table 5.1. Demographic characteristics of household members

	Male	Female	Total*
Household members	331 (47%)	368 (53%)	699
< 1 year	6	10	16 (2%)
1-4 years	36	53	89 (13%)

5-9 Years	49	49	98 (14%)
10-17 Years	67	65	132 (19%)
18-59 Years	156	168	324 (46%)
≥ 60 Years	17	23	40 (6%)

*Data presented in Table 1 were collected during the first round of data collection in December 2016. A total of 682 of the original 699 household members were observed in the second round of data collection in April-May 2017. Three households did not participate in the rainy season collection; two households were not available, and one household refused.

Nighttime human location and sleeping patterns

Time spent away from home

The percentage of the study population observed as away from home peaked in the early evening with 26%-30% away between 6:00pm and 7:00pm and slowly declined. The percentage away was observed to be lowest in the late-night hours, staying steady at approximately 15% from 11:00pm until 4:00am in both the dry and rainy season before rising again from 4:00am to 7:00am. Throughout the night, the percentage of males away from home was approximately double that of females, with a peak of 40% of males away in the early evening in dry season and staying constant at approximately 20% in the middle of the night (Figure 5.3).

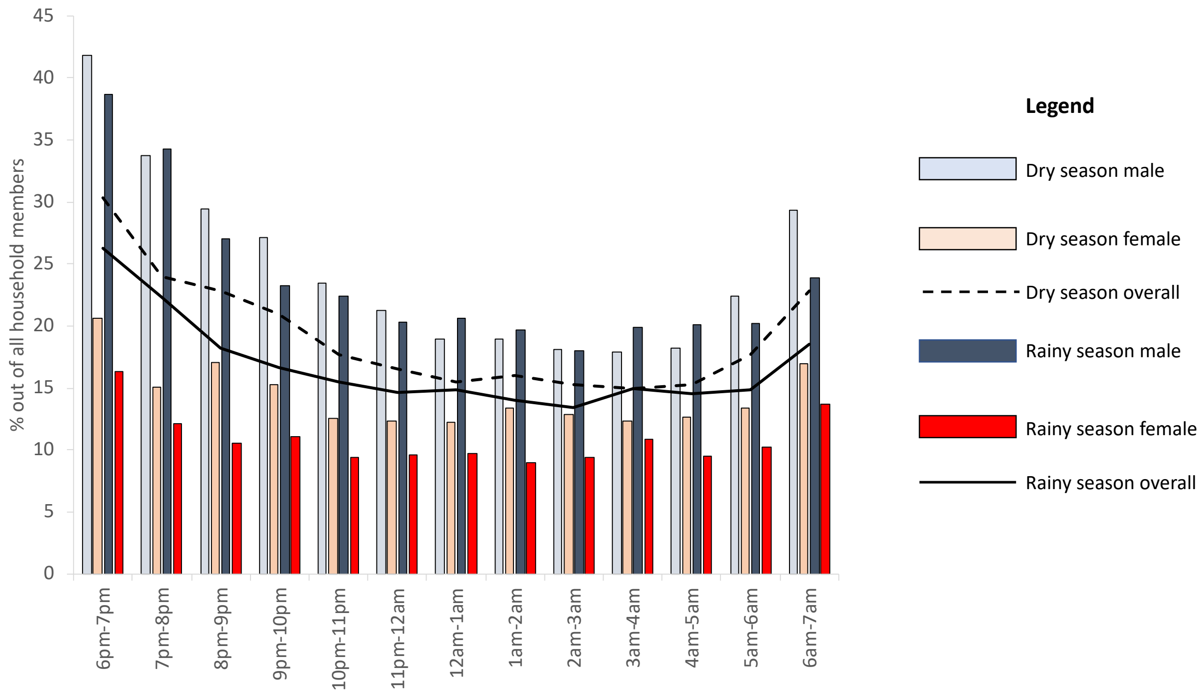

Figure 5.3. Percentage of males and females away from home throughout the night, across seasons.

Time spent in the peri-domestic space

Among study participants observed indoors and directly outside of the home, the percentage of the population outdoors peaked in the early evening hours, with 67% outdoors in the dry season and 51% outdoors in the rainy season between 6:00pm and 7:00pm. The percentage of the population outdoors slowly declined and stayed steady at less than 5% between 11:00pm and 4:00am, when nearly all household members at home were recorded to be indoors and asleep, before beginning to rise again in the early morning between 4:00am and 7:00am (Figure 5.4).

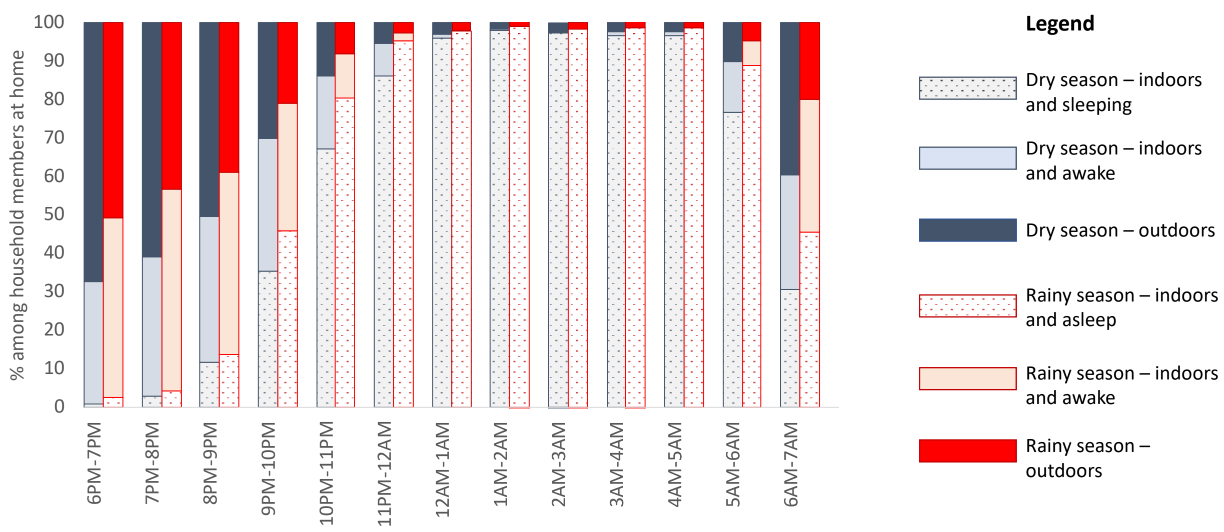

Figure 5.4. Percentage of people outdoors, indoors and awake, and indoors and sleeping throughout the night across seasons, among household members who were observed within the peri-domestic space.

ITN access and use

Assuming one ITN can be used by two people, approximately three quarters (76%) of the study population had access to an ITN in their household. ITN access varied by site, with the lowest level recorded in Miwani and the highest recorded in Bwejuu (Table 5.2).

Among household members at home, ITN use was highest during peak sleeping hours, between 11:00pm and 4:00am. Average ITN use during this time was 56% in the dry season and 62% in the rainy season. Variability was observed across study sites with the lowest levels of net use observed in Miwani and Tunduni across dry and rainy season with an average level of net use of 29% recorded in Miwani in the dry season and 28% in Tunduni in the rainy season during peak sleeping hours. The highest average net use was observed in Bwejuu (79%) and Charawe (76%) in the dry season and Mbaleni (80%) and Charawe (78%) in the rainy season (Figure 5.5). On average, a higher percentage of household members under five years used an ITN with over 70% net use during peak sleeping hours in both the dry and rainy seasons, compared to participants aged 5 years and older who had an average

ITN use of 54% in the dry season and 61% in the rainy season (Figure 5.6). The UAR during peak sleeping hours was 74% in the dry season and 82% in the rainy season, with lowest levels recorded in Miwani and Tunduni (Table 5.2).

Table 5.2. Mean ITN access, use, and use:access ratio (UAR) during peak sleeping hours (11:00pm-4:00am) across season and *shehia*.

Shehia	Dry Season			Rainy Season		
	ITN Access	ITN Use	UAR	ITN Access	ITN Use	UAR
Bwejuu	94%	79%	84%	93%	68%	73%
Charawe	73%	76%	104%	68%	78%	115%
Donge Mchangani	72%	54%	76%	79%	67%	85%
Mbaleni	74%	57%	77%	71%	80%	112%
Miwani	69%	29%	42%	63%	45%	71%
Tunduni	79%	44%	56%	79%	28%	36%
Total	**76%**	**56%**	**74%**	**75%**	**62%**	**82%**

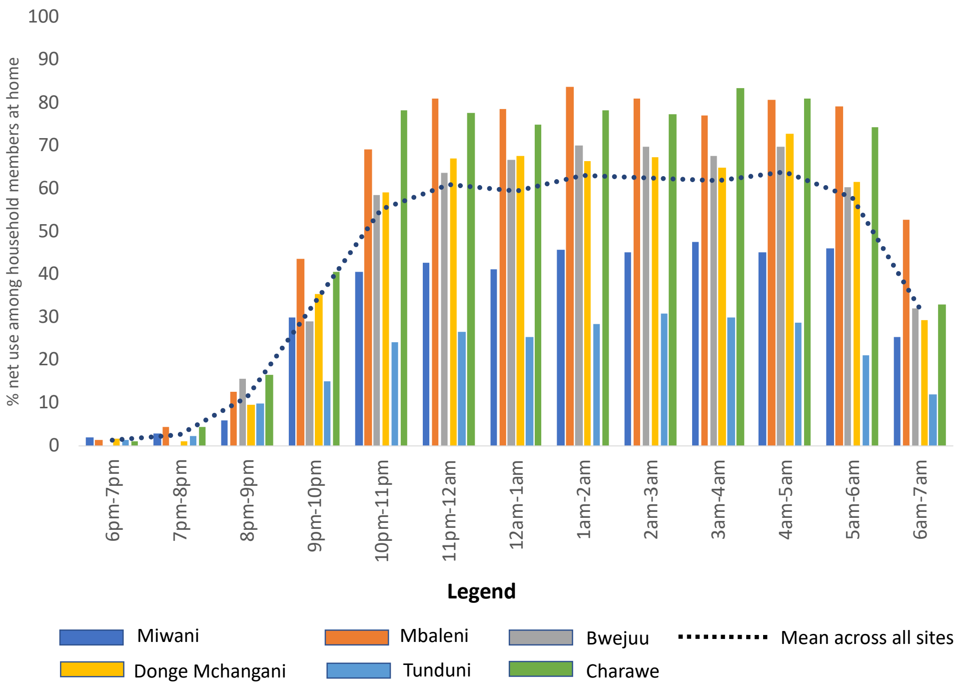

Figure 5.5. Average percentage of ITN use by hour across *shehia* observed in the rainy season, among participants in the peri-domestic space.

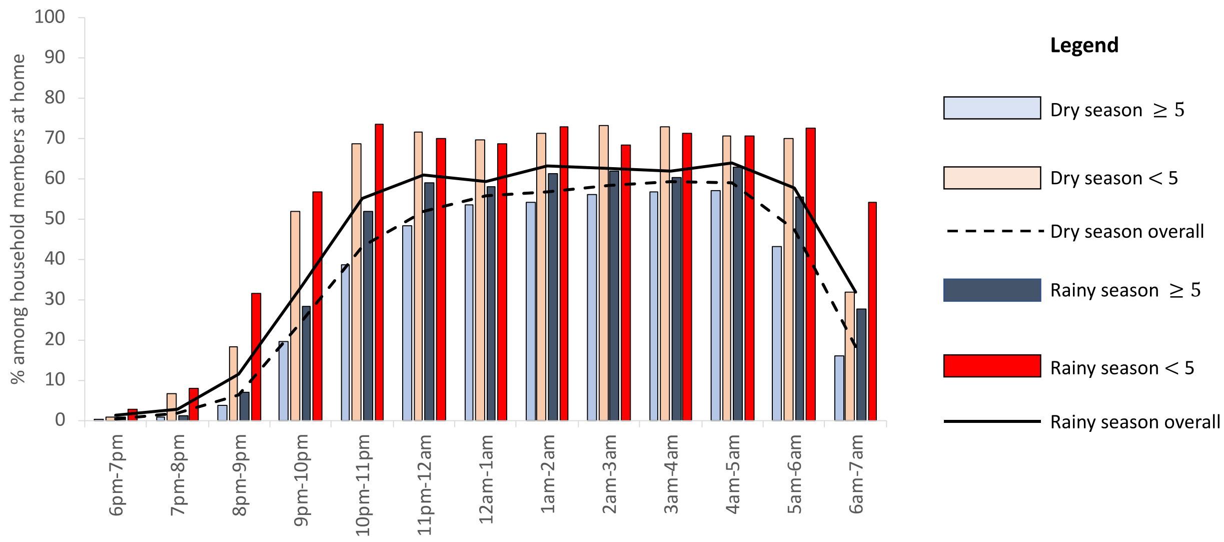

Figure 5.6. Average level of ITN use for participants aged under five years and five years and over, by hour, across seasons

Malaria vector species and biting patterns

A total of 343 female *Anopheles* were collected using the miniaturized double net trap; 92% of all *Anopheles* were collected in the rainy season. Of the *Anopheles* caught with the double net trap, the mean vector biting was the highest in Mbaleni, followed by Miwani and Donge Mchangani. No *Anopheles* were caught using this method in the other three sites. Of all *Anopheles*, 72% (n=248) were caught outdoors, while 28% (n=95) were caught indoors. Within the three sites where *Anopheles* were caught, the number of mosquitoes caught was 56% higher outdoors than indoors in Mbaleni, 85% higher in Donge Mchangani, and more than twice as high in Miwani (Table 5.3).

Anopheles gambiae s.l. was the most common vector species, accounting for 84% (n=289) of malaria vectors caught using this method. PCR analysis was carried out for 284 of the *An. gambiae s.l.* samples, of which over 98% were identified as *An. arabiensis* (n=280) and the remaining were *Anopheles merus* (n=2) and *An. gambiae sensu stricto* (*s.s.*) (n=2). Other *Anopheles* species caught included *Anopheles squamosus* (5 females indoors and 48 females outdoors) and *Anopheles coustani* (1 female outdoors and none indoors). No *Plasmodium* sporozoite positive mosquitoes were identified.

Table 5.3. Rate ratio and 95% confidence interval for mosquitoes caught indoors and outdoors, by *shehia*

Shehia	Location	No. of Female *Anopheles*	Rate Ratio [95% CI]	P-values
Mbaleni	Indoor	62	1	
	Outdoor	137	1.56 [1.13, 2.14]	P<0.01*
Donge Mchangani	Indoor	9	1	
	Outdoor	21	1.85 [0.83, 4.11]	P=0.129
Miwani	Indoor	24	1	
	Outdoor	90	2.33 [1.37, 3.98]	P<0.01*

*Significant difference at the 0.01 level

Patterns of human-vector interaction inside and directly outside of the home

Outdoor biting rates remained relatively consistent throughout the night, while indoor biting peaked in the middle of the night when the highest percentage of the human population was observed to be indoors (Figure 5.7).

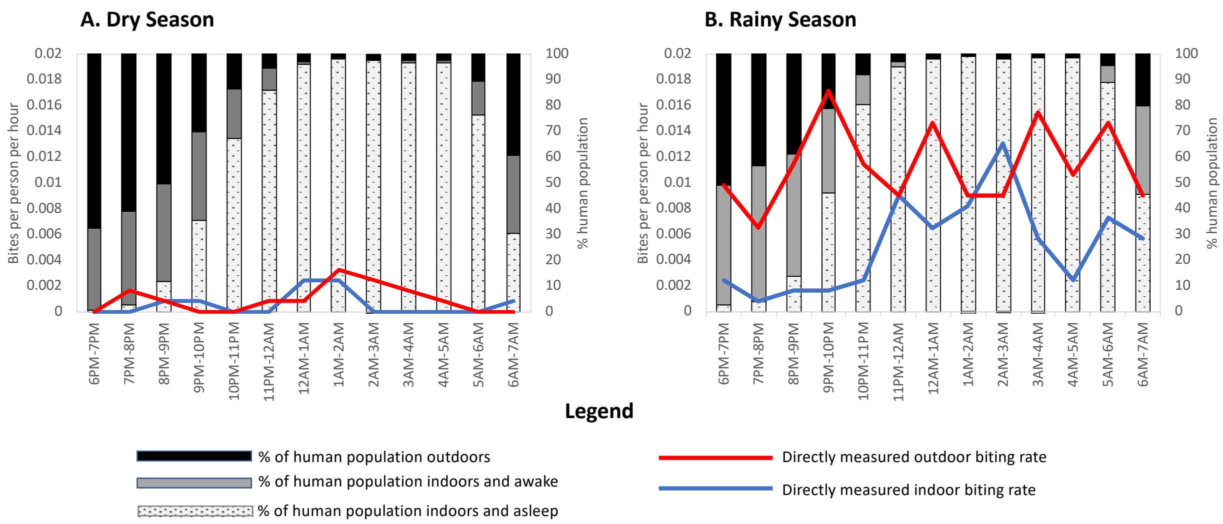

Figure 5.7 Proportion of human population indoors and awake, indoors and asleep, and outdoors throughout the night, overlaid with directly measured indoor and outdoor biting rates for *An. gambiae s.l.*, across seasons. Of *An. gambiae s.l.*, over 98% were *An. arabiensis*.

For an unprotected individual, defined as a person who did not use an ITN at any time during the night, an estimated 79% and 75% of exposure to vector bites occurred indoors ($\pi_{I,u}$) in the dry and rainy seasons respectively and 68% occurred while indoors and asleep **(**$\pi_{S,u}$**)** across seasons (Table 5.4), with indoor exposure peaking in the middle of the night (Figure 5.8).

Use of an ITN while asleep was estimated to directly prevent 66% of exposure to malaria vector bites out of all exposure that would otherwise occur ($P_S{}^*$) and for an ITN user, a majority of remaining exposure was estimated to occur outdoors ($\pi_{O,p}$) (Table 5.4) in the evening hours before sleeping (Figure 5.8). When accounting for the percentage of the study population using an ITN for every hour of the night (Figure 5.5), the population mean personal protection provided by observed levels of ITN use was 39% and 42% in the dry and rainy season respectively (Table 5.4 and Figure 5.8).

Table 5.4 Human exposure patterns to *An. gambiae s.l.* bites by season

Indicator	Dry Season	Rainy Season
Exposure for an unprotected individual		
Percentage of vector bites occurring indoors for an unprotected individual ($\pi_{I,u}$)	79%	75%
Percentage of vector bites occurring while asleep indoors for an unprotected individual ($\pi_{S,u}$)	68%	68%
Exposure prevented by ITN use		
Percentage of all vector bites prevented by using an ITN (P_S^*)	66%	66%
Remaining exposure for an ITN-user		
Percentage of remaining exposure occurring indoors for a protected user of an ITN ($\pi_{I,p}$)	39%	27%
Population mean exposure based on observed level of net use		
Population-wide mean personal protection against biting exposure provided by observed level of ITN use ($P_{S,C}^*$)	39%	42%

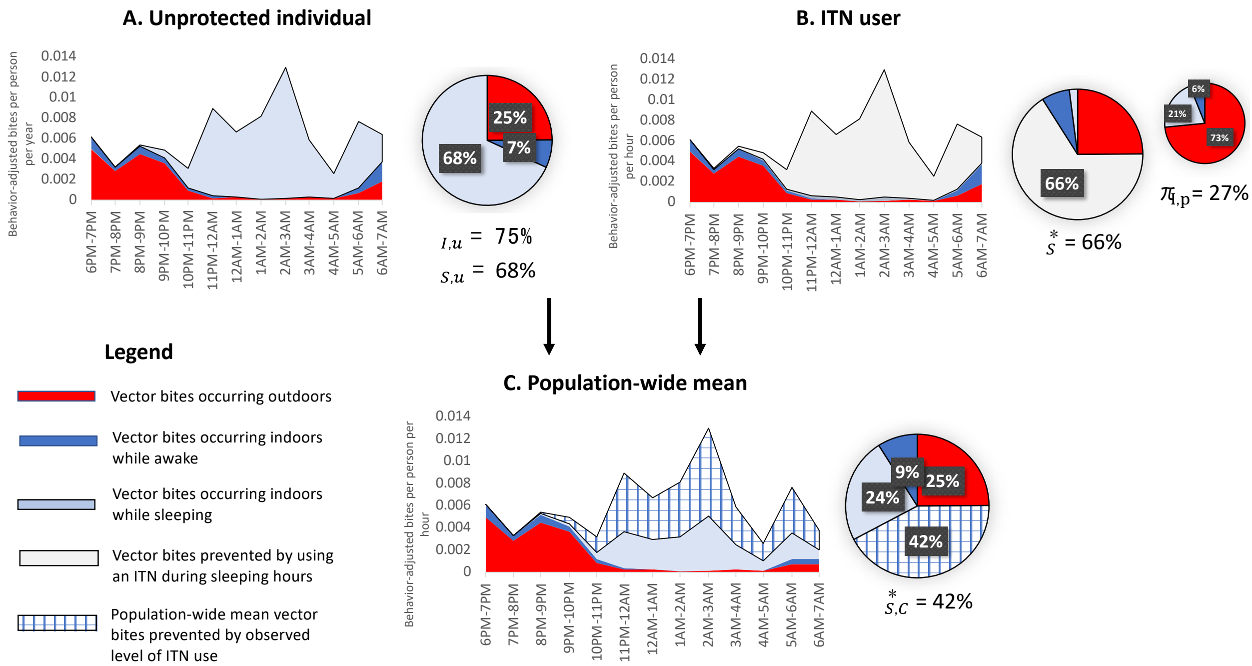

Figure 5.8 Average pattern of exposure to Anopheles gambiae s.l. bites throughout the night in the rainy season for A.) Unprotected individuals, B.) Individuals who use an ITN while asleep, and C.) The population-wide mean exposure to vector bites based on the observed level of ITN use in the study population throughout the night. Of *An. gambiae s.l.*, over 98% were *An. arabiensis*.

5.5 Discussion

A better understanding of intervention use, human activity and sleeping patterns, and how they overlap with local vector behavior, can provide an improved understanding of persistent malaria transmission and guide interventions to protect people when and where they need it. While increasing and sustaining ITN access and use is critical across settings, malaria control and elimination programs should also consider the limitations of current interventions.

Perhaps the most important finding from this work was that current levels of ITN use are estimated to directly prevent less than half of exposure to malaria vector bites. Remaining exposure to vector bites is likely driven by both sub-optimal levels of ITN use in some sites as well as exposure that cannot be prevented by ITN use. Average levels of ITN access and UAR were above 70% across seasons, which is relatively high compared to other settings in sub-Saharan Africa (Koenker et al., 2018, WHO, 2018b). However, variation in levels of use was observed across locations suggesting additional gains could be achieved in some communities. Distribution and promotion of ITNs should continue across sites, with targeted social and behavior change interventions focused on locations with lower access and UAR such as Miwani and Tunduni.

In addition to optimizing the impact of core vector control interventions, it is important to consider gaps that remain. For ITN users, approximately three quarters of remaining exposure occurred outdoors, largely in the hours before sleeping. Qualitative research findings from in-depth interviews and direct observation of nighttime community events in the same study sites provide in-depth information on nighttime activities that can help to inform context-appropriate interventions (Monroe et al., 2019a). Common nighttime activities in these sites included small-scale routine social activities such as gathering to socialize and play cards in the evening, watching television and football matches next to small shops, and entertainment such as going to bars on the weekend. Livelihood activities, lasting all or part of the night, were also commonly reported including security jobs, hunting, and working in hotels or fishing in coastal areas, as well as staying outdoors to guard crops from theft before harvest. Large-scale events such as weddings, funerals, and religious events were observed and reported to last all or most of the night (Monroe et al., 2019a).

Other studies have found challenges to malaria prevention away from home, including logistic and social barriers to ITN use (Monroe et al., 2015, Monroe et al., 2014). However, the feasibility of intervention use may differ depending on the nature of activity. For example, ITN use could be promoted while traveling or visiting friends and family, while supplemental prevention measures would likely be needed to protect people during activities such as socio-cultural events, nighttime occupations, and entertainment which often occur outdoors.

Although the World Health Organization (WHO) does not yet recommend the large-scale deployment of supplemental vector control tools, research is underway to evaluate the effectiveness of interventions such as topical and spatial repellents, insecticide-treated clothing, and improved housing, as well as attractive targeted sugar baits, outdoor traps, and systemic insecticides applied to livestock (WHO, 2019). Larval source management, which could reduce both indoor and outdoor-biting vector populations, is another option that could be considered. Operational research could be useful in Zanzibar and beyond to better understand where and how to deploy these supplemental tools for maximum impact.

An increasing number of countries are now within reach of malaria elimination with 46 countries reporting fewer than 10,000 indigenous cases in 2017 (WHO, 2018b). The epidemiology of malaria has changed in many of these contexts, with cases increasingly clustered geographically and among certain demographic groups (Cotter et al., 2013). Often, a high proportion of cases are observed among men and hard to reach groups, such as migrant populations, and current malaria interventions are unlikely to adequately address these changes (Cotter et al., 2013). In Zanzibar, a higher percentage of males was recorded to be away throughout the night compared to females, and qualitative research findings suggest males are more likely to engage in nighttime occupations, to travel, and to stay outdoors later socializing at night, all of which may impact exposure to malaria vectors. Likewise, travel to and from mainland Tanzania has been found to be a risk factor for malaria infection in Zanzibar(Björkman et al., 2019).

In these contexts, effective targeting of interventions is critical and finer scale information on the epidemiological, ecological, and socio-cultural context is needed, including identification of locations and groups at risk (WHO, 2017c). Additional investigation to better understand networks of higher-risk groups and scenarios, research to link specific activities to malaria infection, and programs targeting these groups with appropriate packages of interventions could be explored in low transmission settings such as Zanzibar.

This study builds on previous studies that have quantified human-vector interaction (Bayoh et al., 2014, Geissbühler et al., 2007, Killeen et al., 2006, Seyoum et al., 2012) to provide programmatically useful information on when and where people are exposed to malaria vectors as well as the activities that may put people at risk. Sites were selected on the basis of having high API in the context of high coverage of ITNs and IRS. However, variation was observed in both vector and human behavior across sites. This finding suggests the value of vector and human behavioral data at the community level to inform targeting of interventions to address specific gaps in protection, particularly in low transmission settings.

Despite the importance of human behavior to understanding patterns of risk, a review of published literature on nighttime human behavior found fewer than a dozen studies over the past two decades that integrated human and vector data (Monroe et al., 2019b). Collecting human and vector data together can provide an improved understanding of exposure patterns and inform when and where supplemental tools might be needed and could be considered in future entomological monitoring and research activities.

This work has a number of limitations. Recruitment of households took place on one day in each site. Households that were away during the time of recruitment or that would be traveling when data collection began were not included in the study. It is possible that the households that were present to consent on the day of recruitment were different from the households that were not or that households that consented may have been different from the few households than those that refused. However, the study team worked with community leaders to schedule recruitment activities during times when a majority of households were likely to be home.

Further, the recorded biting rates may have been impacted by the trapping method used. While, a study by Tangena et. al found no significant difference between numbers of *Anopheles* mosquitoes caught by double net trap and human landing catch (Tangena et al., 2015), the version used in this study had some design differences including its size. When tested by Ifakara Health Institute, the absolute numbers of mosquitoes collected were much lower for the miniaturized double net trap compared to HLC, however indoor and outdoor biting proportions, hourly biting patterns, and species diversities matched previous indoor and outdoor estimates obtained using HLC from the same villages (Limwagu et al., 2019). Despite the potential limitation on absolute numbers, the miniaturized double net trap provided the benefit of an exposure-free option for mosquito collectors, increasing the safety of their work while still allowing the relative biting risk indoors and outdoors to be estimated.

Another potential limitation is where mosquitoes were collected. Mosquito collections were carried out in the peri-domestic setting, leaving a gap in data for places people go when away from home, within their community and beyond. Likewise, it was not possible to measure time spent outdoors or under an ITN for people who were recorded to be away from home. Given that many nighttime activities away from home occur outdoors, the estimate of human exposure to malaria vectors occurring indoors and prevented by ITN use in the peri-domestic setting is likely an over-estimate for the study population as a whole. This finding underscores the importance of addressing outdoor exposure in this context, both in the peri-domestic setting and away from home, and the potential value of mosquito collections in places where people frequently gather at night.

When utilizing direct observation, there is also the potential for reactivity, a phenomenon in which people change their behavior due to the presence of an observer (Bernard, 2012). However, reactivity tends to decrease with the length of the observation and in previous studies was found to have little impact on behaviors of interest (Gittelsohn et al., 1997, Harvey et al., 2009).

Finally, this study did not look at parasite prevalence in the human population or link exposure to vector bites to malaria infection. There is an opportunity to do so in the future for a more complete picture of residual malaria transmission dynamics in Zanzibar and beyond. Despite the limitations, this study provided a high level of information on human behavior as it relates to exposure to malaria vectors..

5.6 Conclusions

In contexts such as Zanzibar, where malaria elimination is in sight, it becomes increasingly important to target interventions effectively. Understanding human behavior and where it intersects with vector behavior will be important for getting to zero locally acquired cases. In the study sites, overall access to ITNs was high and estimated exposure to malaria vectors was low. Opportunities were identified in specific locations and among certain groups to optimize access to and use of ITNs. Additional gaps in protection were identified when participants were outdoors and away from home. The proportion of exposure to malaria vectors occurring outside of sleeping hours suggests that testing of supplemental tools could be explored to enhance elimination efforts. These results should be taken together with data on travel and migration patterns as well as malaria infection dynamics to guide context-appropriate malaria interventions.

5.7 Declarations

Ethics approval and consent to participate

This study received ethical approval from the Johns Hopkins University (IRB# 7390), Ifakara Health Institute (IHI/IRB/No: 035 – 2016) and the Zanzibar Medical Research and Ethics Committee (Protocol #: ZAMREC/0005/OCT/016). All households provided written informed consent for household observations, photos, and mosquito collection.

Consent for publication

No individually identifiable data is presented in this manuscript.

Availability of data and materials

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

Competing interests

The authors have declared that they have no competing interests.

Funding

This work was made possible by the generous support of the American people through the United States Agency for International Development (USAID) and the President's Malaria Initiative (PMI) under the terms of USAID/JHU Cooperative Agreement No. AID-OAA-A-

14-00057 (VectorWorks Project). The contents are the responsibility of the authors and do not necessarily reflect the views of USAID or the United States Government.

Authors' Contributions

AM designed the human behavioral component of the study, developed study protocol and tools, led training and supervision of human behavior data collection team, carried out human behavior and human-vector interaction analysis, and drafted manuscript. DM was responsible for data management for entomology and human behavioral data, developed mobile data collection platform, provided training and supervision for mobile data collection, and contributed to the manuscript. SK and BT oversaw the entomology component of the study, development of entomology tools, training of mosquito collectors, analysis of entomology data, and contributed to interpretation of study results. SM contributed to the study design, provided input on data collection tools, and contributed to interpretation of study results. KH led community entry, contributed to supervision of data collection, and contributed to interpretation of study results. HK, SH, and MF contributed to the study design and provided input on data collection tools. HN contributed to analysis of entomology data. KM contributed to the manuscript and interpretation of study findings. GG and AA contributed to the study concept. FO conceptualized the larger study design, provided high-level support throughout the study, contributed to interpretation of study results, and made significant inputs to the manuscript. All authors reviewed and approved the final manuscript.

Acknowledgements

The authors would like to recognize the hard work and dedication of the data collection teams. The authors would also like to acknowledge Alex Limwagu, for design and set-up of the double-net traps, Amanda Berman for her contributions to mobile data collection, Emily Ricotta and Matthew Lynch for contributions to the study concept, and Revocatus Musiba and Ahmada Ibrahim for contributions to entomology field work. Finally, this work would not have been possible without the participation of household members who welcomed the study team into their homes, the support and partnership of community leaders in the data collection sites, and the technical leadership and commitment demonstrated by the Zanzibar National Malaria Control Program.

Chapter 6: Human behavior and residual malaria transmission in Zanzibar: findings from in-depth interviews and direct observation of community events

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Published in
Malaria Journal 2019 **18**:220

https://doi.org/10.1186/s12936-019-2855-2

6.1 Abstract

Background

Zanzibar has maintained malaria prevalence below 1%, yet elimination remains elusive despite high coverage of core vector control interventions. As part of a study investigating the magnitude and drivers of residual transmission in Zanzibar, qualitative methods were utilized to better understand night-time activities and sleeping patterns, individual and community-level risk perceptions, and malaria prevention practices.

Methods

A total of 62 in-depth interviews were conducted with community members and local leaders across six sites on Unguja Island, Zanzibar. Twenty semi-structured community observations of night time activities and special events were conducted to complement interview findings. Data were transcribed verbatim, coded, and analyzed using a thematic approach.

Results

Participants reported high levels of ITN use, but noted gaps in protection, particularly when outdoors or away from home. Routine household and community activities were common in evenings before bed and early mornings, while livelihood activities and special events lasted all or most of the night. Gender variation was reported, with men routinely spending more time away from home than women and children. Outdoor sleeping was reported during special events such as weddings, funerals, and religious ceremonies. Participants described having difficulty preventing mosquito bites while outdoors, traveling, or away from home, and perceived higher risk of malaria infection during these times. Travel and migration emerged as a crucial issue and participants viewed seasonal workers coming from mainland Tanzania as more likely to have a malaria infection and less likely to be connected to prevention and treatment services in Zanzibar. Some community leaders reported taking the initiative to link seasonal workers to the health care system and required malaria testing to work in their community.

Conclusions

Targeting malaria interventions effectively is critical and should be informed by a clear understanding of relevant human behavior. These findings highlight malaria prevention gaps in Zanzibar, and the importance of identifying new approaches to complement current interventions and accelerate the final phases of malaria elimination. Development and deployment of complementary interventions should consider human behavior, including gender norms that influence exposure to malaria vectors and prevention practices. Expansion of community-level programs targeting travelers and seasonal workers should also be explored.

Keywords Malaria, elimination, residual transmission, outdoor biting, imported case, migration, travel, human behavior, qualitative research, sub-Saharan Africa

6.2 Background

Wide-scale implementation of malaria interventions has led to significant reductions in malaria morbidity and mortality worldwide. The World Health Organization (WHO) estimates that between 2000 and 2015, the rate of new malaria cases declined by an estimated 37% globally, and global malaria deaths fell by 60%, with 6.2 million lives saved(2017b). An estimated three quarters of these gains can be attributed to core vector control interventions, specifically insecticide-treated nets (ITNs) and indoor residual spraying (IRS) (Bhatt et al., 2015a). However, the 2018 World Malaria Report suggests these gains are beginning to level off, with no significant changes in the number of malaria cases or deaths between 2015 and 2017 (WHO, 2018b).

While achieving and sustaining high levels of coverage of core vector control interventions is essential, in many contexts, malaria can persist even once these targets have been achieved. A key challenge is the indoor orientation of ITNs and IRS. Increases in outdoor vector feeding and resting in settings where people spend significant time outside at night may allow vectors to avoid interventions and consequently limit their effectiveness (Durnez and Coosemans, 2013b, Killeen, 2014). An improved understanding of transmission that can persist in the context of high coverage of ITNs or IRS, referred to as residual malaria transmission, will be essential to elimination efforts (Durnez and Coosemans, 2013b, Killeen, 2014, WHO, 2014).

In Zanzibar, the combination of effective vector control interventions with high quality diagnostics and case management has led to a dramatic decline in malaria cases and deaths (Bhattarai et al., 2007, Aregawi et al., 2011). Malaria cases are actively monitored and followed up for investigation and classification through the malaria early detection system and malaria case notification system (PMI, 2018). ITNs were distributed across Zanzibar through universal coverage campaigns (UCC) in 2012 and 2016 with the goal of achieving one ITN for every two people. To sustain high coverage, ITNs have also been distributed continuously through health facility and community-based channels beginning in 2014 (Zanzibar Malaria Elimination Program, 2015). Demographic and Health Survey and Malaria Indicator Survey results show a high use to access ratio in Zanzibar, suggesting that people are largely using the ITNs they have (Koenker et al., 2018). In addition, focal spraying of IRS has been implemented based on village-level incidence data, with over 90% household coverage in spray sites each round (PMI, 2018).

Malaria parasite prevalence has been maintained below 1% for the past decade, and the islands can feasibly aim for elimination (PMI, 2018). In recent years, transmission, while low, has been geographically concentrated in locations with high vector abundance, and areas where residents frequently travel to malaria endemic regions outside of Zanzibar (Hardy et al., 2015b). Results from entomological monitoring from 10 sentinel sites have shown a shift in the malaria vector population from *Anopheles gambiae sensu stricto* (*s.s.*) to *Anopheles arabiensis*, reflecting a shift toward outdoor biting patterns (PMI, 2018). In some locations, *Anopheles funestus* and *Anopheles merus* have also increased. Malaria vector density peaks during the long rains, occurring approximately from April through June (PMI, 2018).

Previous investigations of ongoing transmission have focused on monitoring the behaviors and infectiousness of the malaria vectors and also on case detection and reporting. However, despite growing evidence that malaria cases in Zanzibar are increasingly clustered in certain demographic groups or villages, less attention has been paid to nighttime activity patterns that may contribute to exposure. As part of a larger research study designed to better understand the magnitude and drivers of residual malaria transmission in Zanzibar, this study utilized qualitative research methods to explore nighttime activities and sleeping patterns, individual and community-level risk perceptions, and malaria prevention practices.

6.3 Methods

Study Area

This qualitative study was carried out in December 2016, during the dry season, and April-May 2017, during the long rains, across six shehia (wards) in Zanzibar. Sites were selected from across Zanzibar on the basis of high annual parasite incidence (API>5/1000) and receipt of IRS in 2016. Selected sites were located on Unguja Island, the main island of Zanzibar, and included Bwejuu in the Southern District, Tunduni, Miwani, and Charawe in Central District, and Mbaleni and Donge Mchangani in North B District (Figure 1). The study sites were all within 60 km from Stone Town, Zanzibar's historical capital.

The selected *shehia* varied based on ecological features. Interior *shehia* such as Miwani and Tunduni, were characterized by lush vegetation, trees, and shrubs while Bwejuu and Charawe represented coastal communities (Figure 6.2). Housing construction was both traditional and modern, and included materials such as brick and limestone, metal roofs, sticks and mud. Community members in the selected *shehia* participated in a variety of daily income-generating activities which ranged from fishing in the coastal areas, to farming, animal keeping, and small business activities. Community members were predominantly Muslim, however several communities, such as Miwani and Mbaleni, included a growing number of Christian residents from mainland Tanzania. Local leadership included the *Sheha* and *Assistant Sheha* who were elected to represent community members in each *shehia*.

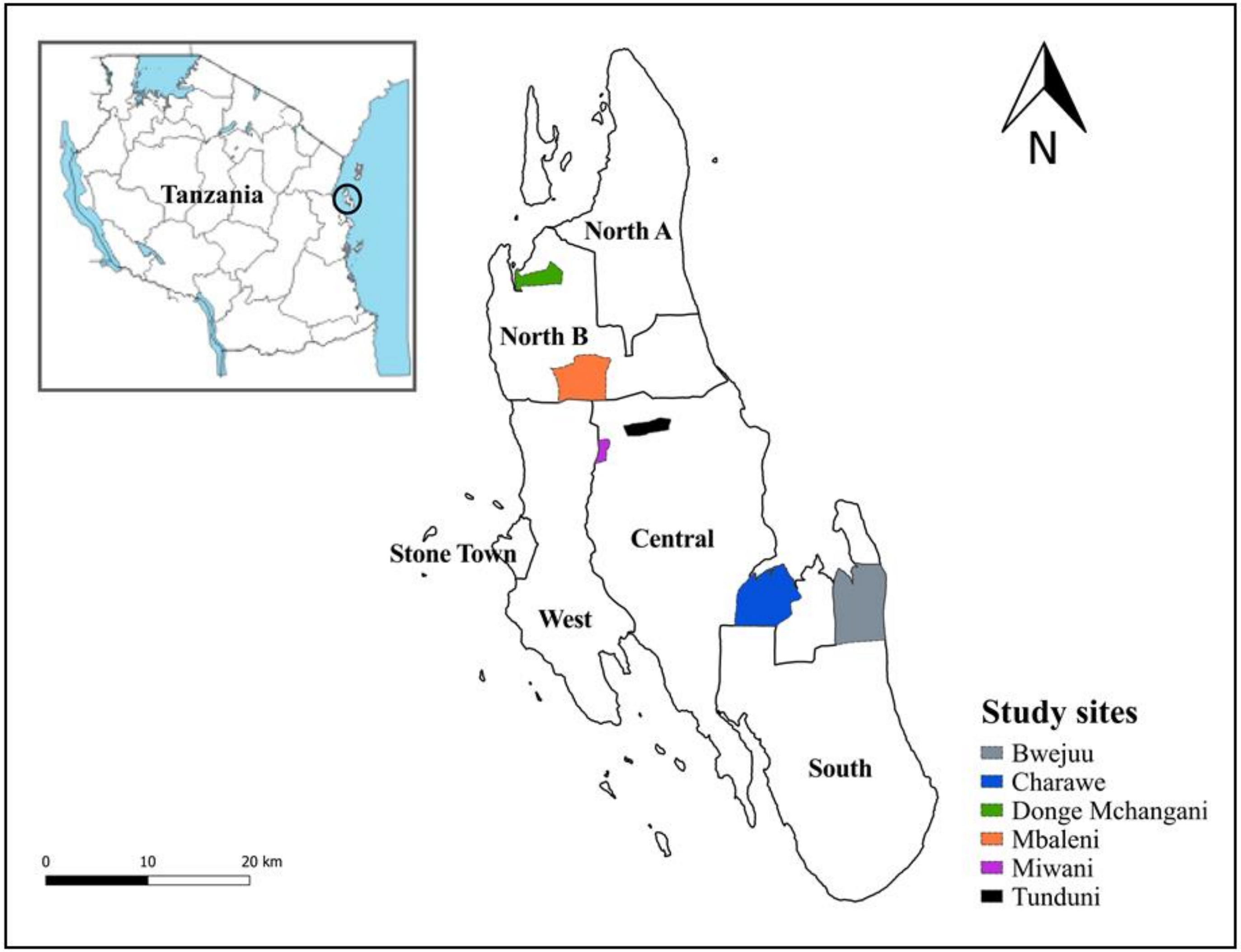

Figure 6.1 Map of study sites

Figure 6.2 Photos of study sites. Clockwise starting from top left, the photos show Bwejuu, Charawe, Tunduni, Miwani, Mbaleni, and Donge Mchangani. Photos taken during field work in December 2016 during the dry season.

Study Design

In-depth interviews (IDIs) were the primary method utilized, with supplemental night time community observations. Participants were eligible to participate if they were 18 years or older. For household IDIs, participants were drawn from among 135 randomly selected households included in the larger study. Households were selected using a random number generator from a list of households provided by the *Sheha* for each site. IDI participants were purposively selected from those households with the help of local leaders, to include representation from males and females of different ages from each site. IDIs were also carried out with community leaders, including the Sheha and his/her Assistant Sheha in each site, to better understand topics of interest at the community level and to identify night time activities and events occurring in outdoor public spaces.

Nighttime community observations were carried out to triangulate findings from in-depth interviews and to provide additional context for understanding community activities and events. Activities that took place away from home but within the study community, were identified with help from the key informants, who provided information on frequency, average attendance, and location.

Data Collection

Data Collection Team

The study employed data collectors from Zanzibar to ensure cultural understanding and sensitivity. Team members were selected on the basis of previous qualitative research experience, fluency in Swahili and English, and performance during training and pilot testing. The qualitative data collection team included three men and three women.

Community Entry

Zanzibar Malaria Elimination Program (ZAMEP) counterparts led a meeting to brief community and district-level leaders from the study sites, held at a central location, followed by visits to each study site. The community entry team worked with local leaders from each community to meet individually with heads of household for each of the selected households and explain the study objectives. At the beginning of the study, participants were briefed on the study objectives, and were notified by the *Sheha* or *Assistant Sheha* if they were selected to participate in an IDI.

In-depth interviews

IDIs were conducted using a semi-structured interview guide developed in English and translated into Swahili prior to data collection. Key topics of interest included nighttime activities and sleeping patterns, individual and community-level malaria risk perceptions, and malaria prevention practices. IDIs with community members were carried out in a quiet, private space, inside or close to the respondent's home. IDIs with community leaders were carried out at the participant's office or home. Interviews lasted 30-90 minutes. Data collectors audio-recorded all interviews and took field notes to capture detail on the setting and non-verbal cues. Supervisors met with the qualitative data collection team on a weekly basis to review emergent themes, provide feedback on data quality, and discuss how to incorporate previous findings into subsequent interviews through an iterative process (Crabtree and Miller, 1999). Follow-up interviews were carried out with a sub-set of community leaders to probe further on emergent themes of interest identified in the review process. Interviews were carried out until thematic saturation was achieved, defined as the point at which additional interviews no longer provided new information on the key topics of interest (Guest et al., 2006).

There were 62 in-depth interviews in total, evenly split across the six sites (Table 6.1). This included 44 household members, 13 community leaders, and follow-up interviews with five community leaders to explore emergent themes in greater detail.

Table 6.1 Interview participant demographics

	Number of interviews	Average age, in years
Community members	44	44.8 (Range: 24, 82)
Men	25	49.1 (Range: 30, 82)
Women	19	39.0 (Range: 24, 62)
Community leaders	13	51.9 (Range: 35, 71)
Men	10	54.3 (Range: 35, 71)
Women	3	43.7 (Range: 39, 48)
Total respondents	57	46.3 (Range: 24, 82)
Men	35	50.6 (Range: 30, 82)
Women	22	39.2 (Range: 24, 63)
Follow-up interviews	5	n/a
Men	4	n/a
Women	1	n/a
Total interviews	62	n/a
Men	39	n/a
Women	23	n/a

Night time community observations

Each nighttime community observation began with the *Sheha* or *Assistant Sheha* walking through the community with study team members to indicate the locations where routine community activities take place. The observers then walked to each location, ensuring at least one observation per location per hour. Data collectors carried out observations in pairs to ensure safety. They recorded the date, season, and location of each observation on a semi-structured form, then added a detailed description of the setting and activities every hour. Each hourly entry included a description of the activities ongoing at the location, approximate number people participating by age and gender, and use of malaria prevention measures, if any. The observation form also included space for the observer to document their own perceptions of what they saw in order to effectively capture both direct observation data and interpretations without mixing the two. For large-scale special events, the study team stayed at the location of the event from the time it began until the time it ended.

A total of 20 nights of community level observation were carried out, of which 17 were of routine activities, defined as activities that occur on a nightly basis. Routine observations were carried out across all sites at least once in both the dry and rainy season. Nighttime observations of routine community activities took place from approximately 6:00pm until the final nighttime activity ended. The end time ranged from 11:05pm to 3:45am for routine nighttime activities in the dry season, and 10:15pm to 3:18am in the rainy season. Routine events observed included buying and selling at local shops, watching television in public spaces, and sitting at *Maskan*. *Maskan* originally referred to places where people of the same political party would go to meet, however the term is now used locally to describe any place where people, generally men, meet to socialize. Three special socio-cultural events were attended when the study team was notified by community leaders of an upcoming event. Large-scale special events were observed from the time they began until the time they ended, or until 7:00am, whichever came first. The three large-scale events observed included a wedding ceremony, a religious ceremony referred to as *Dhikri*, which involved chanting throughout the night, and a rite of passage ceremony for adolescent girls.

Data Analysis

In-depth interviews and key informant interviews were transcribed verbatim in Swahili by the data collection team, including non-verbal cues, then translated to English on an ongoing basis throughout data collection. Each data collector transcribed and translated his or her own interviews. Team supervisors reviewed Swahili transcripts and English translations for quality on an ongoing basis. Following each community observation, observers typed up field notes in English using a template mirroring the data collection form. All electronic files of field notes were collected and reviewed by team supervisors.

Data was analyzed through an iterative process, beginning during data collection through weekly reviews of data and emerging themes, as described above. Following data collection, members of the study team developed a preliminary codebook deductively based upon interview guides and research aims, and inductively through review of transcripts. The codebook included the code, a brief definition, an expanded definition, criteria for using the code, and examples of text from the transcripts to illustrate use of the code (MacQueen et al., 1998). The study team tested the codebook on a random sub-sample of transcripts and met to discuss and review the coding exercise. The codebook was then finalized to reflect feedback from the discussion and to ensure a clear understanding of code definitions across all coders. All in-depth interview transcripts were then uploaded into ATLAS.ti 8, a qualitative data analysis software program for ease of storage, indexing, and retrieval (Atlas.ti, 2017). Members of the study team coded all transcripts in ATLAS.ti using the final codebook. Thematic analysis was used to analyze the qualitative data (Boyatzis, 1998).

Ethical Approval

This study received ethical approval from the Johns Hopkins University (IRB# 7390), Ifakara Health Institute (IHI/IRB/No: 035 – 2016) and the Zanzibar Medical Research and Ethics Committee (Protocol #: ZAMREC/0005/OCT/016). All IDI participants provided written informed consent. The *Sheha* provided oral consent for community observations in public spaces. Heads of household provided written consent for photos. Results were presented back to ZAMEP and the Zanzibar Malaria Elimination Advisory Committee.

6.4 Results

The results present information obtained through IDIs, with supplemental detail and context added from direct observation of community-level activities. Results are organized by theme and include nighttime activities and sleeping patterns, risk perceptions, malaria prevention practices, and travel and migration.

Nighttime Activities and Sleeping Patterns

An illustration of nighttime activities occurring in the evening, early morning, and throughout the night is included in Figure 6.3.

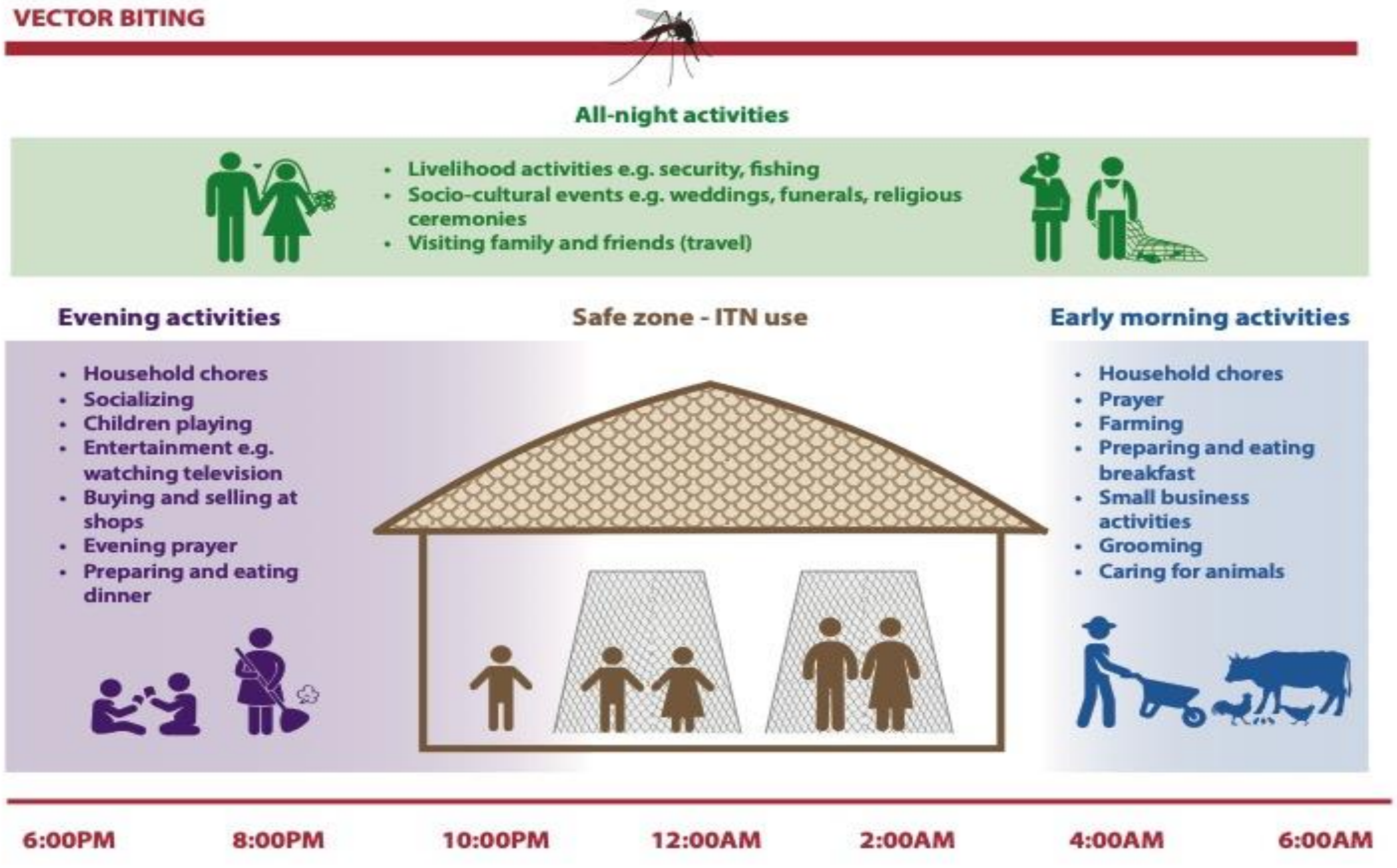

Figure 6.3 Illustration of common night time activities that occur during times when local malaria vectors are active. This includes routine activities in the evening and early morning as well as livelihood activities and special events that can last throughout the night.

Routine Activities

In the peri-domestic space, in and near the home, many women reported doing household activities such as cooking, caring for children, and fetching water at wells in the early evening and at night. Participants also reported doing household chores in the early mornings; women prepared food and cleaned the house while men cared for animals.

Away from home, small-scale social activities, ranging from two to twenty people, were widely reported and observed during the early evening and nighttime. Men gathered at *Maskan,* where they socialized and played cards or other games after finishing their day's work. *Maskan* generally took place in the same locations each night, either outdoors or in semi-open spaces. Women and children were more likely to socialize outdoors nearby their houses with friends or neighbors (Figure 6.4.A).

Watching television or movies was another common social activity that occurred next to small shops or in other semi-covered areas such as market stalls or shacks. In some locations, only men watched television, while at other locations women and children were also observed watching, often in the early evening hours, from 7:00pm to 9:00pm, compared to men who would frequently stay up to midnight. When football matches were being broadcast, young men stayed up to watch until the matches ended, sometimes until 2:00am or later (Figure 6.4.B). On weekends, youth were reported to go to *Viwanja* (entertainment sites, such as bars, that have drinking and dancing). These entertainment activities were most commonly reported in Miwani and Bwejuu and typically ended after midnight. Routine social activities were reported and observed to end earlier in the rainy season compared to the dry season. Football matches were an exception, as a female household member from Donge Mchangani explained, *"people who love football come regardless."*

Buying and selling at local shops was commonly reported and observed. This included permanent shops selling packaged household goods, as well as small stalls selling *chipsi* (French fries), fish, bread, fruit and other foods. Both men and women engaged in small business activities. These shops generally opened in the early evening between 6:00pm and 7:00pm and closed by midnight (Figure 6.4.C). In the rainy season these activities were moved to semi-covered locations or closer to home, and shops generally closed earlier than in the dry season.

During the dry season, some participants reported sleeping outdoors, largely because of the heat. Indeed, participants were observed dozing outdoors in the early nighttime at social gatherings, while watching television, or on verandahs and areas nearby house compounds (Figure 6.5). Young men were observed sleeping outdoors more frequently during the evenings and nighttime, than women or children.

A B C D E

Figure 6.4 Photos of common nighttime activities. **A) A woman and her children sit outdoors on the verandah of their home; B) Community members gather outdoors to watch television; C) A woman prepares *mandazi* (fried dough) indoors before bed to sell the next day; D) A man and woman collect and package charcoal in the early evening; E) Women chant while others sleep on the floor during *Dhikri*, an all-night religious event.**

Figure 6.5 A child sleeps in an open-air space during early evening hours

Across study areas, religious activities were routinely observed. Muslims prayed three times during the night; first, at sunset, then at approximately 8:00pm, and finally, at sunrise. Men generally prayed at the community mosque, while women were more likely to pray at home. Some older children, ages 10 to 14, attended *Madrasa* (Islamic religious school) during the evening hours, from 7:00pm to 9:00pm. Religious activities continued throughout the year.

Livelihood activities, lasting all or part of the night, were commonly reported. In coastal communities, men made a living by fishing, while women and some children harvested seaweed. Along the coast, men often went fishing at night, sleeping in their boats at sea or in temporary shelters along the shore. Fishing activities took place year-round and the time of night depended on the tides and on the cycle of the moon. In some study areas, charcoal making was a common income-generating. It occurred away from the house, at designated locations within the community, and generally took several days to complete. This activity did not require someone to be outside continuously, but rather to intermittently check on the fires (Figure 4D). Additional livelihood activities included security jobs, hunting, and working in hotels in coastal areas. In some locations, men reported staying outdoors to guard their crops from theft before harvest. A male household member from Mbaleni explained, *"They sleep at the area where they keep their stuff. For example, if you plant maize somewhere, you should stay [in] the same place to guard it so it can't be stolen… and taken away by [thieves]."*

Many livelihood activities continued regardless of season. When asked about seasonal differences in livelihood activities, a male community member from Charawe explained, *"The work that people do, they do all the time. Everyone has to eat and make a living whether it's the rainy or dry season."* Farming activities intensified in the rainy season and some participants reported waking up earlier during this time in order to spend more of the morning hours farming. **Special events**

While routine activities were reported and observed to generally finish by midnight, special events continued later, sometimes until dawn. Large-scale social events, including weddings, funerals, and religious ceremonies occurred year-round but were reported to occur more frequently in the dry season. These events were attended by all demographics, including men, women, and children. Events took place in large open outdoor spaces nearby or within household compounds. They brought together people throughout the community, and some attracted visitors from outside the ward.

At one wedding observed by study team members in the rainy season, a group of approximately 50 men and women danced in an open space, while a smaller group of approximately ten drank local brew nearby. The wedding began around 8:00pm and lasted up until 3:00am. During heavy rains, events sometimes moved indoors. For instance, *Dhikri*, a religious event characterized by prayer and chanting, was scheduled to occur outside but was moved indoors because of rain (Figure 4E). A few men remained outside cooking large pots of food under a small roof with no walls. The event lasted from approximately 10:00pm until dawn and attracted men, women, and children from across multiple *shehia*.

Outdoor sleeping was also observed and reported during special events. Large numbers of people gathered and slept in or near the host's home, such as on a verandah, or indoors in community structures such as a mosque with open doors and windows. Women and children would normally sleep indoors inside the host's house while men were more likely to sleep outdoors.

While large-scale events typically lasted from one to several days, participants reported extended changes to sleeping and activity patterns throughout Ramadan, the Islamic holy month characterized by fasting from dawn until dusk. Participants reported staying up at night to pray and spending some or all of the night sleeping outdoors.

Risk perceptions

When asked about the community's most common health problems some participants mentioned malaria as a major concern, others reported it as minor, while others required prompting to mention it at all. Participants also described seasonal fevers but did not associate them with malaria. Participants frequently reported that malaria cases had largely decreased over the years. As a male key informant from Donge Mchangani explained, *"Malaria has decreased because in the past about 10 to 15 people would be diagnosed with malaria, but now only one to two people per month or sometimes no one, so malaria has decreased [to a large extent]."*

Men, women, and children were viewed as being at risk of malaria infection, but for different reasons. Men were perceived as being at risk due to their nighttime social and livelihood activities and travel, women were perceived as being at risk due to time spent outdoors doing household chores and socializing near the home, and children because of their inability to protect themselves. Amongst them, children were seen as being the most vulnerable and having the highest risk of severe malaria infection. A female household member from Charawe provided her view on what puts children at risk*, "They [children] stay and play near big puddles and bushes, and when you put them to bed under a net and leave, they can move to the sides of a bed and touch the net, so mosquitoes bite them."*

When at home during the nighttime, study participants perceived that they were at higher risk of malaria infection outdoors than indoors. They described that it was easier to protect themselves from mosquito bites indoors because prevention methods such as ITNs, IRS, and aerosol insecticide sprays were available. However, a few participants noted that people could also be at risk indoors if they were not under ITNs.

A female household member from Donge Mchangani explained outdoor risk this way, *"when we watch TV (outside), we can spread a mat for children to sleep. Then you concentrate on the TV while the child is getting malaria through mosquito bites."* In a similar way, participants perceived that they were at higher risk of infection when they were away from home (outside the *shehia*). This was largely attributed to lack of access to malaria prevention tools when visiting relatives, going to work, or attending special events away from home.

Alcohol consumption emerged as an important theme related to malaria exposure. It was discussed as a risk factor in three of the sites and was reported most frequently in Miwani. Study participants associated alcohol consumption with spending long periods of time outdoors during the night, and in some cases, falling asleep outside. Men were both observed and reported as more likely to drink. Drinking occurred both on a routine basis, in small outdoor gatherings and at bars, and at some large-scale social events, such as weddings.

Participants perceived a higher risk of biting and infection during the rainy season than the dry season. This was attributed to a greater density of mosquitoes during the rainy season caused by the presence of mosquito breeding sites from water collecting in puddles, ponds and debris (coconut shells, plastic, and garbage) when it rained. A smaller number of participants noted that while mosquito density was higher in the rainy season, risk may be heightened during the dry season due to high levels of outdoor sleeping and lower levels of ITN use.

Malaria prevention

Study participants viewed ITNs as the most important tool for protecting against mosquito bites and malaria infection. It was the primary prevention method participants reported using indoors and was perceived as offering protection both at the household and community level. Across study sites, participants reported high levels of ITN use, with some variation across seasons, sites, and demographic groups.

A female household member from Miwani noted lower levels of ITN use in her community due to lower mosquito density explaining, *"Many people protect themselves using mosquito nets, but in our village nowadays, there aren't many mosquitoes here, so nets are just like decorations to us.*" Low levels of ITN use were reported from participants in Miwani compared to other *shehia* suggesting differences in ITN use patterns across sites. Participants across *shehia* noted that men were less likely to use ITNs consistently, compared to women and children. One female household member from Donge Mchangani confided, *"It's better to tell you the truth. Their father does not sleep under the net. I sleep under it with my child, but my husband does not, he says that with the net it is very hot... Some days he sleeps under the net but some he does not."* Heat was a key barrier to ITN use in the dry season and was reported across participants and sites. As one male household member from Donge Mchangani described, *"During the hot season everything is hot, even the net itself, if you are covered with a net you'll be on fire."*

Alternative prevention methods that were widely available included insecticide sprays and insecticidal coils. Participants reported purchasing these at local shops for use at home, with sprays largely used indoors and coils used primarily outdoors or in semi-open spaces.

Many participants noted the difficulty of malaria prevention outdoors. A female household member from Bwejuu described the challenge this way, *"When you are outside you really can't wear the bed nets, can you?"* While one community leader reported seeing an example of outdoor ITN use, in general, outdoor prevention methods were either less known or not available. For instance, there was strong interest in topical repellents, especially for use when people were away from home working, visiting neighbors, or socializing. However, participants reported that topical repellents were not widely available in the community and were only sold at shops in town.

Some study participants reported that cost was a key barrier in accessing repellents, insecticidal sprays and other alternative malaria prevention methods. Unlike ITNs, which were distributed freely, other methods were only available for purchase at local shops. In some study areas participants mentioned using traditional repellents, made from local plants, that were less expensive. These included tablets that produced mosquito repelling incense (similar to insecticidal coils), and lotions that were applied when outdoors.

Heads of households were primarily responsible for making decisions on purchasing or using malaria prevention methods in the household. Parents reported making decisions in the best interest of their children and were responsible for providing additional or alternative prevention methods if current methods were insufficient, for example, replacing ITNs when they were torn/worn out and buying insecticidal spray to prevent indoor biting.

Housing quality was seen as a key determinant of malaria transmission. Open eaves, unfinished houses, and lack of window screening were viewed as contributing to increased malaria risk. Cost was frequently listed as the key barrier to housing improvements. However, in spite of challenges in housing quality, window screening was commonly reported and observed in the study sites. Window screening served a dual purpose of malaria prevention and providing extra privacy and security. A male household member from Donge Mchangani highlighted the security value, saying*, "If you haven't covered your windows there are thieves, [someone] can put their hand inside if something is nearby and steal it, but screening provides that protection, when you cover (the window) with wire, it is not easy for things to be stolen."*

Education was viewed as a critical component of malaria prevention. Participants described that education on malaria prevention was given at the health facility, through community meetings, and before ITN distribution and IRS campaigns. Community leaders also played an important role in educating community members. Participants reported being satisfied with the level of education provided, but noted that frequent and consistent education, particularly for non-users of ITNs, is crucial.

Migration and Travel

Migration and short-term travel were viewed by participants as a critical challenge to malaria elimination in Zanzibar. Participants reported traveling to mainland Tanzania to work, visit family, and for special events such as weddings and funerals. In some study sites, there had also been an influx of migrants and visitors coming to work from across Zanzibar, mainland Tanzania, and other parts of East Africa. Seasonal workers were reported to come for farming, to operate small businesses, and work in hotels in coastal areas. Some came seasonally, for a few months, while others stayed for longer periods, even settling permanently.

Increased presence of migrants in study areas was described as being responsible for imported cases as well as subsequent local infections. A male household member from Bwejuu explained*, "There's an influx of people from outside coming into this town...There's almost as many people from outside here as there are locals, and that makes it worrisome."* Additionally, visitors were perceived as less likely to be linked to community channels for malaria treatment and prevention such as the health facility, community health committees, or community leaders. Seasonal workers and other visitors were likewise viewed as less likely to have access to or use ITNs that are available to other members of the community, making them more vulnerable to infections. Both household members and key informants noted the importance of providing ITNs to visitors. A male household member from Donge Mchangani explained, *"We interact with our friends from Tanzania mainland and they come more and more every day and they need nets."*

Community leaders in three study sites reported examples of how these challenges were already being addressed, or how they planned to address them in the immediate future, through initiatives spearheaded at the *shehia* level. In these sites, visitors will be required to report to the *Assistant Sheha* and *Sheha* when they arrive and get tested for malaria as a prerequisite for living and working in the *shehia*. Key informants in one site reported that this initiative has already been implemented and has led to identification and treatment of positive malaria cases.

6.5 Discussion

Targeting malaria prevention interventions requires an understanding of when and where people are being exposed to malaria vectors. These results provide a richer understanding of human behavioral factors that can impact exposure risk and inform malaria elimination efforts in Zanzibar.

Zanzibar has one of the most intensive and successful programs for malaria control and elimination in sub-Saharan Africa, including wide-scale implementation of effective vector control tools, case management, and social and behavior change communication. While the islands have experienced significant reductions in both vector density and malaria infection, current vector control interventions, namely ITNs and IRS, may not be sufficient for eliminating local transmission (Govella and Ferguson, 2012b).

This study revealed that in Zanzibar, as in other settings in sub-Saharan Africa, a range of routine activities occur during times when malaria vectors are active (Monroe et al., 2014, Monroe et al., 2015, Dunn et al., 2011, Monroe et al., 2019b). A 2010 study by Dunn *et al.* described malaria risk behaviors in rural Tanzania and established that routine social, household and livelihood activities around dawn and dusk including socializing outdoors, fetching water, fishing and farming could increase risk of exposure to mosquito bites and infection (Dunn et al., 2011).

Large-scale socio-cultural events and livelihood activities were identified that lasted throughout the night, disrupting usual sleeping patterns and making ITN use during any part of the night a challenge. This finding is consistent with a number of recent studies highlighting the importance of ‘special’ socio-cultural events in malaria-related risk (Alaii et al., 2003, Dunn et al., 2011, Monroe et al., 2015, Monroe et al., 2014). Studies in Ghana and Uganda identified social barriers to ITN use away from home such being perceived as proud or even disrespectful for using ITNs during important social events. They also identified logistical constraints, including not having a place to hang an ITN at social events, and resource limitations such as not having extra ITNs with which to travel (Monroe et al., 2015, Monroe et al., 2014).

To date, there are few tools designed to protect people outdoors that have sufficient evidence to support a WHO recommendation. Tools that are in the development pipeline should address existing gaps in protection and be appropriate to the context in which they will be used. The results suggest discrete times of the year and setting profiles that can help to inform development and deployment of supplemental interventions. This includes inside the home, directly outside of the home, fixed locations within the community where people routinely gather, large-scale events, livelihood activities, and travel.

Understanding how gender norms impact risk of exposure to malaria is also important for targeting vector control tools and social and behavior change interventions (Dunn et al., 2011, 2007). In Zanzibar, women were more likely to serve as primary caregivers, and perform daily tasks that were oriented around the household, including childrearing, household chores and small businesses close to home such as selling food and charcoal making. Women with children also stayed closer to the house during the nighttime, often socializing with neighbors and friends near their home.

Conversely, men's routine activities had a higher level of physical mobility, keeping them outdoors and away from their home for longer periods during the nighttime. Across seasons, men stayed outdoors later and went to sleep later after spending the night watching television, chatting, and socializing at *Maskan*. In some sites, men also reported drinking alcohol, which was perceived to increase risk behavior, such as staying outdoors late into the night. Men were more likely to engage in nighttime livelihood activities, including security jobs, protecting crops, hunting, and fishing which keeps them outdoors during peak biting times. These findings are consistent with a trend seen in many countries moving toward elimination where adult males represent a rising proportion of malaria cases (Cotter et al., 2013). This trend has been largely influenced by migration and outdoor livelihood activities that increase exposure to malaria vectors, including fishing, agriculture, military, mining, and forest work (Jacobson et al., 2017).

Travel and migration emerged as a central consideration for malaria elimination in Zanzibar among study participants. This finding is consistent with a recent review of travel history among malaria cases in Zanzibar which showed more than half of cases had traveled outside of Zanzibar in the previous month (PMI, 2018). In this study, many residents perceived that travelers, returning residents, and seasonal workers from Mainland Tanzania are responsible for new malaria cases, representing a key threat to malaria elimination in Zanzibar. Even when residents perceived overall malaria transmission rates to be low, they still believed that there was a risk of resurgence of malaria due to travel and migration. These results are consistent with the findings of a 2012 study in Zanzibar in which participants expressed a fear that imported cases from the mainland could put local communities at risk (Bauch et al., 2013). Research across a number of settings in sub-Saharan Africa have documented an association between travel from higher to lower transmission areas and malaria risk (Lynch et al., 2015, Yukich et al., 2013, Smith et al., 2017), and available evidence suggests that targeting imported cases is pivotal to malaria elimination efforts (Le Menach et al., 2011).

Livelihood activities and occupations such as tourism, farming, and fishing were seen as key drivers of short-term migration. For instance, farmers from mainland Tanzania moved into some study sites to farm and cultivate land often arriving during planting season and staying through harvest season when they were paid for their work. Participants also perceived that seasonal workers had lower access to prevention methods that were available to residents such as ITNs distributed through community channels. Seasonal workers and migrants were seen as less likely to seek health care resources, and more likely to engage in nighttime occupations and activities that put them at higher risk of infection.

Participants in this study noted that community level malaria prevention programs often missed or were not accessible to seasonal workers and migrants. These included ITN distribution programs and community-level education on malaria prevention. In some study sites, seasonal workers and visitors were required by the *Sheha* to register and get tested as a requirement for staying in the community. These community-level initiatives have the potential to ensure prompt testing and treatment for groups at higher risk of malaria infection. Complementary approaches for elimination should therefore include efforts to protect the migrant workforce, travelers, and guests from infections and ensure improved access to prompt diagnosis and treatment for these groups. ZAMEP could consider formalizing and expanding community-level programs to other sites with high malaria incidence and high levels of seasonal workers and travelers, while maintaining leadership at the community-level. Additional interventions tailored to these groups could also be explored such as community health programs encouraging residents to travel with ITNs, testing and treatment for seasonal workers, and providing a basic package of interventions for high-risk travelers. This approach is consistent with approaches being used in malaria elimination contexts in the

Greater Mekong Sub-Region. The current WHO malaria elimination strategy for the Greater Mekong Sub-Region emphasizes the importance of increasing access to diagnostic and treatment services and prevention measures for mobile and migrant populations (WHO, 2015).

Limitations

Qualitative research has inherently different objectives and methods compared to quantitative research (Pope and Mays, 1995), and it is crucial to interpret all study results in the context of the strengths and limitations of the methods used. The sample size in this study was designed to achieve theoretical saturation and not wide-scale generalizability. Further, self-reported information can be subject to bias, including social desirability bias in which participants provide responses they believe will be socially acceptable rather than responses that reflect their true experiences or perspectives (Grimm, 2010). To reduce the potential for social desirability bias, the study team conducted all interviews in private settings and reminded participants that there was no right or wrong answer to questions. Direct observation creates the potential for reactivity, a phenomenon in which participants alter their normal behavior in response to the presence of an observer (Bernard, 2012). A few cases of reactivity, such as participants talking to or engaging with observers, were carefully recorded, and generally appeared to have a minimal impact on study results. Further, the combination of in-depth interviews and direct observation allowed for triangulation of information across methods. Notwithstanding the limitations, these findings provide deeper insight into participants' perspectives and experiences that would not be possible through more structured methods.

6.6 Conclusions

In Zanzibar, and other pre-elimination settings, targeting interventions effectively is critical, and should be informed by a clear understanding of relevant human behavior. Gaps in malaria prevention identified in this study included routine household and community activities occurring during non-sleeping hours as well as livelihood activities and large-scale social events that often last throughout the night. There is an opportunity to explore the use of supplemental vector control tools and accompanying social and behavior change interventions to help address these gaps. Migration and travel of malaria infected individuals from higher transmission settings into Zanzibar must also be addressed to reach elimination. Existing community structures provide potential mechanisms for addressing gaps in protection, as well as targeting higher risk groups such as travelers and seasonal workers. Building on these existing systems to target interventions should be explored to limit both local and imported malaria cases.

6.7 Declarations

Ethics approval and consent to participate

This study received ethical approval from the Johns Hopkins University (IRB# 7390), Ifakara Health Institute (IHI/IRB/No: 035 – 2016) and the Zanzibar Medical Research and Ethics Committee (Protocol #: ZAMREC/0005/OCT/016). All IDI participants provided written informed consent. The *Sheha* provided oral consent for community observations in public spaces. Heads of household provided written consent for photos. Results were presented back to ZAMEP and the Zanzibar Malaria Elimination Advisory Committee.

Consent for publication

Written consent was obtained for photos where people are identifiable. The consent form included information on dissemination and display of the photos.

Availability of data and materials

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

Competing interests

The authors have declared that they have no competing interests.

Funding

This work was made possible by the generous support of the American people through the United States Agency for International Development (USAID) and the President's Malaria Initiative (PMI) under the terms of USAID/JHU Cooperative Agreement No. AID-OAA-A-14-00057 (VectorWorks Project). The contents are the responsibility of the authors and do not necessarily reflect the views of USAID or the United States Government.

Authors' Contributions

AM led study design, development of study protocol and data collection tools, oversaw data collection, led data analysis and interpretation, drafted manuscript outline and sections of the manuscript, and managed inputs to the manuscript. KM helped supervise data collection, contributed to data analysis and interpretation, and drafted sections of the manuscript. FO conceptualized the larger study design, contributed to development of data collection tools, provided input on interpretation of study results, and provided significant input on the manuscript. MF, SM, HK, and ML contributed to study design and development of data collection tools and provided significant input on the manuscript. KH led community entry, facilitated data collection activities, and provided input on interpretation of study results. FA contributed to the manuscript and provided input on interpretation of study results. AA contributed to study design and provided support for field work. GG contributed to study design and provided feedback on the manuscript. SH contributed to development of data collection tools, provided significant input on the manuscript, and provided high-level social science support. All authors reviewed and approved the final manuscript.

Acknowledgements

The authors would like to thank everyone who made this study possible. This includes the study participants for taking the time to share their valuable experiences and community leaders in the study sites for ensuring the success of all components of the study. The authors are grateful to the data collection team who worked diligently and professionally to build trust with the study communities and collect high quality data. This includes Safia Ali, Khairati Salum Selemani, Mwatima Khamis, Masoud Fadhil, Faki Haji Faki, and Masoud Hindi. The authors would like to acknowledge Brooke Farrenkopf who contributed to codebook development and transcript coding, Dickson Msaky who helped with selection of photos for the manuscript and created the study site map, and Mwinyi Khamis who supported community entry activities. The authors would also like to thank Seth Irish and Jenny Carlson for providing feedback on the manuscript.

Chapter 7: Methods and indicators for measuring patterns of human exposure to malaria vectors

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Published in
Malaria Journal 2020 **19**:207

https://doi.org/10.1186/s12936-020-03271-z

7.1 Abstract

Background

Effective targeting and evaluation of interventions that protect against adult malaria vectors requires an understanding of how gaps in personal protection arise. An improved understanding of human and mosquito behavior, and how they overlap in time and space, is critical to estimating the impact of insecticide-treated nets (ITNs) and determining when and where supplemental personal protection tools are needed. Methods for weighting estimates of human exposure to biting *Anopheles* mosquitoes according to where people spend their time were first developed over half a century ago. However, crude indoor and outdoor biting rates are still commonly interpreted as indicative of human-vector contact patterns without any adjustment for human behavior or the personal protection effects of ITNs.

Main text

A small number of human behavioral variables capturing the distribution of human populations indoors and outdoors, whether they are awake or asleep, and if and when they use an ITN over the course of the night, can enable a more accurate representation of human biting exposure patterns. However, to date no clear guidance is available on what data should be collected, what indicators should be reported, or how they should be calculated. This article presents an integrated perspective on relevant indicators of human-vector interactions, the critical entomological and human behavioral data elements required to quantify human-vector interactions, and recommendations for collecting and analyzing such data.

Conclusions

If collected and used consistently, this information can contribute to an improved understanding of how malaria transmission persists in the context of current intervention tools, how exposure patterns may change as new vector control tools are introduced, and the potential impact and limitations of these tools. This article is intended to consolidate

understanding around work on this topic to date and provide a consistent framework for building upon it. Additional work is needed to address remaining questions, including further development and validation of methods for entomological and human behavioral data collection and analysis.

Keywords Insecticide-treated nets, human-vector interaction, human-vector contact, exposure, residual malaria transmission, outdoor biting, outdoor transmission

7.2 Background

Insecticide-treated nets (ITNs) have accounted for an estimated two thirds of malaria cases prevented in the past decade (Bhatt et al., 2015a). However, their effectiveness is limited against mosquitoes that feed when people are outdoors, or indoors but awake and active. Furthermore, the scale-up of ITNs can contribute to shifts in species composition, as well as shifts in vector behavior (e.g. toward early evening and early morning biting, increased outdoor resting and biting, and more frequent feeding upon animals) which may further attenuate vector control impact (Killeen et al., 2017a, Killeen, 2014, Durnez and Coosemans, 2013a).

Quantifying and characterizing gaps in personal protection against mosquitoes, defined as the proportional reduction of biting exposure an individual experiences as a direct result of personal use of a protection measure, requires information on the behaviors of vectors and humans, as well as when and where they intersect. Methods for factoring spatiotemporal interactions between vectors and humans into biting exposure estimates were developed as early as the late 1960s and early 1970s (Elliott, 1968, Garrett-Jones, 1964, Elliott, 1972). A number of more recent articles have also underscored the importance of including human behavior when investigating biting risk, and the value of biologically meaningful coverage indicators (Killeen et al., 2014, Kiware et al., 2012, Lindblade, 2013).

Despite the importance of human behavior to understanding malaria transmission dynamics, relatively few studies have investigated it (Monroe et al., 2019b, Sherrard-Smith et al., 2019).

A review of published literature between 2000 and 2017 identified fewer than a dozen studies in sub-Saharan Africa that integrated entomological and human behavioral data to enable more meaningful interpretation (Monroe et al., 2019b, Sherrard-Smith et al., 2019). Likewise, a systematic review and meta-analysis of mosquito feeding behavior identified a surprising absence of data on human location and sleeping patterns needed to quantify risk of mosquito biting (Sherrard-Smith et al., 2019). The review identified 250 data sets measuring mosquito biting time across Africa but only 22 of these data sets had documented human location, only seven documented human sleeping patterns, and only three had collected necessary human and vector data in the same time and place (Sherrard-Smith et al., 2019).

Crucially, calculation methods for weighting exposure estimates according to human location can alter interpretations when compared to those suggested by entomological observations alone (Killeen et al., 2018, Killeen, 2018, Sougoufara et al., 2018a, Huho et al., 2013a). For example, for a mosquito population that feeds both indoors and outdoors, the overwhelming majority of exposure events for an unprotected person may still occur indoors if mosquitoes actively seek blood throughout the night when most people are asleep inside their houses (Figure 7.1).

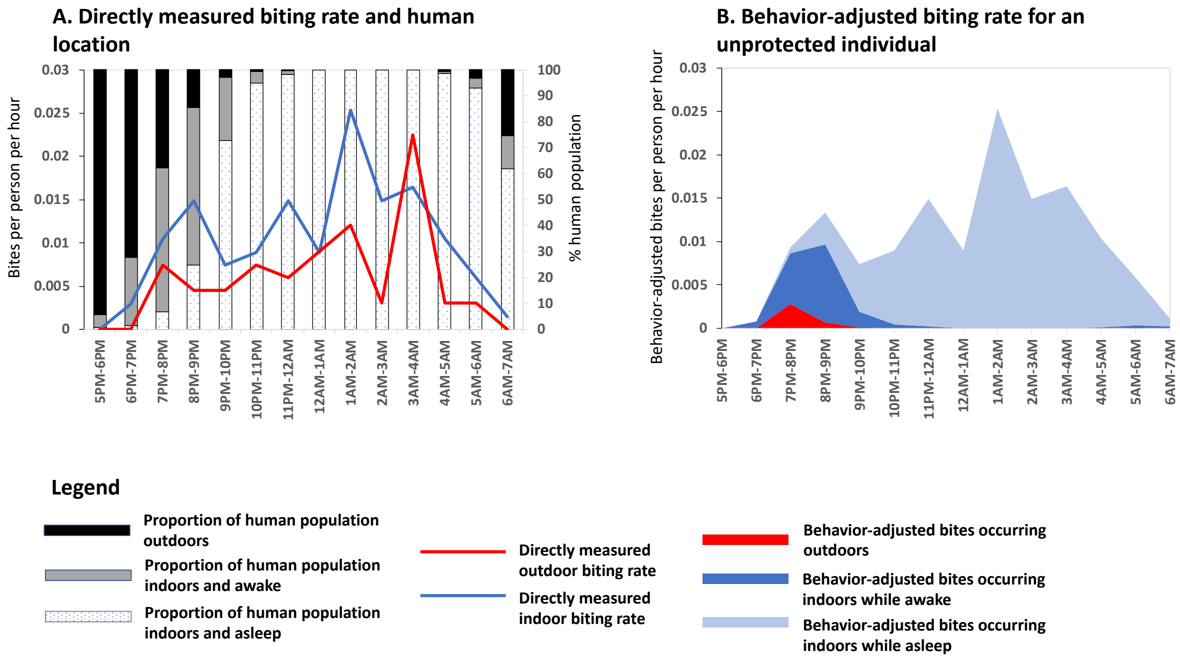

Figure 7.1 Example of directly measured and behavior-adjusted estimates of human exposure to malaria vectors from Asembo, western Kenya in 2011. Mosquito biting data was collected using human landing catches from June through July 2011 and human behavioral data was collected using a cross-sectional survey conducted from July through August 2011 (Bayoh et al., 2014). Series A shows the proportion of the human population 1) outdoors 2) indoors and awake, and 3) indoors and asleep throughout the night, overlaid with directly measured indoor and outdoor biting rates for *An. arabiensis*. Based on biting density alone, the estimated percentage of vector bites occurring indoors = 63%. Series B integrates vector and human behavior data to show behavior-adjusted cumulative exposure to vector bites for an unprotected individual. The percentage of vector bites occurring indoors for an unprotected individual ($\pi_{I,u}$)= 97% and the percentage occurring while asleep indoors for an unprotected individual ($\pi_{S,u}$) = 84%.

Despite their utility, such quantitative indicators of when and where interactions between humans and vectors occur remain under-utilized, and no clear guidance is available on what data should be collected, what indicators should be reported, or how they should be calculated. Further, what little methodological literature exists is somewhat scattered, with inconsistent definitions and notation in different reports at different development stages of the methodology.

Beyond the implications for personal protection from mosquito bites, such numerical estimates for gaps in practically-achievable personal protection are also crucial determinants of how well ITNs function to control vector populations due to mosquito contact with the insecticides applied to them (Barreaux et al., 2017, Durnez and Coosemans, 2013b, Killeen, 2014, Killeen et al., 2014). The strong preferences for human blood that make some African *Anopheles* such efficient malaria vectors also render them vulnerable to population control with insecticidal personal protection measures like ITNs (Killeen, 2014, Killeen et al., 2014, Killeen et al., 2017a, Killeen et al., 2013). Reduced vector population abundance, survival rate, feeding frequency and human-feeding probability, underpin equitable community-level *mass effects* that account for much of the benefits of widespread ITN use (Bradley et al., 2015, Killeen et al., 2017a, Magesa et al., 1991). Successful suppression of a vector population depends directly upon the extent of personal protection ITNs provide for two reasons: (1) The degree of personal protection not only influences rates of human exposure to mosquitoes but also rates of mosquito exposure to the active ingredients of ITNs (Gatton et al., 2013). (2) Personal protection is often what motivates end users of ITNs and drives utilization rates once access is provided (Loll et al., 2013).

However, vector population suppression is a much more complex phenomenon and is also limited by other vector behaviors such as feeding on animals (Takken, 2002, Killeen et al., 2017a, Waite et al., 2017), early exit from houses (Killeen et al., 2017b), and physiological resistance to insecticides (Gleave et al., 2018, Hemingway et al., 2016), none of which is within the scope of this article. Instead, this article focuses specifically on how best to measure and interpret behavioral determinants of personal protection in the field. Building on existing approaches in the literature, this article presents an integrated perspective on relevant indicators of human-vector interactions, the critical entomological and human behavioral data elements required to quantify human-vector interactions, and recommendations for collecting and analyzing such data.

7.3 Methods for Measuring Human-Vector Interaction

Indicators of human-vector interaction patterns

Human-vector indicators can provide a clearer picture of where (indoors or outdoors) and when (time of night) exposure to malaria vectors occurs by accounting for human location and intervention use throughout the night. Relevant indicators include: 1) The proportion of vector bites occurring indoors for an unprotected individual ($\pi_{I,u}$), which represents the maximum possible personal protection any indoor intervention could provide. 2) The proportion of vector bites occurring indoors during sleeping hours, for an unprotected individual ($\pi_{S,u}$), which represents the maximum possible personal protection any intervention targeting sleeping spaces could provide. 3) The proportion of all vector bites prevented by using an ITN (P_S^*), which represents the protection provided against vector bites to someone using an ITN during sleeping hours. 4) The proportion of remaining exposure occurring indoors for a protected user of an ITN ($\pi_{I,p}$), which represents how much remaining (residual) exposure occurs indoors for an individual who uses an ITN. This indicator is particularly useful for understanding where residual malaria transmission is occurring once high coverage with ITNs is achieved and the relative merits of adding supplemental interventions that act indoors and/or outdoors in that context. 5) The population-wide mean personal protection against biting exposure provided by community-level coverage of humans with ITNs ($P_{S,C}^*$), which represents the community average level of personal protection, accounting for the proportion of people who use an ITN each night while asleep. This summary indicator is particularly useful for adjusting field measurements of mosquito biting rates to account for this community-wide mean level of personal protection.

While indicators 3-5 focus on the personal protection provided by ITNs, similar indicators may be calculated for mosquito-proofed housing, and other personal protection measures such as repellents or treated clothing. All indicators, when possible, should be disaggregated by vector species and by human population groups (e.g. by sex and age categories) as behaviors can vary across species and groups. Equations for calculating population-level indicators of human-vector interaction are presented in Box 1 and an example using vector and human behavior data from Asembo, western Kenya is used to comparatively illustrate these indicators in Figure 7.2.

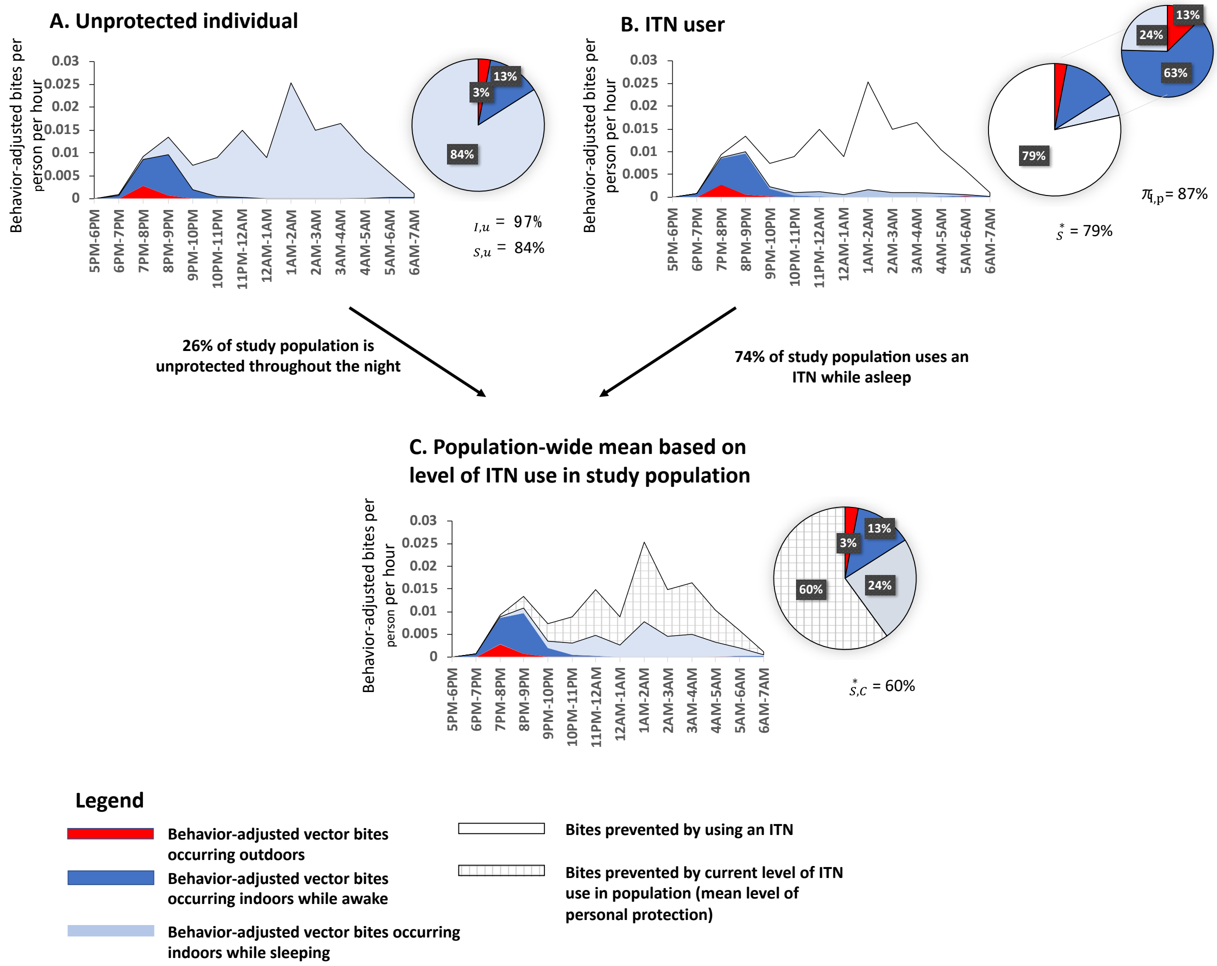

Figure 7.2 Example of indicators calculated using vector and human behavior data from Asembo, western Kenya in 2011 (Bayoh et al., 2014). Series A shows the behavior-adjusted estimates of exposure to *An. arabiensis* bites for an unprotected individual. Series B shows behavior-adjusted estimates of exposure to vector bites for an ITN user. ITNs were assumed to prevent approximately 94% of bites while in use based on reference estimates from experimental hut trials. The percentage of all vector bites prevented by using an ITN (P_S^*) = 79% and the proportion of remaining exposure occurring indoors for a protected user of an ITN ($\pi_{I,p}$)=87%. Series C shows the population-wide mean exposure to vector bites. In this site the proportion of the population that reported using an ITN while asleep the previous night was 74% (arrows). Therefore, the population-wide mean personal protection against biting exposure given the reported community-level coverage of people using an ITN ($P_{S,C}^*$) is 60%.

Box 7.1 Equations for calculating summary indicators of human-vector interaction patterns. In order to maintain consistency and enable easy comparison with field-relevant literature, the following notation provides an updated, harmonized, and clarified version of that most commonly used in published articles quantifying human-vector interactions. However, examples of alternative notation for conceptually similar parameters can be found in the mathematical modeling literature and are also valid. In the notation presented here, "π" refers to the average proportion of human exposure to vector bites that occurs under a certain condition. The first subscript is used to indicate the location of bites (I=indoors; O=outdoors; S=sleeping space). The second subscript is used to indicate whether the indicator is referring to someone who is protected by an ITN (p) during sleeping hours or unprotected throughout the night (u). The following equations are intended to reflect a twenty-four-hour period to account for mosquito biting activity and human behaviors over the course of a full day, although for practical purposes hours of full daylight in which Anopheles malaria vectors in most settings are inactive may be assumed to be negligible. An Excel® spreadsheet template is provided to calculate these indicators from raw data using the examples presented in Figures 7.1-2.

1. Proportion of vector bites occurring indoors for an unprotected individual ($\pi_{I,u}$) (Bayoh et al., 2014, Killeen et al., 2006, Moiroux et al., 2014, Seyoum et al., 2012): This is an indicator of the maximum possible protection any indoor intervention could provide and is expressed as the number of bites received indoors over a 24-hour period divided by the total number of bites received indoors and outdoors over the same 24 hour period. It is calculated as the sum of the measured indoor vector biting rates (B_I) for each one-hour time period (t) over a 24-hour period weighted by the estimated proportion of humans indoors (I) at that time, divided by the total location weighted exposure (Equation 1 denominator), i.e. itself plus the sum of the outdoor biting rates weighted by the proportion of humans outdoors (O, where O=1-I) at each time over the same 24-hour period:

$$\pi_{I,u} = \frac{\sum_{t=1}^{24} B_{I,t}\, I_t}{\sum_{t=1}^{24} B_{I,t}\, I_t + B_{O,t} O_t} \quad \text{(Eq.1)}$$

It may sometimes be useful to instead express this summary indicator as its complement, the proportion of bites occurring outdoors for an unprotected individual ($\pi_{O,u}$)(Killeen et al., 2013):

$$\pi_{O,u} = 1 - \pi_{I,u} \quad \text{(Eq.2)}$$

2. Proportion of vector bites occurring while asleep for an unprotected individual ($\pi_{S,u}$) (Bayoh et al., 2014, Huho et al., 2013a, Kamau et al., 2018, Killeen et al., 2006, Seyoum et al., 2012): An indicator of the maximum possible protection any intervention targeting indoor sleeping spaces could provide. It is expressed as the number of vector bites received while asleep indoors divided by the total number of bites received indoors and outdoors during a 24-hour period. It is calculated as the sum of the indoor vector biting rates (B_I) for each one-hour time period (t) over a 24-hour period weighted by the estimated proportion of humans sleeping (S) indoors at that time, by the sum of the indoor and outdoor biting rates respectively weighted by the proportions of humans indoors and outdoors at each time over the same 24-hour period:

$$\pi_{S,u} = \frac{\sum_{t=1}^{24} B_{I,t} S_t}{\sum_{t=1}^{24} B_{I,t} I_t + B_{O,t} O_t} \quad \text{(Eq.3)}$$

One important limitation of this calculation is that it assumes all sleeping spaces are indoors, which may not be the case in all settings.

3. Proportion of all vector bites directly prevented by using an ITN ($P_S{}^*$)(Cooke et al., 2015, Geissbühler et al., 2007, Moiroux et al., 2014, Thomsen et al., 2016): An indicator of *the de facto* protection provided against all indoor and outdoor bites by using an ITN, allowing for non-use while awake and active. It is calculated as the product of the proportion of exposure occurring indoors while asleep and the personal protection against bites (feeding inhibition) provided by an ITN while in use (*ρ)*. Data on personal protection provided by an ITN while in use can be obtained from standardized experimental hut trials, in which it is referred to as *feeding inhibition.* Feeding inhibition is defined as the percentage of mosquitoes that are prevented from taking a blood meal out of all mosquitoes that would otherwise do so inside an experimental hut (Okumu and Moore, 2011). Weighting these estimates of personal protection while in use (ρ) by the patterns of relevant human and mosquito behaviors, the proportion of all vector bites prevented by using an ITN may be calculated as follows:

$$P_S^* = \rho\pi_{S,u} = \frac{\rho\sum_{t=1}^{24} B_{I,t} S_t}{\sum_{t=1}^{24} B_{I,t} I_t + B_{O,t} O_t} \text{ (Eq.4)}$$

4. Proportion of remaining exposure occurring indoors for a protected user of an ITN ($\pi_{I,p}$) (Killeen et al., 2006, Moiroux et al., 2014, Seyoum et al., 2012): An indicator of how much of the remaining exposure occurs indoors for an individual who uses an ITN and where supplemental tools should be targeted (i.e. indoors, outdoors, or both). It is calculated by adjusting the estimate of $\pi_{I,u}$ to allow for the indoor personal protection provided by using an ITN:

$$\pi_{I,p} = \frac{(\sum_{t=1}^{24} B_{I,t} I_t) - \rho(\sum_{t=1}^{24} B_{I,t} S_t)}{(\sum_{t=1}^{24} B_{O,t} O_t + B_{I,t} I_t) - \rho(\sum_{t=1}^{24} B_{I,t} S_t)} \quad \text{(Eq.5)}$$

It may sometimes be useful to instead express this summary indicator as its complement, the proportion of bites occurring outdoors for an ITN user ($\pi_{O,p}$):

$$\pi_{O,p} = 1 - \pi_{I,p} \quad \text{(Eq.6)}$$

5. Population-wide mean personal protection against biting exposure provided by observed level of ITN use (*C*) in the community ($P^*_{S,C}$): While ITNs can feasibly be used during sleeping hours, not all members of a population can or do use an ITN. This is an indicator of *population-wide mean level of personal protection provided by current levels of ITN use*. Calculated simply as the product of the proportion of human population using an ITN each night and the overall personal protection provided by an ITN, allowing for the attenuating effects of exposure occurring when the user is active outside the net.

$$P^*_{S,C} = \frac{\rho \sum_{t=1}^{24} B_{I,t} C_t}{\sum_{t=1}^{24} B_{I,t} I_t + B_{O,t} O_t} = \rho\, \pi_{S,p} C \quad \text{(Eq.7)}$$

Critical data elements

Measuring human exposure to malaria vectors requires timed estimates of indoor and outdoor vector densities as outlined below and representative estimates of the human population indoors and outdoors, awake and asleep, and using personal prevention measures, over the full period of vector feeding activity. Given the potential variation in both vector and human behavior, it is important to capture this data across seasons when possible. It is also helpful to know the approximate level of personal protection, in terms of bite prevention, provided by an ITN during the times when it is used. Such entomological estimates of personal protection are typically expressed as proportional blood feeding reduction, defined as the percentage of mosquitoes that are prevented from taking a blood meal out of all mosquitoes that would otherwise do so inside an experimental hut. Suitable estimates for commonly-used products may be obtained from published experimental hut studies, ideally from the nearest and most relevant settings with similar vector populations (WHO, 2013). Human behavioral data should include representative estimates of the proportion of the human population indoors versus outdoors, sleeping versus awake, and under the protection of an ITN throughout the night. In other words, where people are, whether they *could* feasibly use an ITN, and whether they *are* using an ITN. When possible, such human behavior data should ideally be collected in a disaggregated format that is linkable to de-identified individual human study participants. This format allows aggregation into estimates for the mean proportion of the human population indoors, sleeping, and under the protection of an ITN at each time of the night, but also allows for assessment of the epidemiological importance of behavioral differences between individuals. A summary of recommended data elements is included in Box 7.2.

Box 7.2 Summary of critical entomological and human-behavioral data elements for quantifying the distribution of human exposure to malaria vectors across times of the night and indoor versus outdoor locations.

Entomological data:

- Local and directly comparable measurements of indoor and outdoor biting rates for individual vector species, separately for each hour over the full period of feeding activity.
- Reference estimates for the personal protection provided by ITNs while actually being used, expressed in terms of proportional human blood feeding reduction.

Human behavioral data:

- Local estimates of the proportions of the human population who are indoors versus outdoors for each hour of the night.
- Local estimates of the proportions of human population who are asleep or trying to sleep versus awake and active, for each hour of the night.
- Estimate of proportion of human population using an ITN for each hour of the night.

Considerations for entomological data collection

Indoor and outdoor biting rates can be assessed through human landing catches (HLC) (Silver, 2007) or an alternative method verified to reproduce representative exposure density distributions by capturing host-seeking mosquitoes. While HLC has been traditionally referred to by entomologists as the "gold standard" method, it should not be undertaken lightly as a default method and may not be permitted in some contexts for ethical reasons, such as where arboviral transmission may occur. Before any alternative method can be considered adequate for surveying human exposure patterns it must first be compared with HLC to determine equivalence indoors versus outdoors, over the course of the night, across settings, and across seasons (Box 7.3).

None of the validation steps described in Box 3 is particularly difficult and a range of under-utilized alternatives to HLC exist that could be suitable (Silver, 2007, Clements, 1992). Although no exposure-free method has yet been identified that completely satisfies all the requirements described in Box 5, only slight discrepancies are observed between HLC and some of the latest electric grid (EG) trap prototypes (Meza et al., 2019, Govella et al., 2016). However, some limitations and uncertainties remain regarding the performance and reliability of EGs (Sanou et al., 2019) and they have the potential to be somewhat laborious and hazardous to use in practice. More practical and reliable exposure-free alternatives to HLC requiring no electrical power source would be desirable in terms of convenience, scalability and safety. New double net trap designs, including a miniaturized version developed and applied to survey human exposure patterns indoors and outdoors, are emerging that might address this need once evaluated against the criteria in Box 3 (Limwagu et al., 2019).

One of the most commonly used methods for surveying malaria vector densities, the Centers for Disease Control and Prevention (CDC) light trap was originally designed for indoor use, generally catches fewer mosquitoes outdoors, and can have variable outdoor sampling efficiency between studies, seasons, and mosquito species (Silver and Service, 2008). It is, therefore, not suitable for comparing indoor and outdoor biting densities and thus not recommended for measuring the entomological indices described in Box 2.

An important priority for future research in this area should be the specific adaptation of safe, convenient methods for measuring the entomological metrics described in Box 2 and evaluating those mosquito trapping methods in terms of the performance criteria detailed in Box 3. In the meantime, investigators relying on EGs, double net traps, or any other alternative, should include such assessments in their study designs as an essential internal quality assurance component of their studies.

Box 7.3 Criteria for validating alternative methods to human landing catches for quantitative assessments of human patterns of exposure to mosquito bites. A method should ideally meet all criteria. If there are variances, they must be measured and adjusted for to achieve the necessary equivalency.

(1) **Relative performance compared to HLC must be consistent indoors and outdoors.** Note however, that because the derived metrics of human exposure are expressed and used as proportions, the method does not need to have equivalent absolute efficiency. If an alternative method is more (or less) efficient indoors than outdoors when compared

to HLC, the method will yield correspondingly biased estimates of *where* human exposure occurs. As an example, in particular setting it may be acceptable if an alternative method catches only 30% of the number of mosquitoes obtained by HLC with the same sampling effort in the same times and places, so long as that relative efficiency is 30% indoors and 30% outdoors. Lessons may be learned from early efforts to develop customized EGs for this purpose; initial prototypes had higher relative efficiency outdoors than indoors (Maliti et al., 2015), so further prototypes were developed to address these shortcomings (Meza et al., 2019, Govella et al., 2016) and some discrepancies remain (Sanou et al., 2019).

(2) **Those indoor and outdoor relative capture rates must remain constant throughout the night.** In simple terms, if both relative capture efficiencies average 30% over the course of the night, this needs to reflect steady estimates of 30% throughout the night. If instead this reflects the mean of an unstable device with 40% relative sampling efficiency at the start of the evening that declines to 20% by the following morning, the method will yield correspondingly biased estimates of *when* human exposure occurs. This criterion is of particular relevance to battery-powered traps (Silver, 2007). Important lessons may be learned from early efforts to evaluate commercially-available electrocuting grids for this purpose; this approach failed because relative capture efficiency faded as battery charge drained over the course of the night (Majambere et al., 2013, Maliti et al., 2015).

(3) **The capture method should have consistently density-independent sampling efficiency relative to HLC.** It is essential that a method is proven to satisfy this criterion, so that it can be reliably applied across a range of locations and seasons without compromising reliability or utility for comparing results. For example, if a method has a sampling efficiency of 30% relative to HLC when vector densities are

low, it should also be 30% at high vector densities rather than tail off to 20% (or increase to 40%) as capture bags fill with mosquitoes,, batteries drain faster, or human operators become overwhelmed. While this has not yet proven an issue for purpose-built electrocuting grids (Maliti et al., 2015), the same cannot be said for CDC light traps (Briët et al., 2015).

Collections should be carried out for all hours of vector feeding activity. This is referred to simply as “night” for the purposes of malaria vectors, although this may include early evenings and mornings. Ensuring that the fringes of mosquito activity are captured, which may require 14 hours of collections or more in some locations, will improve accuracy of the measures of human-vector interactions and correct interpretations of data (Killeen et al., 2013). (Killeen et al., 2013). Given the importance of even minor fractions of outdoor exposure that may occur before dusk and after dawn to sustaining residual malaria transmission (Killeen, 2014, Govella and Ferguson, 2012a, Sherrard-Smith et al., 2019, Sougoufara et al., 2018b), surveying even low levels of biting activity during these early and late stages of mosquito activity cycles is critical.

It is also important to be able to disaggregate biting rate profiles for individual vector species within taxonomic groups and complexes, many of which differ in their time of biting, preference for indoor or outdoor biting, and efficiency as vectors. This is especially important where the individual vector species contribute differentially to overall malaria transmission and also have different biting behavior profiles as may be observed between *Anopheles gambiae sensu stricto, Anopheles arabiensis and Anopheles funestus* (Lwetoijera et al., 2014a, Russell et al., 2011, Durnez and Coosemans, 2013a). It is therefore important that the results of morphological or molecular identifications of individual specimens can be linked to the field data detailing where, when, and how they were captured (Kiware et al., 2016).

While this may sound obvious, it is not the case for most malaria vector behavior data. Indeed, only three published estimates for any of the summary indicators described in Box 1 unambiguously relate to a single, clearly identified species, rather than mixture of species within a complex or group (Killeen et al., 2018).

Mosquito densities are variable across nights and locations, and the distribution across indoor and outdoor environments often changes according to season and micro-climatic conditions (Ngowo et al., 2017, Magbity and Lines, 2002, Smith et al., 1995). Mosquitoes may also shift host-seeking behaviors as an adaptive response to insecticidal pressure from indoor interventions (Thomsen et al., 2016). Therefore, ensuring sufficient replicates across locations and seasons is key to establishing long-term trends in behavior patterns of local mosquitoes.

Indoor and outdoor mosquito collections are generally carried out in the peri-domestic setting, inside and directly outside of homes, which may not accurately reflect exposure to malaria vectors when people are away from home. Therefore, in some contexts, collections should be considered in additional locations of interest within the community where people may be at risk of exposure, for instance forest camps, as well as among migrant and mobile populations (Gryseels et al., 2015, Durnez et al., 2013).

In addition to indoor and outdoor mosquito collections, estimates of human vector interactions require an estimate of personal protection provided by ITNs while in use. Context-specific, local measurements of biting reduction achieved by ITNs, mosquito-proofed housing, or other relevant protection measures are neither necessary nor realistic to expect for every setting. For most commonly used ITN products, reference estimates are available from several experimental hut evaluations across tropical Africa and Asia, although these may vary between products, locations and species. The most geographically and ecologically relevant of these published values can be used in the calculations described in

Box 7.1, albeit with the caveat that variability may arise from context-dependent differences in the condition of these products under conditions of use in the real world.

In addition to the critical data elements outlined in Box 7.2, when possible, the environmental characteristics within each house used for indoor human landing catches, particularly in terms of repellents, irritants and physical barriers that reduce mosquito densities in the house should also be captured. In addition to any behavior-modifying active ingredients used for ITNs and IRS, structural features such as closed eaves, complete ceilings, and screened windows, and wall surface substrate need to be carefully considered when collecting and interpreting data (Sherrard-Smith et al., 2018). Additional variables that may influence biting patterns include habitual cooking locations, house size, and type of livestock present indoors and outdoors. While these fine details may not be necessary for population-level or district-level recommendations envisaged here, they can help to identify major sub-groups within the population, which may require specific recommendations.

Considerations for human behavioral data collection

Different methods have been used to estimate the proposed human-behavioral data elements. To date, no "gold standard" has been established for collecting this data. Examples of methods used to measure human behavior identified in the literature include direct observation (Bugoro et al., 2011, Geissbühler et al., 2007, Huho et al., 2013a, Monroe et al., 2015, Finda et al., 2019), providing a digital watch to a household member and having him/her record information for each household member at specified times (Cooke et al., 2015), and using survey questions (Bayoh et al., 2014, Bradley et al., 2015, Geissbühler et al., 2007, Huho et al., 2013a, Kamau et al., 2018, Killeen et al., 2006, Moiroux et al., 2014, Russell et al., 2011, Seyoum et al., 2012, Thomsen et al., 2016). When selecting a methodological approach, it is important to consider its strengths, limitations, feasibility, as well as potential biases in the chosen method. It is also important to consider the scale at which it can realistically be applied (village, district, or national) and whether it can provide individual-level data that can be disaggregated and linked to other complementary data such as malaria infection status, socioeconomic status, education, and other potential risk factors.

Survey questions have to date been the most widely used option for collecting the proposed human behavioral data elements. In addition to the standard survey questions on ITN use described in the current Roll Back Malaria Household Survey Indicators for Malaria Control (DHS, 2013a), information on location and sleeping patterns throughout the night can be collected, for example using a set of five additional questions asked for each household member (Box 4). Variations of the survey questions put forward in this paper have been used in previous studies (Bayoh et al., 2014, Geissbühler et al., 2007, Huho et al., 2013a, Killeen et al., 2006, Msellemu et al., 2016, Seyoum et al., 2012), including one that triangulated the results of survey questions with direct observation data (Geissbühler et al., 2007). When survey questions are used, the phraseology of the questions and locally appropriate translations are crucial to ensure a clear understanding by study participants and accurate responses. Even when implemented well, there are a number of limitations associated with surveys, including the potential for bias in responses (Van de Mortel, 2008). Additionally, using a small set of questions, such as those presented in Box 4, requires making assumptions to estimate an individual's hourly location throughout the night, rather than measuring directly for each hour or time interval. For an individual who reported using an ITN the night before, this approach assumes he or she was under the protection of an ITN consistently from the time they reported sleeping until the time they reported waking up. Therefore, this approach inherently will not capture micro-level behaviors such as getting in and out of bed throughout the night, sleeping up against the net, or leaving it partially open during the night (Harvey et al., 2017, Msellemu et al., 2017).

Direct observation of human behavior by mosquito collector, household member, or trained data collector can provide a high level of detail on human behaviors throughout the night, compared to survey questions. However, reactivity, described as a change in behavior due to the presence of an observer, must be considered (Bernard, 2012). This phenomenon tends to decrease over time suggesting the potential value of multiple nights of observation or an acclimation period (Gittelsohn et al., 1997, Harvey et al., 2009). Certain groups or activities may be inherently easier to observe than others, which can bias results. If observations are taking place in the peri-domestic setting only, it is important to consider how time spent away from home will be measured and recorded. This is particularly important when occupations such as fishing, forest work, or migratory farming are practiced, as these may result in significant exposure to mosquito bites far from people's homes (Gryseels et al., 2015). When possible, data collection should be considered in additional locations where people spend significant time overnight, such as farm plots (Nonaka et al., 2010, Swai et al., 2016a, Edwards et al., 2019). Community entry is critical to the success of observations. Therefore, prior to conducting observations, community leaders and household members should be fully briefed on the objectives of the study and the reason for observation. Further, observations require adequate supervision to ensure data quality, and if data collectors are from outside of the study community, a clear security plan to maintain safety throughout the night should also be put in place. The decision on who will carry out observations may depend on a number of factors including available resources and security. It is important to consider how the identity of the observer (household member, community member, or trained data collector) might impact the quality of the data as well as the behavior of household members being observed.

There are a variety of platforms for collecting the critical data elements (Box 7.2) and programs can select the option that works best for them based on the considerations outlined here. Platforms for collecting critical human behavioral data elements include routine entomological monitoring, national surveys, and stand-alone research studies. Collecting human behavior data within entomological surveillance sites provides an opportunity to collect vector and human behavior data within the same population sample and to track changes across seasons and over time. Many countries now conduct routine entomological surveillance, which often includes monitoring indoor and outdoor biting rates. Collecting a small set of human-behavioral variables (Box 7.2) in conjunction with ongoing entomological collections could provide an opportunity to improve the decision-making value of data from these programmatic surveillance platforms; if both types of data can be disaggregated down to matching one-hour periods or disaggregated at least to small enough time intervals to intuit the potential for indoor interventions to protect community members.

Including a standard set of relevant questions in large-scale surveys (Box 7.4), such as malaria indicator surveys, provides the opportunity to collect information across a broad demographically and geographically representative sample, allowing comparison of human behavior across settings without substantively increasing time or resource inputs. When using such national-scale survey platforms, it may not be possible to ensure the person(s) answering the survey questions is knowledgeable about household members' behavior, which represents a limitation of this option. Further, it is difficult to capture seasonal trends in human behavior due to the intermittent, cross-sectional design of most large-scale surveys and entomological and human behavioral data may not be available from the same time and place.

Stand-alone research studies may also include layered entomological and human behavioral data, and it can be valuable to collect epidemiological data in the same population sample. This data can, and when possible, should be collected during epidemiological evaluations of vector control tools (Killeen et al., 2017b).

There are inherent trade-offs between the level of detail that can be obtained and the scale at which a method can be implemented. When possible, use of multiple methods and method triangulation of the results from such different, complementary approaches should be considered to mitigate limitations of individual methods.

Box 7.4 Suggested survey questions that can be used as part of a stand-alone survey or included as part of a national survey. These questions can be asked in addition to standard survey questions on ITN use described in the current Roll Back Malaria Household Survey Indicators for Malaria Control. Defined categorical options should be offered as answers. For time-related questions 1, 2, 4 and 5, options are hour-long time periods starting every hour e.g. 18:00 to 19:00, 19:00 to 20:00 etc.

1. During what time period did [name] go to sleep yesterday?
2. During what time period did [name] wake up today?
3. Did [name] sleep indoors or outdoors last night?
4. If [name] slept indoors, during what time period did [name] finally go indoors for the evening last night?
5. If [name] slept indoors, during what time period did [name] first go outdoors for the day this morning?

Considerations for statistical analysis and sample size calculation

The variability and reliability of these estimates should be presented using the 95% confidence interval calculated from data sets of adequate sample size, containing multiple observations of human and vector behavior through space and time. It is possible to estimate sample sizes of proportions by classifying human behaviour or mosquito behaviour into categories. When considering the toolbox of vector control interventions that are currently available, appropriate classifications for human behaviour may be categorised as 1) indoors asleep, 2) indoors awake or 3) outdoors. Similarly, after estimating average bedtime as a cut off, vector mosquitoes may be classified by the proportion of bites that occur 1) indoors before bed, 2) indoors after bed 3) outdoors. While this is a simplification, it is adequate to allow the calculation of minimum sample sizes to precisely detect a specified difference at either the individual (household), or village (cluster) level provided some information on the variability in human and vector behaviour is available *a priori* to account for differences between villages (Hayes and Bennett, 1999). Other methods commonly used for estimating mosquito data are simulation based methods, which detect true effect sizes for specified densities of mosquitoes biting indoors or outdoors as well as the expected statistical uncertainties (Johnson et al., 2015). Regardless of the method, data used for the sample size calculation should be obtained locally.

7.4 Discussion

Ongoing transmission of malaria is a direct result of the overlap between human and vector behaviors, and intervention access and use. It is essential to look at these pieces together for a more complete picture of malaria exposure. This information can inform selection of appropriate vector control tools for implementation in a particular scenario, guide prioritization of interventions in resource-constrained environments, and allows for monitoring of temporal changes in performance of interventions that may be influenced by human and/or vector behavior. For example, given the Kenya example illustrated in Figures 7.1-2, programs might wish to focus on indoor-oriented interventions to further reduce the indoor nighttime exposure to *An. arabiensis*. With increasing resistance to pyrethroids reported among malaria vectors throughout sub-Saharan Africa, continued indoor biting despite high coverage of ITNs may indicate a need to distribute piperonyl butoxide (PBO) or next generation nets. Likewise, monitoring would provide insights into to whether the proportion of exposure to vector bites occurring outdoors is stable or changing over time, as even small increases in outdoor exposure have the potential to impact transmission dynamics (Sherrard-Smith et al., 2019). In other contexts, exposure patterns may point to the need for outdoor interventions to protect people when outdoors and awake, or to the importance of strengthening behavior change interventions to increase ITN use during sleeping hours.

Longitudinal data across seasons can highlight the impact of seasonal variation in vector and/or human behavioral data. For example, in some contexts, people may spend more time outside when the weather is hot, compared to when the weather is cool or rainy (Monroe et al., 2015, Monroe et al., 2019a). Outdoor sleeping and large-scale socio-cultural events may also increase during this time and sleeping patterns may differ during planting and harvesting seasons (Monroe et al., 2015, Monroe et al., 2019a). ITN use can also vary seasonally due to factors such as heat, mosquito density, and perceived malaria risk (Koenker et al., 2019). Disaggregation of these indicators by age and sex can help programs to further target interventions by demographic group, where needed. For example, in some settings, adolescent and adult males spend more time outdoors at night, are more likely to engage in nighttime livelihood activities, and more likely to sleep outdoors (Monroe et al., 2015, Monroe et al., 2019a, Monroe et al., 2019b, Ahorlu et al., 2019). These socio-demographic factors should be considered in combination with biological factors such as transmission intensity, vector density, and EIR when interpreting the data and considering how additional interventions could be targeted.

The approach presented in this paper provides improved estimates of biting risk by accounting for the availability of human hosts indoors and outdoors as well as the protection provided by an ITN or other personal protection measures. Beyond biting risk, there are wide-ranging applications for this approach. The key parameter values estimated by considering human-vector interaction can be used as input values and/or to validate host-vector interaction-based models, with the potential to improve their prediction accuracy (Chitnis et al., 2008, Churcher et al., 2015, Griffin et al., 2010, Kiware et al., 2012, Kiware et al., 2017). Transmission modeling integrates metrics that describe mosquito and human interaction, net use and IRS coverage, to holistically determine the efficacy of vector control interventions and the corresponding probable epidemiological impact (Kiware et al., 2017, Eckhoff, 2011, Griffin et al., 2016, Griffin et al., 2010). These models make assumptions about the exposure to infectious bites that remains after deploying ITNs or IRS to a community that are already based on data such as those outlined above. Therefore, improving the quality and quantity of these data can help refine transmission and statistical model predictions of public health impact (Bhatt et al., 2015a, Winskill et al., 2017).

Previous work has highlighted the importance of heterogeneity in entomological inoculation rates for malaria transmission (Smith et al., 2007) as well as the subsets of humans and mosquitoes contributing most to transmission (Gonçalves et al., 2017). The changes suggested for the collection of routine data that are made here will not directly address how heterogeneity in exposure risk within and between individuals across nights might affect malaria burden or control efforts. When possible, the suggested practices for collection of routine data should be implemented in a manner that allows these indicators to be directly linked to epidemiological outcomes like malaria incidence and prevalence, so that the importance of such underlying heterogeneities in exposure risk and intervention suitability can be better understood.

Further, while the approach presented here is useful for measuring patterns of human exposure to malaria vectors, complementary qualitative data is needed to characterize relevant nighttime activities, sleeping patterns, and intervention use in greater depth, to better understand groups that may be at higher risk, as well as to identify barriers and facilitators to malaria prevention in different contexts (Monroe et al., 2019a, Monroe et al., 2015, Monroe et al., 2014). This information can be used to guide selection and deployment of context-appropriate interventions.

7.5 Conclusions

Collecting and integrating a minimum set of human behavioral data elements - the proportion of the human population indoors, asleep, and using an ITN throughout the night - with hourly indoor and outdoor mosquito biting rates can provide a more accurate measure of when and where people are at risk and how best to protect them. This information can help to guide National Malaria Control Programs in deploying interventions targeting specific vector and human behaviors and inform target product profiles for new tools (Killeen et al., 2017b). If collected and used consistently, the critical data elements and indicators presented in this article can contribute to an improved understanding of how malaria transmission persists in the context of current interventions and how exposure patterns may change as new vector control tools are introduced, as well as the potential impact and limitations of these tools. This article is intended to consolidate understanding around work on this topic to date and provide a consistent framework for building upon it. Additional work is needed to address remaining questions, including further development and validation of methods for entomological and human behavioral data collection and analysis.

7.6 Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Competing interests

The authors have declared that they have no competing interests.

Funding

This work was made possible by the generous support of the American people through the United States Agency for International Development (USAID) and the President's Malaria Initiative (PMI) under the terms of USAID/JHU Cooperative Agreement No. AID-OAA-A-14-00057 (VectorWorks Project). The contents are the responsibility of the authors and do not necessarily reflect the views of USAID or the United States Government.

Authors' contributions

AM, SM, FO, SK, and GK conceptualized the manuscript. **AM** drafted the manuscript and SM, FO, SK, NFL, HK, ESS, JG, and GK made significant contributions to the content. All authors reviewed and approved the final manuscript.

Acknowledgements

The authors would like to thank Drs. Eric Ochomo, Seth Irish, Lia Florey, Matthew Lynch, and Nicodemus Govella for their feedback on this manuscript.

Chapter 8: Discussion

The need for improved targeting of interventions is becoming increasingly urgent in the context of stalled progress and an uncertain funding landscape. To optimize malaria prevention efforts, it is critical to identify context-specific approaches that will produce the highest impact. These approaches must be informed by an understanding of when and where gaps in prevention occur. This thesis highlights important opportunities to better measure, characterize, and address gaps in malaria prevention. Key areas to consider include levels of intervention access and use, product effectiveness, and gaps in protection that remain in the context of good coverage of core vector control interventions (Figure 8.1). This information can point to discrete opportunities for action including structural or social and behavioral interventions, and/or supplemental vector control tools. While presented here as separate challenges, these issues are often related and should be positioned within the broader social, economic, and political context.

8.1 ITN Access

ITN access is the most important predictor of use, and in most places, a high proportion of people with access to ITNs within their households use them (Koenker and Kilian, 2014).To date, few countries have achieved and sustained target levels of access, suggesting that additional gains in malaria prevention can be achieved by increasing access to ITNs (Koenker et al., 2018). Access can be achieved and sustained by ensuring an appropriate number of ITNs is distributed through efficient distribution channels.

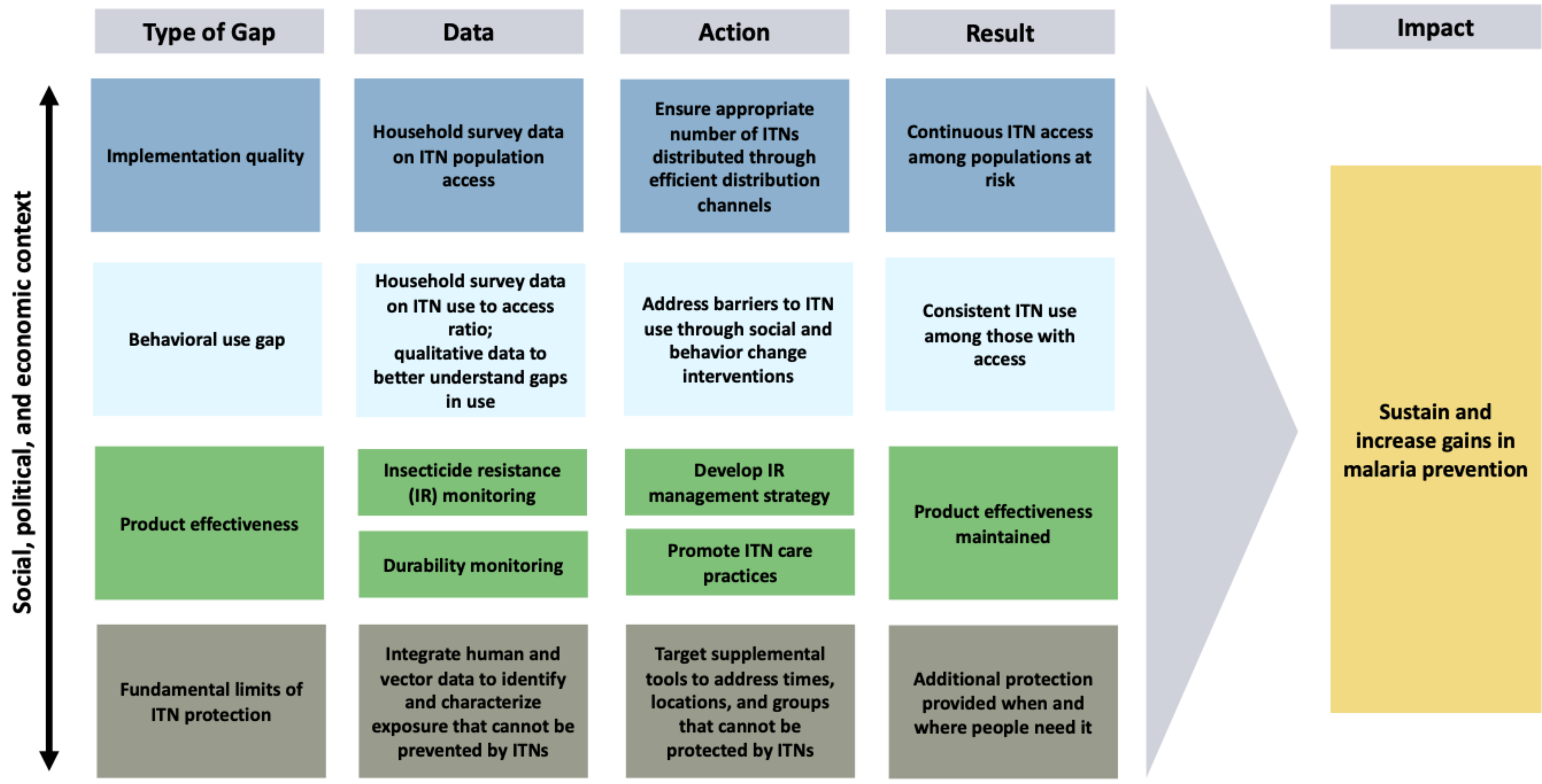

Figure 8.1 Opportunities to close the malaria prevention gap
Four key areas can be considered to help close the malaria prevention gap: implementation quality of interventions, levels of use of the intervention, the effectiveness of the intervention, and protection gaps that can remain. The social, economic, and political landscape can also have an impact across malaria prevention efforts and can significantly impact broader malaria transmission dynamics.

An increase in the quality and number of available distribution channels has been achieved in recent years. Mass distribution campaigns remain an important mechanism for distribution in many settings, particularly for achieving high levels of coverage rapidly. However, mass distribution campaigns are generally carried out every three years and gaps in coverage can begin to appear soon after distribution due to factors such as deterioration of the ITNs, loss of ITNs, and population growth (Kilian et al., 2010). A number of countries have begun utilizing continuous distribution channels, including school, health facility, community, and commercial sector channels, as part of their ITN strategy (Koenker et al., 2013b, Willey et al., 2012, Eze et al., 2014, Grabowsky et al., 2007, Stuck et al., 2017, Girond et al., 2018, Zegers de Beyl et al., 2017). The WHO now recommends use of continuous distribution channels in combination with mass distribution campaigns to ensure high levels of access are maintained without interruption (WHO, 2017a).

8.2 ITN Use

While reported use is generally high among those with access, this is not the case in all contexts. Understanding barriers and facilitators to use in settings and among groups with sub-optimal levels of use can help to inform effective social and behavior change interventions. Key factors influencing ITN use identified in Ghana and Zanzibar are consistent with results from other research studies which identified heat and low perceived risk as primary barriers, and disease prevention, a good night's sleep, and personal experience with the disease as key motivators (Pulford et al., 2011, Msellemu et al., 2017).

An important addition is the need to define the concept of use more broadly. National malaria surveys include standardized questions on ITN use the previous night (DHS, 2013a). While this indicator is useful for estimating population-level use, it fails to account for a number of key factors that may impact its accuracy in measuring the extent of protection currently provided by ITNs, as well as the maximum level of protection that could be obtained. Factors such as patterns of nighttime indoor and outdoor sleeping and activity, variability in sleeping spaces, differences in net use across seasons, among others, are not reflected in this measure. ITN use is a complex behavior that can vary by time of night, season, and over time. A more holistic understanding of ITN use practices and times when ITN use is not feasible is needed, particularly in settings where a large gap between access and use remains. This information can help to shape effective social and behavior change interventions aimed at closing the gap between access and use.

8.3 Product Effectiveness

Beyond access and use, it is important to ensure the malaria prevention tool that is used is effective in a given context. In the case of ITNs this involves understanding ITN durability, including physical integrity, attrition, and insecticidal content and bio-efficacy over time. Durability monitoring can provide important information on how environmental and human behavioral factors can impact durability of different ITN products under field conditions. Human behavior can contribute to ITN wear and tear or maintenance and can have a significant impact on the longevity of ITNs. Research studies in Nigeria found that net survival varied significantly across different socio-ecological settings based on household behaviors (Kilian et al., 2015). Effective care practices, especially tying nets up when they are not in use and careful tucking and untucking, can extend the life of a net. Behavior change communication has been successfully utilized to increase effective care practices and extend ITN longevity (Helinski et al., 2015, Koenker et al., 2015). Effective maintenance practices should be promoted to help ensure available ITNs stay in good condition and are able to provide high levels of protection for as long as possible.

In addition to ITN durability, susceptibility of local malaria vectors to the insecticide can have a significant impact on the protection provided by an intervention. Insecticide resistance in malaria vectors is widespread across all five WHO regions that have ongoing malaria transmission. It affects all vector species and insecticide classes and has increased globally over the past decade (WHO, 2012a, WHO, 2018a). Selection of vector control tools should take into consideration the susceptibility of local malaria vectors and monitoring of resistance intensity and mechanisms is important to inform programmatic decision-making. Managing insecticide resistance will be important to sustaining gains in malaria control, and can be achieved through insecticide rotation, use of combinations of insecticides, development of insecticides with new modes of action, as well as using insecticides only when and where they are most appropriate (WHO, 2018a).

There have been a number of recent innovations aimed at fighting insecticide resistance. Research studies on chlorfenapyr, an insecticide that works through a new mode of action, have provided evidence that it is effective at killing resistant mosquitoes (N'Guessan et al., 2016, Bayili et al., 2017). Pyriproxyfen, which inhibits mosquito growth and reproduction, combined with permethrin, the standard insecticide treatment for ITNs, has shown some benefit over permethrin alone in areas with resistant vectors (Tiono et al., 2018, Lwetoijera et al., 2014b, Ngufor et al., 2014). The addition of a synergist, piperonyl butoxide (PBO), to pyrethroid nets has also been investigated. Available evidence suggests pyrethroid-PBO nets are more effective than standard pyrethroid nets in settings with insecticide resistance (Gleave et al., 2018, Protopopoff et al., 2018). While pyrethroid-PBO nets can help to maintain protection in some settings, they should not be considered a tool for insecticide resistance management, and broader insecticide resistance management strategies are essential (WHO, 2017b).

Development and deployment of insecticide-based solutions to combat resistance can be costly. It is important to consider sustainable, complementary approaches that do not rely on insecticides as part of integrated vector control strategies. Effective environmental management played a fundamental role in the historic decline of malaria in many parts of the world, and should continue to be considered a critical component of integrated vector management approaches (Packard, 2007). Environmental management has been shown to reduce the incidence of malaria, without relying on insecticides (Keiser et al., 2005). It can include long-term changes to land, water, or vegetation such as installing drains, draining swamps, or other engineering approaches, or temporary changes to the environment such as intermittent irrigation to reduce breeding sites (Keiser et al., 2005).

It can also include changes to human habitations that can limit human contact with malaria vectors (Keiser et al., 2005). Housing improvements, such as screened windows and closed eaves, can protect people during all times they are indoors and are not dependent on daily user compliance. Available evidence suggests that housing improvements are associated with reduced risk of malaria transmission (Tusting et al., 2015, Wanzirah et al., 2015). In Zanzibar, many households in the study sites had already begun screening their windows to prevent mosquitoes and other insects from entering, as well as to increase privacy and security within their home. There is an opportunity to accelerate this trend toward housing improvements by promoting the perceived benefits for both malaria prevention and privacy, exploring lower-cost solutions for wider adoption, and ensuring that the housing improvements carried out are effective at preventing mosquitoes from entering.

8.4 Identifying and targeting exposure that remains

While optimizing the impact of ITNs through high levels of access and use of effective products is essential, ITNs alone will not be sufficient in many contexts to eliminate malaria. To close the malaria prevention gap, it is crucial to understand when and where people continue to be exposed to malaria vectors, what they are doing during these times, and which groups of people are at greatest risk. This understanding requires integration of data on intervention use, and human and vector behavior throughout times when local malaria vectors are active. This thesis brought together in-depth measurement and characterization of human and vector behavior that can contribute to a more complete picture of malaria transmission dynamics.

Common categories of night time activities emerged across studies in sub-Saharan Africa identified through the review of published literature and were consistent with findings of the primary research study in Zanzibar. Gaps in protection can occur for large segments of the population during routine night time activities occurring outside of sleeping hours and during special socio-cultural events such as weddings or funerals, as well as for certain groups such as people who engage in night time occupations, travelers, and migrant or displaced populations (Gryseels et al., 2015, Dunn et al., 2011, Monroe et al., 2015, Monroe et al., 2014).

These categories of activities and groups of people can help to drive development and deployment of supplemental tools to target remaining exposure. While there are few supplemental tools that currently have a WHO recommendation, there is some evidence for tools that are currently available or in the pipeline. A systematic review and meta-analysis of vector control tools beyond ITNs and IRS found that the most evidence exists for insecticide-treated materials, mosquito-proof housing, larval source management, spatial repellents, and topical repellents (Williams et al., 2018). Additionally, mass drug administration with ivermectin can kill vectors that feed on treated humans and reduce malaria infections (Foy et al., 2019).

Spatial repellents or push-pull systems could provide protection to those carrying out household chores in the peri-domestic space or at fixed social or entertainment venues. Spatial repellents have the potential to prevent malaria vectors from entering a space (Achee et al., 2012), while push-pull systems utilize both repellents (push) and attractant-baited traps (pull) to reduce vector populations (Menger et al., 2014).While these interventions have the potential to reduce human exposure to malaria mosquitoes, to date, there is not sufficient evidence on their impact on malaria infection to recommend wide-scale use (Maia et al., 2018).

People engaged in night time occupations, such as security or fishing, may benefit from personal protection measures. Topical repellents have the potential to reduce individual exposure to malaria vectors, however there is not sufficient evidence to suggest topical repellents reduce malaria incidence, and compliance remains a critical concern (Govere et al., 2000, Le et al., 1994, Maia and Moore, 2011, Ogoma et al., 2012, Maia et al., 2018). Insecticide-treated clothing has been shown to reduce exposure to malaria vectors in some contexts, and in a smaller number of studies, protection against malaria infection (Kimani et al., 2006, Banks et al., 2014). Personal protection measures, including topical repellents, insecticide-treated clothing, and spatial repellents do not have sufficient evidence for a WHO recommendation for use as a public health intervention at this time. However, topical repellents and insecticide-treated clothing are recommended for personal bite prevention in certain population groups (WHO, 2019).

Effective targeting of supplemental interventions is particularly important in countries moving toward elimination. Often, a high proportion of cases are observed among men and hard to reach groups, such as migrant populations, and current malaria interventions are unlikely to adequately address these changes (Cotter et al., 2013). In these contexts, effective targeting of interventions is critical and finer scale information on the epidemiological, ecological, and socio-cultural context is needed, including identification of locations and groups at risk (WHO, 2017c). In Zanzibar, seasonal workers were perceived as being at higher risk of being infected with malaria and as having less access to prevention and treatment services. Additional investigation to better understand networks of higher risk groups, research to link specific activities to malaria infection, and programs specifically targeting these groups with appropriate packages of interventions should be explored.

8.5 Gender considerations for malaria prevention

Gender norms can vary across settings and over time and can have a significant impact on a range of health behaviors and outcomes (Albrecht et al., 2003). Gender norms can impact all aspects of malaria prevention, including access to and use of prevention measures, ITN care and repair practices that can impact longevity and product effectiveness, as well as patterns of malaria exposure related to division of labor within the household, participation in entertainment activities or employment outside of the household, sleeping patterns, and travel (WHO, 2007, Tolhurst and Nyonator, 2006, Dillip et al., 2018).

The shift toward universal coverage of ITNs is designed to close gender gaps in protection, and research from this thesis suggests that gains in ITN access can further improve use among groups with sub-optimal levels of use. While women of reproductive age and young children are rightfully prioritized when there are insufficient ITNs for household members, age and gender disparities begin to disappear as access increases, though they may not disappear entirely.

While access is a primary determinant of use, a number of studies have noted gender disparities in ITN use, with a higher proportion of women using an ITN compared to men (Garley et al., 2013, Graves et al., 2011, Kateera et al., 2015). In some contexts, such as in the qualitative work in Ghana, gender norms were reported to impact use of ITNs due to a perception that strong men do not need to use them. Gender norms can also influence product effectiveness and longevity through ITN maintenance practices. Studies across several sites found that daily net care fell within women's household responsibilities, though both men and women expressed motivation to maintain nets. (Loll et al., 2014, Dillip et al., 2018, Scandurra et al., 2014, Hunter et al., 2014). Inclusive messaging is needed to promote ITN use and proper care practices among males and females of all ages.

The review of published literature on nighttime human behavior found some gender differences in night time activities. Women were more likely to spend time outdoors in the peri-domestic setting, inside or nearby the home doing household chores, while men were more likely to spend time away from home at night for entertainment or livelihood activities, and more likely to sleep outside. This finding was echoed in the primary research in Zanzibar where women and children spent more time in the peri-domestic setting, while adolescent and adult men spent more time away from home. In this context, males were also more likely to come to Zanzibar from mainland Tanzania for seasonal work. Identification of higher risk groups and targeted interventions, such as occupation-based vector control interventions, could be useful, particularly in elimination contexts (Cotter et al., 2013).

8.6 Research for improved policy and practice

In addition to ensuring the right data is collected and integrated, it is essential that research findings are available and useful for programmatic and policy-level decision-making. The future of malaria prevention must be built on leadership from affected countries and local solutions. Primary research in this thesis was undertaken in partnership with malaria control and elimination programs and local research institutes with the goal of providing programmatically useful recommendations. Partners were directly involved in data collection and analysis and interpretation of data, and final results were presented back to the malaria control and elimination programs and partners. In Zanzibar, the results were also presented to the Zanzibar Malaria Elimination Advisory Committee and will help to inform Zanzibar's malaria elimination strategy moving forward.

Parts of this thesis were shared and discussed at a number of international forums that can help to shape policy. This includes a workshop on residual malaria transmission hosted by the WHO and Ifakara Health Institute; a symposium at the American Society of Tropical Medicine and Hygiene meeting; presentations at the Alliance for Malaria Prevention, the

RBM Vector Control Working Group, the RBM Monitoring and Evaluation Reference Group, and the Multi-lateral Initiative on Malaria meetings; and through multiple presentations to PMI headquarters and mission staff.

Chapter 9: Conclusions

To sustain and increase gains in malaria prevention, improved targeting of context-appropriate packages of interventions will be critical. This thesis highlighted opportunities to better measure, characterize, and address human behavioral gaps in malaria prevention. This information will allow for more effective programmatic responses, whether through strengthening existing tools or through development and deployment of complementary interventions.

The protection provided by ITNs, a core vector control tool, can be optimized by ensuring high levels of access, use, and product effectiveness. Access is the most important determinant of ITN use and gaps in population access suggest additional gains can be achieved through increasing access in most contexts. Sustaining high levels of ITN access can also reduce age and gender gaps in use, ensuring that all people at risk are protected. While achieving and sustaining high levels of access is critical, it is also important to understand why some people with access to an ITN do not use it consistently or care for it properly. This thesis highlighted the importance of viewing use practices through a broader lens. Information on patterns of ITN use among those with access, and individual and contextual barriers to consistent use, can help to inform effective social and behavioral interventions.

While significant protection can be provided by ITNs with high levels of access and use, there are times when people can be exposed to malaria vectors when ITN use is not feasible. This may include routine night time activities, night time occupations, large scale events, and travel and migration. It is crucial to understand the protection conferred by ITN use, as well as gaps in protection that require supplemental tools and approaches. A clear and integrated understanding of human activity and sleeping patterns, intervention use, and local vector behavior can dramatically improve our understanding of malaria risk.

This thesis contributed to an improved understanding of malaria prevention in sub-Saharan Africa through a range of methodological approaches, including secondary analysis of large-scale survey data from ten countries in sub-Saharan Africa, primary research utilizing quantitative and qualitative methods, a review of the published literature, and development of a standardized approach to measuring human exposure to malaria vectors. Evidence that comes out of this work will help to inform malaria control and elimination programs through effective targeting of existing tools, complementary tools, and social and behavior change interventions.

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YOHANNES, M. & BOELEE, E. 2012. Early biting rhythm in the Afro-tropical vector of malaria, Anopheles arabiensis, and challenges for its control in Ethiopia. *Med Vet Entomol,* 26**,** 103-5.
YUKICH, J. O., TAYLOR, C., EISELE, T. P., REITHINGER, R., NAUHASSENAY, H., BERHANE, Y. & KEATING, J. 2013. Travel history and malaria infection risk in a low-transmission setting in Ethiopia: a case control study. *Malaria journal,* 12**,** 33.
YUKICH, J. O., ZEROM, M., GHEBREMESKEL, T., TEDIOSI, F. & LENGELER, C. 2009. Costs and cost-effectiveness of vector control in Eritrea using insecticide-treated bed nets. *Malaria journal,* 8**,** 51.
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Curriculum Vitae

Profile

Global health professional with over 10 years of experience working in East, West, and North Africa. Expertise in infectious diseases, specializing in malaria research and programs. Recognized expert in targeting and optimization of vector control tools, residual malaria transmission, and development of methods and indicators for integrating human behavioral and entomological data. Extensive experience leading diverse research teams in field-based settings. Strong record of publishing research findings in peer-reviewed journals and presenting at international forums. Broad-based program management experience including provision of technical assistance to field programs, work planning, budget tracking, and ensuring submission of timely, high-quality deliverables for large-scale global health programs. Strong written and oral communication skills with the ability to communicate effectively to a range of audiences. Known as someone who takes initiative, identifies and cultivates mutually beneficial partnerships, and effectively bridges research and programmatic priorities.

Experience

Senior Program Officer, Johns Hopkins Center for Communication Programs (CCP): 2017-present

- Providing technical expertise to improve long-lasting insecticide-treated net (LLIN) distribution systems through VectorWorks, a 5-year US Agency for International Development (USAID) project.
- Responsible for conceptualizing, designing, and overseeing research activities related to optimization of vector control tools, identifying the magnitude and drivers of residual malaria transmission, and development of methods and indicators for measuring human-vector interaction.
- Translating research findings into programmatic recommendations.
- Identifying and cultivating research partnerships and strengthening capacity for social science research.
- Providing technical input and high-level oversight for VectorWorks country programs.
- Engaging at global level to share knowledge and best practices through the American Society of Tropical Medicine and Hygiene (ASTMH), the Alliance for Malaria Prevention (AMP), and the Roll Back Malaria Vector Control Working Group (VCWG).
- Leading development and roll-out of gender training for CCP headquarters and field staff through CCP's Gender Community of Practice.
- Carrying out formal supervisory duties.

- Working as part of team to develop and implement Center-wide initiatives to increase employee engagement.
- Part of successful proposal-writing teams for USAID, Unitaid, and DFID-funded projects.

Program Officer I/II, CCP: 2014-2017

- Oversaw project activities for VectorWorks Ghana, including provision of technical assistance to the project's field team, tracking a $2 million annual budget, and work planning.
- Spearheaded gender analysis, development of a project-wide gender strategy, and integration of gender considerations across project activities. Developed and facilitated gender training for project field teams.
- Carried out process evaluation of Zanzibar's continuous LLIN distribution system and put forward actionable recommendations for improvement.
- Led concept note and protocol development for a residual malaria transmission study in Zanzibar. Hired and trained data collection team and supervised a team of 20 in the field. Cultivated effective partnerships with Ifakara Health Institute and the Zanzibar Malaria Elimination Program.
- Spent seven weeks in a field-based setting conducting a qualitative study on outdoor sleeping patterns and nighttime activities in northern Ghana. Published results and presented findings at the American Society of Tropical Medicine and Hygiene, the Alliance for Malaria Prevention, and the Vector Control Working Group meetings.
- Spearheaded Center-wide staff engagement initiative.
- Identified and cultivated new, synergistic research collaborations.

Visiting Research Scientist, Ifakara Health Institute: 2016-Present

- Collaborating on research studies investigating the magnitude and drivers of residual malaria transmission in East and West Africa. Responsible for leading and providing capacity strengthening for human behavioral research.
- Designed and led qualitative research workshop to meet an expressed need for capacity strengthening.

Qualitative Researcher, Rakai Health Sciences Program (RHSP): 2013

- Conducted a qualitative evaluation of the PeerCARE study, a randomized trial designed to assess the effectiveness of a peer support intervention on HIV care engagement and preventive care utilization among pre-ART adults in Rakai District, Uganda.
- Responsible for development of qualitative research protocol and tools.
- Directed the efforts of a Ugandan research team in the collection of data to improve the PeerCARE intervention and maximize its efficiency.
- Built in-country capacity and sustainability by providing training in qualitative data analysis, such that study team members could provide technical guidance in the future.

Graduate Student Researcher, Johns Hopkins Center for Communication Programs: 2013

- Responsible for analyzing data from the Uganda Culture of Net Use study and synthesizing the results into two manuscripts for publication in a peer-reviewed journal. Drafted, edited, and managed the manuscripts prior to publication and conducted the associated literature reviews. Presented the findings to the Alliance for Malaria Prevention.

Research Assistant, Johns Hopkins Bloomberg School of Public Health: 2012- 2013

- Systematically reviewed and synthesized the results of published studies on HIV prevention interventions in low and middle-income countries. Worked independently and as part of a research team to conduct primary and secondary literature searches, to identify the epidemiological quality of studies, and to abstract, code, and synthesize research findings. The results of this research were used to inform World Health Organization guidelines for HIV prevention programs.

Health Development Volunteer, United States Peace Corps: 2010- 2012

- Lived in a field-based setting in rural Morocco and worked with a diverse range of stakeholders to develop and carry out program activities.
- Conducted an extensive community needs assessment which informed the development and implementation of a primary school health curriculum, maternal and child health classes and educational video, and organization of a community-wide health screening event.
- Selected by Peace Corps to develop and lead training activities for 60 new Peace Corps Volunteers on how to initiate and sustain effective health education programs in rural communities.

English Teacher, YBM ECC English Academy: 2008- 2009

- Developed and implemented lesson plans at a private English academy.
- Taught daily English classes to children ages 7-15.
- Monitored and measured student progress and completed monthly reports.

LEAD Director, FIVER Children's Foundation: 2008

- Planned and facilitated leadership programs for approximately 70 youth from under-served communities in New York City; programs included health and relationship education, ethics, wilderness training, and college preparation activities.
- Supervised a staff of 8 counselors, wrote reports and evaluations, and communicated with parents.

Intern, Women Fighting AIDS in Kenya: 2007

- Assisted in provision of comprehensive services to HIV-positive women and children. Conducted outreach, education, and nutrition programs. Contributed to development of HIV/AIDS peer-education training program.

Education
Swiss Tropical and Public Health Institute
Degree received May 2019 | PhD in Epidemiology and Public Health, Health Interventions

Johns Hopkins Bloomberg School of Public Health
Degree received January 2014 | MSPH in International Health, Social and Behavioral Interventions Program

- Global Health Field Research Award Recipient*:* Awarded one of six Field Research Awards granted by the Johns Hopkins Center for Global Health in 2013. The award funded a research proposal to measure the impact of peer health workers on engagement and retention in care among people newly diagnosed with HIV in Rakai, Uganda.

- Center for Global Health Scholarship Recipient: Awarded one of eight Global Health Scholarships out of the 2012 incoming class of MPH and MSPH students at Johns Hopkins Bloomberg School of Public Health. Selected based on academic excellence and demonstrated commitment to the field of global health.

Washington University in St. Louis
Degree received May 2008 | Double major in Psychology and African Studies, minor in Women and Gender Studies

- Study abroad in Kenya: Spring 2007
- Senior Capstone: *"Closer to Home: Health and Mental Health Concerns of African Refugees Living in St. Louis"*

Relevant Publications/Presentations/Posters

- **Monroe, A.,** Moore, S., Okumu, F., Kiware, S., Lobo, N., Koenker, K., Sherrard-Smith, E., Gimnig, J., Killeen, G. *Methods and indicators for measuring patterns of human exposure to malaria vectors.* Malaria Journal, June 2020.
- **Monroe, A.,** Mskay, D., Kiware, S., Tarimo, B., Moore, S., Haji, K., Koenker, H., Harvey, S., Finda, m., Ngowo, H., Mihayo, K., Greer, G., Ali, A., Okumu, F. *Patterns of human exposure to malaria vectors in Zanzibar and implications for malaria elimination efforts*. Malaria Journal, June 2020.
- **Monroe, A.** *Social and behavioral considerations for effective vector control interventions.* Oral presentation,VCWG meeting, February 2020.
- Ahorlu, C., Adongo, P., Koenker, H., Zigirumugabe, S., Sika-Bright, S., Koka, E., Tabong, P., Piccinini, P., Segbeya, S., Olapeju, B., **Monroe, A**. *Understanding the gap between access and use: a qualitative study on barriers and facilitators to insecticide-treated net use in Ghana*. Malaria Journal, December 2019.
- Mwanga, E., Mmbando, A., Mrosso, P., Stica, C., Mapua, S., Finda, M., Kifungo, K., Kafwenji, A., **Monroe, A.,** Ogomo, S., Ngowo, H., Okumu, F. *Eave ribbons treated with transfluthrin can protect both users and non-users against malaria vectors*. Malaria Journal, September 2019.
- **Monroe, A.**, Mihayo, K., Okumu, F., Finda, M., Moore, S., Koenker, H., Lynch, M., Haji, K., Abbas, F., Ali, A., Greer, G., Harvey, S. *Human behaviour and residual malaria transmission in Zanzibar: findings from in-depth interviews and direct observation of community events*. Malaria Journal, July 2019.
- **Monroe, A.**, Moore, S., Koenker, H., Lynch, M., Ricotta, E. *Measuring and characterizing night time human behaviour as it relates to residual malaria transmission in sub-Saharan Africa: a review of the published literature.* Malaria Journal, January 2019.
- Olapeju, B., Choiriyyah, I., Lynch, M., Acosta, A., Blaufuss, S., Filemyr, E., Harig, H., **Monroe, A.**, Selby, RA., Kilian, A., Koenker, H. *Age and gender trends in insecticide-treated net use in sub-Saharan Africa: a multi-country analysis.* Malaria Journal, November 2018.
- **Monroe, A.** *Why is malaria transmission persisting in some contexts despite high coverage of vector control tools, such as LLINs and IRS? Results from recent studies across three WHO Regions*. Symposium organizer and chair, ASTMH Annual Meeting, October 2018.
- **Monroe, A**., Mihayo, K., Harvey, S., Moore, S., Lynch, M., Koenker, H., Ali, A., Msaky, D., Haji, K., Greer, G., Kiware, S., Okumu, F. *Human behavior and residual transmission in Zanzibar: insights from in-depth interviews and community*

observation of night time community events. Poster presentation, ASTMH Annual Meeting, October 2018.

- Musiba, R., Tarimo, B., **Monroe, A.,** Msaky, D., Mihayo, K., Chilla, G., Shubis, G., Greer, G., Mcha, J., Ali, A., Okumu, F., Kiware, S. *Characterization of outdoor mosquito biting and resting behaviors as one of the drivers of ongoing malaria transmission in Zanzibar.* Poster presentation, ASTMH Annual Meeting, October 2018.
- **Monroe, A.,** Zigirumugabe, S., Koenker, H., Lynch, M., Segbeya, S., Kpabitey, R., Malm, K., Olapeju, B., Babalola, S., Ahorlu, C. *Understanding the gap between access and use of insecticide treated nets in Ghana: a qualitative study across three ecological zones*. Poster presentation, ASTMH Annual Meeting, October 2018.
- Msaky, D., Chilla, G., Musiba, R., Shubis, G., Mihayo, K., **Monroe, A.**, Mcha, J., Haji, K., Tarimo, B., Kiware, S. *The implementation and impact of adapting technologies to support residual malaria transmission research: a case study in Unguja Island, Zanzibar.* Poster presentation, ASTMH Annual Meeting, October 2018.
- **Monroe, A**. *Quantifying the malaria prevention gap: proposed indicators for measuring human-vector interaction.* Oral presentation, WHO Roll Back Malaria Monitoring and Evaluation Reference Group Meeting, September 2018.
- **Monroe, A.** *Human behavioral considerations for measuring and characterizing residual malaria transmission.* Symposium oral presentation, Multilateral Initiative on Malaria Conference, April 2018.
- Zegers de Beyl, C., Acosta, A., **Monroe, A.**, Nyanor-Fosui, F., Ofori, J.K., Asamoah, O., Hornston, S., Gerberg, L., Fotheringham, M., Kilian, A., Koneker, H. *Impact of a 15-month multi-channel continuous distribution pilot on ITN ownership and access in Eastern Region, Ghana.* Malaria Journal, March 2018.
- **Monroe, A.**, Nakigozi, G., Ddaaki, W., Mulamba Bazaale, J., Gray, R., Wawer, M., Reynolds, S., Kennedy, C., Chang, L. *Qualitative insights into implementation, processes, and outcomes of a randomized trial on peer support and HIV care engagement in Rakai, Uganda*. BMC Infectious Diseases, January 2017.
- **Monroe, A.**, Asamoah, O., Lam, Y., Koenker, H., Psychas, P., Lynch, M., Ricotta, E., Hornston, S., Berman, A., Harvey, S. *Outdoor Sleeping and other night-time activities in northern Ghana: implications for residual malaria transmission and malaria prevention*. Malaria Journal, January 2015.
- **Monroe, A.** *Outdoor sleeping and other night-time activities in northern Ghana: implications for malaria prevention*. Oral presentation, VCWG meeting, January 2015.
- **Monroe, A.** *Where nets are not enough: Recent findings on non-use of LLINs and thoughts about the need for alternatives.* Oral presentation, AMP meeting, January 2015.
- Leonard, L., Diop, S., Doumbia, S., Sadou, A., Mihigo, J., Koenker, K., Berthe, S., **Monroe, A.**, Bertram, K., Weber, R. *Net use, care and repair practices following a universal distribution campaign in Mali*. Malaria Journal, November 2014.
- **Monroe, A.** *Potential implications of outdoor-sleeping behaviors and nighttime activities for malaria control in Upper West and Northern Regions of Ghana*. Poster presentation, ASTMH Annual Meeting, November 2014.
- **Monroe, A.** *Impact of a Peer Intervention on Engagement in Prevention and Care Services among HIV-Infected Persons Not Yet on Antiretroviral Therapy: A Qualitative Evaluation of a Randomized Trial in Rakai, Uganda*. Oral presentation, International Conference on HIV Treatment and Prevention Adherence, June 2014.

- Lam, Y., Harvey, S., **Monroe, A.**, Muhangi, D., Loll, D., Kabali, A., Weber, R. *Decision-making and intra-household allocation of bednets in Uganda: Do households prioritize the most vulnerable members?* Malaria Journal, May 2014.
- **Monroe, A**., Harvey, S., Lam, Y., Muhangi, D., Loll, D., Kabali, A., Weber, R. *"People will say that I am proud": a qualitative study of barriers to bed net use away from home in four Ugandan districts*. Malaria Journal, March 2014.