ANTI-MALARIAL INTERVENTIONS IN EAST AFRICAN COUNTRIES: AVAILABILITY, COMPLIANCE AND IMPLICATIONS FOR CONTROL

by

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To my father, Gerald P. Larson (1948-1974)

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CHAPTER I

INTRODUCTION

1.1 Introduction

1.1.1 Malaria

Malaria is a major threat to human health worldwide and is found almost exclusively in the poorest countries on the planet. Malaria is caused by the entry and subsequent reproduction of one of 5 species of the Plasmodium parasite into the human bloodstream and transmitted from and to mosquitoes of the genus Anopheles. Malaria is a major cause of mortality and sickness, particularly in children in Sub-Saharan Africa [Organization, 2011]. True prevalence and incidence numbers are unknowable due to the deep problem of data quality in malaria endemic countries. However, it is estimated between 600,000 and 2,000,000 deaths can be attributed to malaria. It was estimated that there were over 200 million cases in 2010, in addition to numerous undetected and asymptomatic cases[Laishram et al., 2012, Murray et al., 2012]. Despite vast successes in eliminating malaria from once endemic areas, transmission persists around the globe. Strategies to control, prevent and treat malaria exist, but the scale of the disease and its deep association with entrenched poverty, economics and politics prevent easy eradication[Mills et al., 2008].

Malaria is not only a result of poverty, but also a cause of poverty. It not only causes individual human suffering at the most vulnerable stages of life, but engenders wide economic suffering in populations [Gallup and Sachs, 2001]. The worlds most malarious countries are not only characterized by low gross domestic product (GDP), but also historically have seen the lowest rates of economic growth[Sachs, 2002]. The direction of causality and associations may be spurious, but it is known that the scope of the disease robs monies that might be spent addressing other health needs, and depletes government funding for schools, infrastructure and community investment. On a household level, monies that might go to educating children or even investment into small enterprises goes to buying bed nets, medications and, at worst, paying funeral expenses[Jimoh et al., 2007, Onwujekwe et al., 2000]. Thus, combating malaria is not only salient for the protection of human health, but also for the health and welfare of future generations, whose destiny is increasingly entwined with the world community.

1.1.2 Objective

Broadly, this dissertation will focus on deliverable anti-malarial interventions in the context of three sub-Saharan African countries, all located in or proximally to East Africa. We shall first explore spatial issues of malaria, taking infrastructural and social factors into account. We shall then explore the problem of inequities in use and possession of insecticide treated bed nets (ITNs) in two different geographic contexts under two different delivery strategies. Finally, we will investigate the problem of increasing availability of artemisinin combination therapies (ACTs) in remote and isolated regions.

This research is relevant as the interventions we focus on in this dissertation have direct impacts on human health. Knowing the specific factors which hinder or encourage access, availability and compliance could help prevent disease, reduce mortality and improve the long term health of people in some of the most at-risk areas of the world.

1.2 Specific Aims of this Dissertation

This dissertation will address challenges to increasing accessibility and availability of malaria interventions through four distinct aims:

First, we will characterize Plasmodium infection in the context of human and infrastructural factors and urbanicity using a geo-located household level data set covering eight districts of Malawi. We shall draw spatial inferences using freely available GIS data including population, roads, water bodies and rivers and locations of public health facilities.

Second, we will explore the relationship of insecticide treated (ITN) net possession and use in Malawi. ITNs in Malawi are overwhelmingly distributed at fixed locations, usually at publich health facilities. We will explore how spatial access and availability impact household possession and use of ITNs to protect small children. We will again leverage the same data set as in the first aim. We will make recommendations for strategies to increase access to ITNs by hard to reach populations.

Third, we will examine the issue of compliance to ITNs in the context of a comprehensive, direct to household, no cost distribution of nets. We will use a survey of households in an area of intense transmission along Lake Victoria in Kenya.

Finally, we will examine issues of availability of Artemisinin Combination Therapies (ACTs) in Accredited Drug Dispensing Outlets (ADDOs) in two isolated and undeveloped regions of Tanzania. We will take advantage of longitudinal survey of ACT stocking in all ADDOs from both regions. We will explore how new products diffuse through drug markets in rural Tanzania and explore determinants of stocking and characteristics of "early adopters." From the results, we will make recommendations for ways to increase access to new pharmaceutical products in isolated and resource poor areas.

1.2.1 Insecticide Treated Nets

Insecticide Treated Nets (ITNs) provide inexpensive, safe and effective protection against malaria infection and are recommended by the World Health Organization and a core tool in malaria control programs worldwide[World Health Organization, 2007]. ITNs not only prevent Anopheline vectors from biting humans, but the insecticide impregnated in the fabric also kills mosquitoes on contact, preventing mosquitoes from simply biting someone proximal. In addition, vectors lose opportunities for reproduction, overall vector numbers are reduced and transmission is reduced in the community. ITNs are cost effective, averting an estimated $48 per DALY[Goodman et al., 1999] and preventing cases at a mere $3.26 each[11]. Scale up of ITN use worldwide has been associated with vast reductions in malaria incidence and other health conditions [Lim et al., 2011].

There is evidence for broad mass effects from high community use of ITNs. One study in Ghana indicated positive effects [Klinkenberg, 2010] in urban settings. In that study, children living within 300m of a household using ITNs were shown to have higher hemoglobin concentrations than children who lived more than 300m away from ITNs. Hawley, et al concluded, through a case control study of Kenyan villages, that ITNs impart protective effects to all household compounds within 300m of a household that uses ITNs [Hawley et al., 2003]. Maxwell, et al. indicated that un-netted villages proximal to villages that used ITNs had lower levels of malaria infection, although distance effects were not explored in their paper [Maxwell, 2002].

Investigators have speculated that there may be two negative effects imparted by widespread ITN use. First, researchers suspect that long term use of ITNs reduce the overall number of childhood infections and thus reduce the immunitive capacity of the individual later in life, leaving one vulnerable to more severe bouts of disease. Second, it is though that the repellent nature of the treated nets may divert mosquitos to bite unprotected individuals more frequently, thus increasing risk for those who do not sleep under nets [Quinones, 2000].

Insecticide treated nets have been associated with significant decreases in Anophelene vectors [Mbogo, 1996] although blood parasite levels remained unchanged. Community effects of ITNs in Kenya, has been associated with changes in the spatial distribution of Anophelene vectors, with decreasing number of A. funestus being seen with decreasing distances away from communities which are widely covered by ITNs [Gimnig, 2003]. Reductions in the numbers of A. gambiae along Lake Victoria have also been associated with scale ups in ITN use[Bayoh et al., 2010] though two studies indicated that A. gambiae numbers remained unchanged even when ITN coverage was high [Gimnig, 2003, Quinones et al., 1998]. There has been no evidence that nets affect the gonotrophic cyle of A. gambiae [Quinones et al., 1997].

1.2.2 Literature on Insecticide Treated Nets

The number of new publications on ITNs has been growing rapidly. Early work on treating nets with Permethrin based insecticides started in the early 1980s. Researchers experimented with treating nets and clothing with Permethrin to determine its effectiveness in repelling and killing blood-sucking arthropods [Dremova, 1982]. Loong et al. performed early trials to determine mosquito mortality upon contact with insecticide treated net material, and the extent to which Permethrin remained on nets given simulated every day wear and tear [Loong, 1985]. An early study in the Gambia indicated that ITNs reduced the odds of clinical malaria by 50%. Investigators also noticed important age effects. Telling were early suggestions that compliance varied among ethnic (and likely SES) groups and that use of nets were lowest amongst teenagers and highest amongst adult women. Men in the trials used nets far less than women. Authors also noticed a variety of factors which influence the decision to use nets, such as privacy and perceived protection from other pests [Bradley, 1986, MacCormack and Snow, 1986].

(Figure 1.1).

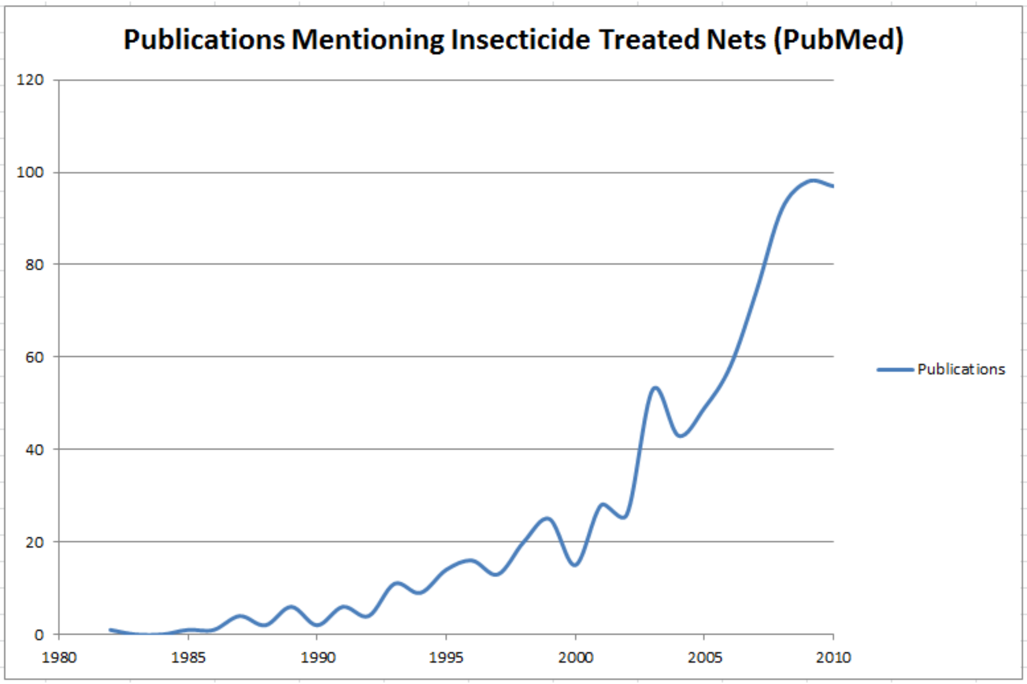

Figure 1.1: Publications mentioning "insecticide treated nets" on PubMed

Trials in Malaysia noted high success in control of vectors numbers and malaria infections initially, but found that as net condition and regular compliance waned from the start of the study period, blood parasite levels in randomized ITN groups matched those of non-ITN groups. Their research indicated that ITN success or failure depends on a complex network of ecological, sociological, cultural and practical factors[Hii, 1987]. A trial in Tanzania indicated that having a single person sleeping under a treated bednet in the household, reduced the number of mosquito bites of unprotected persons by half. In contrast, one person sleeping under an untreated net increased the number of bites of unprotected persons [Lines et al., 1987].

A trial in the Gambia indicated that while children who slept under ITNs had fewer clinical episodes of malaria, overall parasite rates were unchanged between treatment and control groups. Their research suggested that ITNs extended the amount of time that mosquitoes probed for blood meals and had little effect on the number of bites received [Snow et al., 1987]. In a separate trial, The same group noted a 90% reduction in Anopheline vectors in a treatment village compared to a control village, and, over the course of a year found that villages where children slept under ITNs had far fewer clinical episodes of malaria and lower parasite concentrations. However, the authors noted that nets were most effective in low to medium transmission areas and were likely less effective in areas/times of heavy transmission [Snow et al., 1987].

Access to ITNs is largely dependent upon the method of distribution and cost. Most public distributions of ITNs occur out of health facilities, requiring that household representatives travel to health facilities to obtain them. Some direct to household distributions do occur, but largely strategies rely on central points of distribution such as community events or fixed schools or health facilities[Skarbinski et al., 2011, O'Meara et al., 2011] .

Cost is a major barrier to the scale up of ITN coverage[Agha et al., 2007, Mathanga and Bowie, 2007, Matovu et al., 2009]. Requiring that households pay for them, often results socio-economic gradients in ITN possession. Some argue that selling goods enhances sustainability of interventions and expands access as for cost goods can be integrated into already existent market infrastructure[Population Services International, 2003]. Some authors have argued that there are psychological effects of having paid for a product or sunk costs effects where households value goods more

after expending household resources for them[Arkes and Blumer, 1985]. Research from Zambia has indicated that households that are more willing to pay for water treatment packs, are more likely to use them but found no evidence of sunk costs, i.e. households value goods more because of past investment[Ashraf et al., 2010]. They posit that there are positive effects to charging for health related goods, though evidence suggests that increased price is associated with a decreased likelihood of ownership[Cohen and Dupas, 2010]. The issue of user fees for all heath interventions is contentious and highly debated in the literature [World Bank, 1987, Ridde and Haddad, 2009, Nabyonga Orem et al., 2011, Wilkinson et al., 2001, Shaw and Griffin, 1995, Abdu et al., 2004, Gilson, 1997, Chuma et al., 2009, Gilson and McIntyre, 2005, Ridde and Morestin, 2011, Uzochukwu and Onwujekwe, 2004, James et al., 2006, Guo, 2012, Litvack and Bodart, 1993] [Bonu et al., 2003] [Mubyazi et al., 2010]
.

1.2.3 Pharmaceutical Interventions

Effective medicines to treat malaria incidents have long existed. Possibly the earliest medicine to treat malaria was quinine, derived from the bark of cinchona trees and long used by the Quechua people in Peru. Its anti-malarial properties were discovered and the bark was brought to Europe in the 17th century[Flackiger, 1879]. Though quinine was largely replaced in the mid 1940s following the discovery of chloroquine[Slater and ebrary, 2009], it continues to be used in the treatment of complicated malaria in Sub-Saharan Africa[Sinclair et al., 2012]. Increasing parasite resistance to chloroquine and subsequent increases in complicated malaria and mortality has resulted in a decline in its use[Trape, 2001]. artemisinin, a derivative of the plant Artmisa annua, had been used by Chinese herbalists for more than 2,000 years in the treatment of malaria and other illnesses. It is now a treatment of choice for P.falciparum malaria, often given in combination with other malaria drugs[Organization, 2011]. artemisinin Combination Therapies (ACTs) are preferred over mono-therapies because the cocktail of medications is thought to slow the development of drug resistance. artemisinin resistance has already been noted to have occurred along the Thai-Cambodia border and it is feared that it will spread to SSA[Friedrich, 2012, Mugittu et al., 2006, Phyo et al., 2012, Uhlemann and Fidock, 2012, White, 2010, Yeung et al., 2010]. As there are few other pharmaceutical options on the horizon, widespread resistance could erase many of the gains seen in the past few years.

Despite proven successes of ACTs in treating falciparum malaria, improving access to them by populations at risk remains a challenge[Organization, 2011]. High cost and political hurdles prevent widespread access to ACTs in the areas which have the highest case burdens. The Affordable Medicines Facility malaria was a factory gate subsidy mechanism that sought to expand access to ACTs, by bringing the wholesale price paid by private drug sellers down to that paid by public providers. Privates shops, which largely sold chloroquine based medications, a number of which were rendered ineffective by growing resistance, would then be incentivized to sell ACTs at a price that customers could afford. Access to ACTs (usually under the brand name Coartem) would be expanded, and chloroquine based medications such as Sulfadoxine/pyramethanine (SP) (Fansidar) would finally be pushed out of the market[Laxminarayan and Gelband, 2009]. The program attracted harsh criticism from a number of international groups due to fears that it would undermine publicly funded health delivery, mistreat individuals who did not actually have the disease, be given by untrained individuals with motivations of profit rather than health delivery and foster artemisinin resistance through incomplete dosing[Siva, 2009, Arrow, 2012, Wayne, 2012].

1.2.4 Problems of Delivery

The success or failure of any health intervention is based on the simple issue of whether end users can access it or not. Even when completely acceptable to and desired by end users interventions are useless if they are unavailable or affordable. Delivery methods can range from fully private for profit sale of nets in markets, to mixed public/private/NGO delivery strategies which distribute nets through local health services at dedicated events, to fully public delivery of ITNs through routine services. ITNs can be given at no cost, can be subsidized by international donor groups or governments, or can be sold as any other commercial product. A review of ITN delivery methods in a number of SSA countries found differences in ITN coverage and use by different types of delivery systems[Webster et al., 2007]. Specifically, the researchers found that high ITN ownership was obtained by delivering ITNs free of charge by piggy-backing on to vaccination campaigns, and was lowest for mixed public/NGO delivery methods which offered low cost nets delivered through routine health facilities. Interestingly, though it might be considered an outlier given the context, unsubsidized nets delivered through the informal sector in the Gambia showed the highest rates of use among target groups of young children and pregnant women. Models have shown that mass delivery strategies should be supplemented by delivery through ante-natal clinics to effectively target young children, who face the greatest risk for mortality [Okell et al., 2012].

1.2.5 Problems of Accessibility and Proper Use

Even if households have access to malaria interventions, there is no guarantee that they will use them and no guarantee that they will use them in the manner required for full effectiveness. A major complaint of ITNs is that they are hot, particularly in the hot rainy seasons of SSA. It has also been noted that certain types of ITNs cause itchiness [Banek et al., 2010, Sharma et al., 2009, Zaim et al., 2000] and the authors have observed households discontinue using certain types of nets in favor of others because of this complaint. Sleeping arrangement and household construction have also been associated with consistent compliance to ITN use[Iwashita et al., 2010]. Caregivers are known to break up doses of medications for malaria in SSA, compromising effectiveness. Providers have also been recorded as having given half doses to reduce costs and serve more patients. Incomplete dosing could also raise the threat of drug resistance[White et al., 2009].

CHAPTER II

URBANICITY FEATURES ALTER PLASMODIUM INFECTION RISK IN MALAWIAN CHILDREN AGED 6-59 MONTHS

2.1 Abstract

Background: Malaria prevalence is known to be lower in "urban" areas compared with "rural" areas. The multifactorial nature of urban and rural spaces suggest this designation is not dichotomous, but rather represents a continuum of conditions. The misclassification of urban and rural conditions could hamper intervention targeting for diseases which are linked either positively or negatively to urbanicity. We suggest a composite measure of urbanicity using freely available GIS layers, and test it using a broad household level malaria survey of 6-59 month old children in Malawi.

Methods: A composite measure of urbanicity for Malawi was constructed using freely available data for locations of health facilities, roads, rivers, lakes and electricity lines along with census derived population density. Distances to locational features were applied to a point based grid for all of Malawi. The internal reliability of these variables to measure urbanicity was tested using Cronbach's alpha and Guttman's lambda 6. A principal component analysis (PCA) based composite measure was produced for all points on a fine grid throughout Malawi. Malaria prevalence was measured using a household level survey from 2007. Children from

randomly selected households were tested for infection and a demographic survey was performed and GPS locations were recorded. Population density and distance to locational features, along with the composite measure of urbanicity were assigned to each household for assessment. Statistical relationships of all factors were tested against Plasmodium parasitemia status using bivariate and multivariate regression based methods, including potential household level confounding factors such as insecticide treated net use and household material wealth.

Results: Urbanicity features were correlated with one another, but there appeared to be moderate levels of internal reliability to measure the latent variable of urbanicity. Graphical methods showed that urban and rural gradients exist throughout Malawi, even within areas classified as "urban" and "rural" by the Malawi Government. Individual factors associated with urban and rural divides were found to be associated with Plasmodium infection in children. The composite measure of urbanicity had a graded though non-linear but inverse relationship with Plasmodium infection. Statistical tests confirmed associations for most components in bivariate models. Multivariate models confirmed associations of urbanicity factors even when controlling for gender, age, insecticide treated net use and material wealth status.

Conclusions: Composite measures of urbanicity can be created for developing countries from freely available data layers. These measures are applicable to common disease outcomes such as malaria. We found that community-level factors associated with human settlements and urban development were predictive of decreased risk for malaria in children, even in the presence of more traditional household-level prevention such as ITN use. To conserve public health resources, policy makers should target disconnected rural communities which suffer from inadequate access to health services including malaria treatment and prevention, rather than broadly defined "rural" areas.

2.2 Introduction

Health outcomes differ between urban vs. rural areas of developing countries. Prevalence malaria, for example, is generally found to be lower in urban than in rural areas[Bousema et al., 2012] though the manner in which "urban" spaces are distinguished from "rural" spaces are generally ill defined. Many studies use urban/rural designations as suggested by political bodies. These designations were often intended for administrative purposes[Vlahov and Galea, 2002] and have little to do with topographical, infrastructural and economic landscape and are uninformative for assessing patterns and determinants of disease. Some research has been done to create more constructive measures of "urban" and "rural" in developing countries [Novak et al., 2012, Dahly and Adair, 2007]. However, the focus of those studies was on urban spaces, rather than on health across a developmental gradient that may cover an entire country.

2.2.1 Malaria along the urban and rural spectrum

In terms of malaria, vast differences in prevalence between urban and rural spaces are often explained by observations indicating fewer opportunities for both vector reproduction and availability of human blood meals in urban settings. Urbanized areas are considered less favorable for most competent Anopheles species, particularly due to the paucity of suitable breeding sites that leads to lower mosquito densities in cities [Trape, 2001, Lindsay et al., 1990]. Urban house structures tend to reduce access of adult mosquitoes to humans at night, thus reducing transmission [Lindsay et al., 2002]. Furthermore, the increased density of humans in urban locations may reduce the per capita number of human blood meals [Trape, 2001, Smith et al., 2004].

Autochthonous malaria has been eliminated from most regions of North America, Europe and even South Africa, but many conditions have contributed to these changes. Macro- and micro-socio-economic improvements, better housing conditions and increased levels of education are considered largely responsible. The construction of railroads, for example, coincided with rapid declines in malaria in the southern United States as market opportunities drew people away from waterfronts[Ackerknecht, 1977]. Malaria elimination in Italy occurred as agriculture and land cultivation expanded[Snowden, 2006]. Urbanization typically results in smaller family units and household size, which has been associated with successful malaria elimination[Hulden, 2010]. Although no single factor can be credited for reducing malaria incidence, most research suggests that such changes have been related to components of economic development. Evidence from several sub-Saharan African (SSA) countries suggests that declines in malaria incidence over the past decade began before the scale-up of malaria interventions such as ITNs, IRS and expanded drug accessibility[O'Meara et al., 2011]. Such reduction in malaria incidence could be the result of rapid urbanization and development in some SSA countries. Although urban settings can be associated with negative outcomes for some health conditions, SSA cities have experienced higher life expectancy, lower childhood mortality, better childhood nutrition, and higher vaccination rates than that in rural SSA areas [Leon, 2008]. For malaria, studies in SSA have found differences along gradients of rural, peri-urban, and urban settings [Hay et al., 2005, Byrne, 2007]. Other investigations in developing countries have looked at urbanicity gradients as risk factors for chronic diseases [Allender et al., 2011, Popkin and Gordon-Larsen, 2004]. Finer-scale, composite measures of urbanicity have been associated with caloric intake, number of days breast feeding and BMI in the Philippines, for example [Dahly and Adair, 2007].

If factors associated with urbanization that successfully reduce Plasmodium transmission in large urban spaces can be identified, they may be somewhat transportable to other contexts. Though much attention is given to the large of cities in SSA, certain characteristics that define urban areas can be found even in smaller urban and partly rural areas. These characteristics, such as improved housing, accessible and available health care, greater population density, and access to transportation and markets exist to varying degrees throughout SSA, and may be influencing the malaria burden. Conversely, characteristics associated with rural settings such as small-scale cropping, nearby standing water, poor housing, and inadequate health services can also be found in some urban areas [De Silva and Marshall, 2012, Alemu et al., 2011, Nduka and Kalu, 2011, Rakotomanana et al., 2010, Ngom and Siegmund, 2010, Thwing et al., 2009, Siri et al., 2008, Wang et al., 2006, Keiser et al., 2004].

2.2.2 Research Goals

We will attempt to create a measure of urbanicity which measures access to social services, transport infrastructure, electricity and population density. We will also take proximity to sources of water and areas potentially poorly suited for large human settlements into account. We will illustrate that rural like spaces exist within and proximate to "urban" areas and that urban-like spaces exist in "rural" areas. As a test case, we will see whether our measure is applicable to malaria prevalence in an area of intense transmission, while controlling for potential confounding factors.

2.3 Methods

2.3.1 Creating a Measure of Urbanicity

We opted to use freely available data layers of features common to developing countries. Our goal was to create a measure of urbanicity which would not require detailed, on the ground surveys (as many other measures have used. Rather, we seek to create a utilitarian measure that can take advantage of data that is easily obtained for any developing country. We settled on five components related to urban areas: health services, transportation infrastructure, population density and availability of electricity.

With some exceptions, colonial powers tended to establish cities in Sub-Saharan Africa far from swamps and fresh water bodies whereas residents of rural areas tend to live in close proximity to water sources. Even within cities, areas of better means tend to be located at higher elevations and away from areas where water can collect. Thus, we have included layers of both rivers and lakes into the measure.

Data Sources

Health Facility (HF) locations in Malawi, both public and private, were comprehensively surveyed in 2003 by the Japan International Cooperation Agency (JICA). The geo-coordinates for each HF, in addition to facility type, ownership and funding source were included in the database [Japan International Cooperation Agency (JICA), 2000]. Spatially-referenced data for elevation, water bodies and rivers and transportation networks in Malawi were downloaded from the website of DIVA-GIS [Hijmans et al., 2004]. Enumeration area level population density was obtained from the Malawi National Statistical Office[Malawi National Statistical Office, 1998]. Locations of power lines were obtained from the African Development Bank Group [African Development Bank Group, 2012]. These environmental data, the georeferenced HF data, and the surveyed household location data were integrated into a Geographic Information System (GIS) database using ArcGIS (ver. 10.0). (See Figure 2.1)

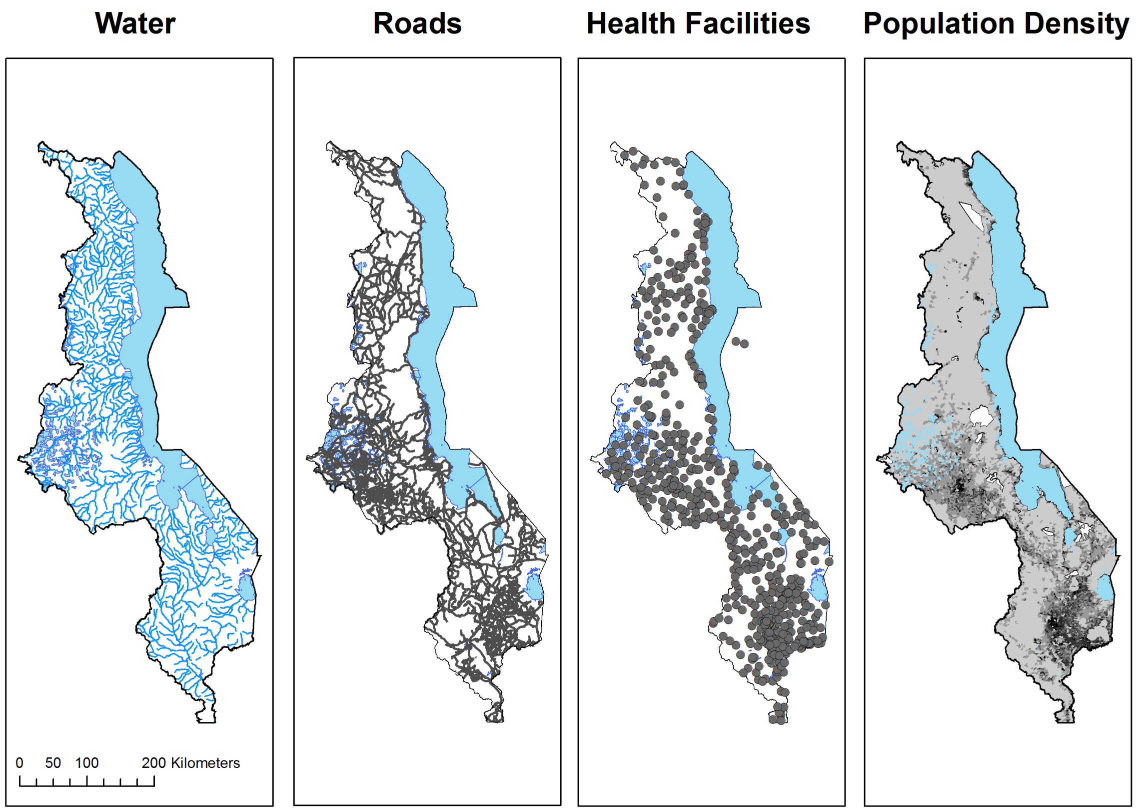

Figure 2.1: GIS layers for water (rivers and lakes), roads, health facilities and population density.

Creating the Urbanicity Measure

A fine grid (1km) across the map of Malawi was created. Distances to all locational features were calculated for each point on the grid using straight line distances. Each points was assigned the population density of the enumeration area it fell in.

"Urbanicity" cannot be directly measured but the variables we select for our composite measure should have some level of internal consistency. To confirm that the measures chosen all represent the latent variable of urbanicity, an internal reliability analysis was performed. Three measures of internal reliability were used. First, simple Pearson correlation coefficients were examined. Cronbach's α is likely the most common method of measuring internal consistency, used often in psychological and educational studies where several items are used to measure latent, unmeasurable variables[Bland and Altman, 1997]. Finally, Guttman's λ 6 is also presented for comparison[Guttman, 1945]. Though Cronbach's α is commonly presented in reliability studies, Guttman's λ is considered superior in some cases, as it is more robust to an increasing number of terms.

As all variables are continuous and not easily weighted or scored, principal components analysis (PCA) was used to create a final composite measure, a common data reduction technique for creating single measures from a set of correlated variables.Values of the first principal component were applied back to the point grid of Malawi and maps were created.

2.3.2 Malaria Case and Household Survey

Data on malaria cases came from a survey of 6,094 households in eight Districts throughout Malawi conducted during April/May 2007 (Figure 1). Within each District, from 16 to 30 Enumeration Areas (EAs) were chosen at random. Within each

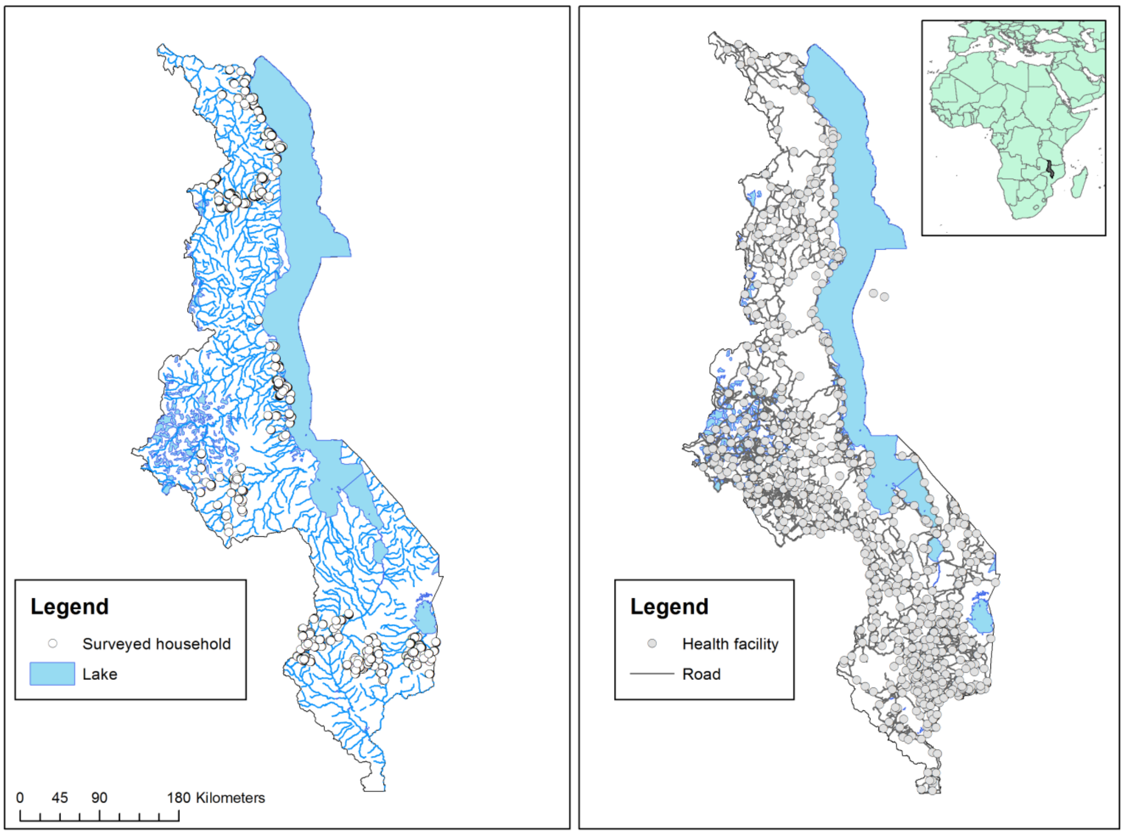

Figure 2.2: Maps of Malawi showing (a) locations of households in the Northern, Central and Southern Regions surveyed during the 2007 sampling period and (b) Health facilities and major roads throughout the country.

EA, 10 to 81 households were randomly selected and, following informed consent of the parent or guardian, one child between 6 and 59 months of age was identified for inclusion in the survey. Demographic information on household members was collected from the maternal head of household and a finger-prick blood sample was taken from the surveyed child.

Blood samples were then visually assessed by trained microscopists for presence or absence of any species of Plasmodium. Household-level characteristics such as home construction, water sources, type of toilet, and possession of livestock, electronic goods, light sources and transportation were recorded. A principal components analysis (PCA) procedure was performed and the first principal component was used to create a continuous measure of material assets that was considered a proxy for socioeconomic status (SES) [Filmer and Pritchett, 2001]. This measure was then divided into quintiles to categorize the SES of each household. The geographic location of each house was recorded using a GPS unit. All information was entered into a Microsoft Access database. The Institutional Review Boards at the College of Medicine, University of Malawi and the US Centers for Disease Control and Prevention (CDC) approved the study protocol.

2.3.3 Statistical Methods

Evaluations of associations between continuous variables and a dichotomous measure of Plasmodium infection status (positive or negative) were performed using standard t-tests. Next, patterns of association were graphically assessed using a local regression method a line was fitted to illustrate trend.

We first tested associations between household and demographic covariates and malaria status using t-tests and chi-square tests for continuous and categorical variables, respectively. Next, we used logistic regression models to test associations with both bivariate and multivariate models to determine if associations held in the presence of potential confounders. As we were interested in the specific patterns of association between features of urbanicity and parasitemia, a generalized additive logistic regression model was implemented. This allowed us to apply a smoothing function for the continuous measure covariates. The smoothing function allows flexibility in estimation, eliminating the need for assumptions of linearity, and allowing visualization and better assessment of patterns of association. Estimates of log odds and standard errors were presented for non-smoothed covariates. This smoothing function produces visual plots and tests for association, but does not provide parameter estimates. Thus, for reference, linear parameter estimates were also provided. Significance of associations of parasitemia with all covariates was tested both in bivariate and multivariate models. Finally, because predictors may not all act additively in relation to parasitemia risk, we also explored potential interactions between smoothed covariates of interest and parasitemia risk using chloropleth maps. All analyses were performed using R (ver. 2.15.1) statistical software.

2.4 Results

2.4.1 Urbanicity Measure

Most of the measures used to evaluate urbanicity were only weakly correlated with one another (Table 2.1). Distance to health facilities and road, however, had a correlation coefficient of 0.5. A reliability analysis showed that the variables chosen only had moderate internal reliability (see Table 2.3) though analysis of both Guttman's λ and Cronbach's α suggested that all variables should be included.

A PCA based composite measure was produced and the values of the first principal component were mapped for all locations on a fine point grid of Malawi (see Figure 2.4. All variables were included in the first principal component (see Table

2.2) though there appeared to be two major groups of variables (Figure 2.3. One represented human factors such as population density, roads and health facilities and the other represented proximity to water. Power lines in Malawi tend to run alongside rivers and other bodies of water.

Using the variables available to us, areas of high urbanicity were to be found throughout Malawi, even in areas not classified as "urban" by the Malawian Government. Likewise, there was heterogeneity even within and around "urban" spaces. Areas that were found to be highly urban, according to our measure were proximal to areas that were classified as very rural, particularly in the area surrounding the capital, Lilongwe City.

2.4.2 Parasitemia Survey

822 (13.5%) of surveyed children were slide-positive for Plasmodium infection (see table 2.4). The mean age of children included in the survey was 25 months. Parasitemia risk varied by household construction type, water sources, and toilet types. Other information on household possessions such as livestock, media items and transportation was collected and included in the aggregate measure of SES, but, are not individually analyzed in this study.

2.4.3 Distances to Geographic Features

Children with Plasmodium parasites lived, on average, significantly further (7.8 km) from the nearest HF compared to those without infection (6.5 km away) (Table 1). Similarly, Plasmodium-positive children lived further (1.26 km) from the nearest road than those who tested negative (0.96 km). However, infected children lived closer to a lake body (13.49 km) than those who were not infected (26.89 km). Infected children resided in less dense (3,915 people/ea) than children who were not

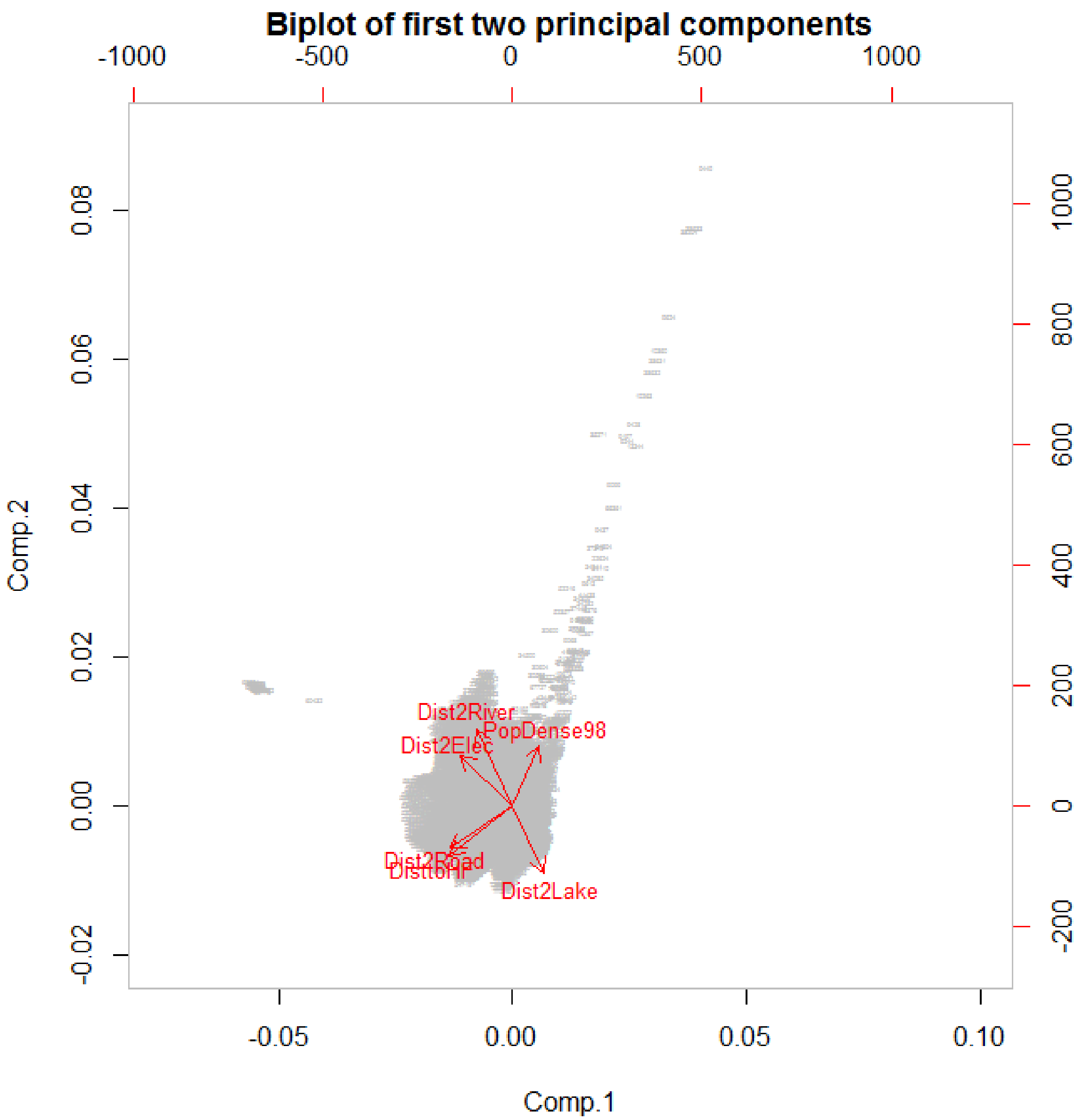

Figure 2.3: Biplot of first two principal components of urbanicity factors.
Cities are heterogeneous in terms of factors associated with urbanicity. Likewise, urban-like areas exists in rural areas.

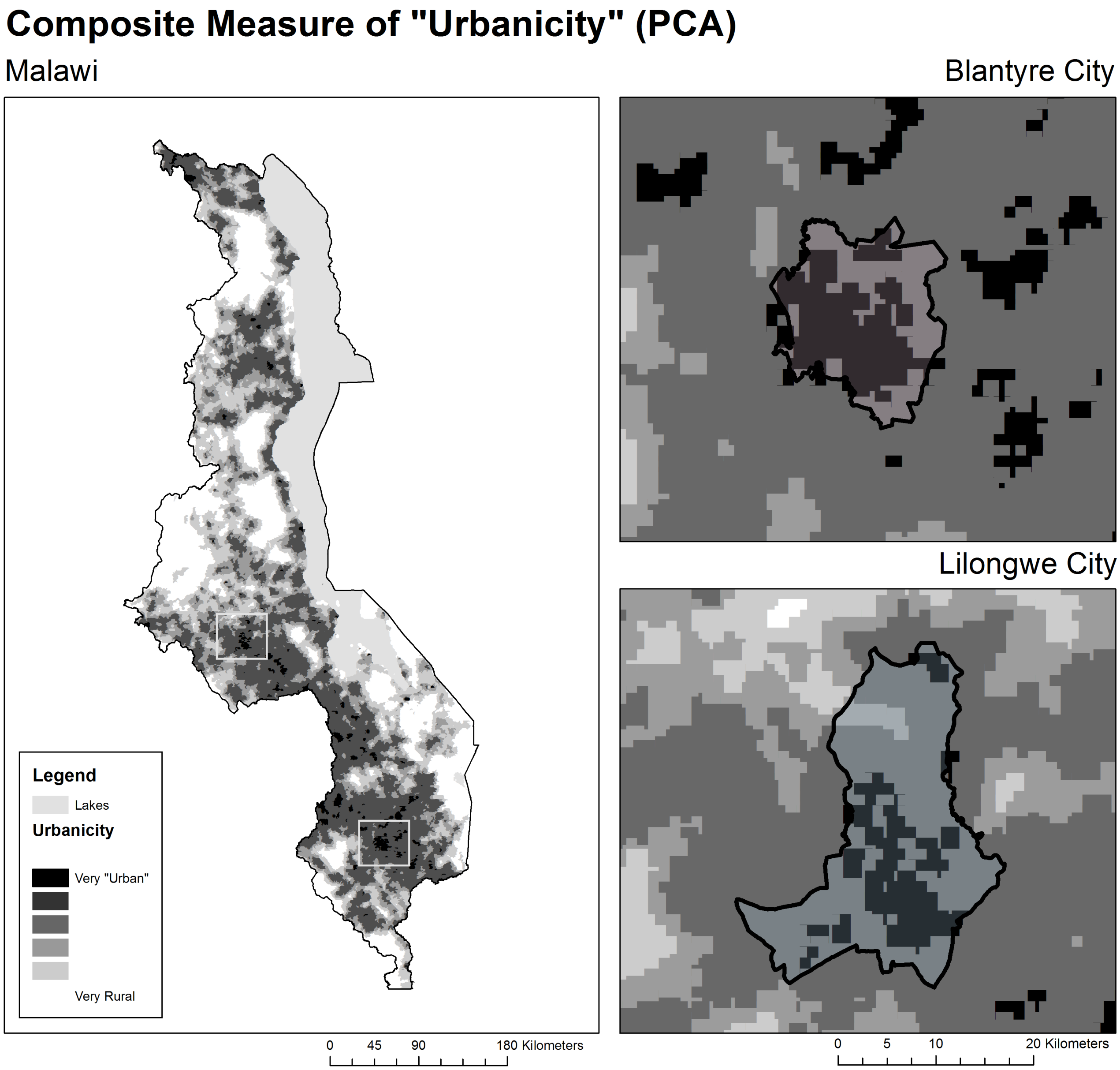

Figure 2.4: PCA weighted composite measure of urbanicity at all points throughout Malawi. Heterogeneity of urbanicity with the cities of Blantyre and Lilongwe are shown.
Cities are heterogeneous in terms of factors associated with urbanicity. Likewise, urban-like areas exists in rural areas.

infected (7,961 people/ea).

Similar results were found using a Loess regression methodology (Figure 2.5). Distance of households to the nearest HF was strongly predictive of malaria risk (Figure 3a). The probability of infection increased from 6% to 30% with increasing distance to HFs. Household distance to the nearest road also had a graded, positive relationship to prevalence of Plasmodium parasitemia (Figure 3b). Although t-tests comparing overall means previously indicated proximity to water was not associated with parasitemia risk, graphical assessment suggested a relationship for households located within 5 km of a river (Figure 3e). The risk of parasitemia decreased significantly with increasing distance from a lake(Figure 3d). Population density appeared have no relationship with parasitemia risk (Figure 3f).

2.4.4 Relationships of Urbanicity to Parasitemia

Figure 2.7 shows the smoothed bivariate relationship of the composite measure of urbanicity with the probability of being parasitemic. Though parasitemia risk declines with increased urbanicity, there is one notable break point. Parasitemia risk is flat for very rural areas (.20), then begins to decline suddenly, converging to zero for very urban areas.

2.4.5 Regression-Based Associations

Bivariate logistic regression models indicated that ITN use was highly predictive of reduced parasitemia (Table 2.5). Gender was not a significant predictor of parasitemia in children. Using the poorest quintile as a reference, SES had an inverse relationship with parasitemia; the wealthiest groups had the lowest likelihood of testing positive for Plasmodium parasites, compared with the poorest groups. In other bivariate models, age, distance to nearest HF, distance to lake, and population

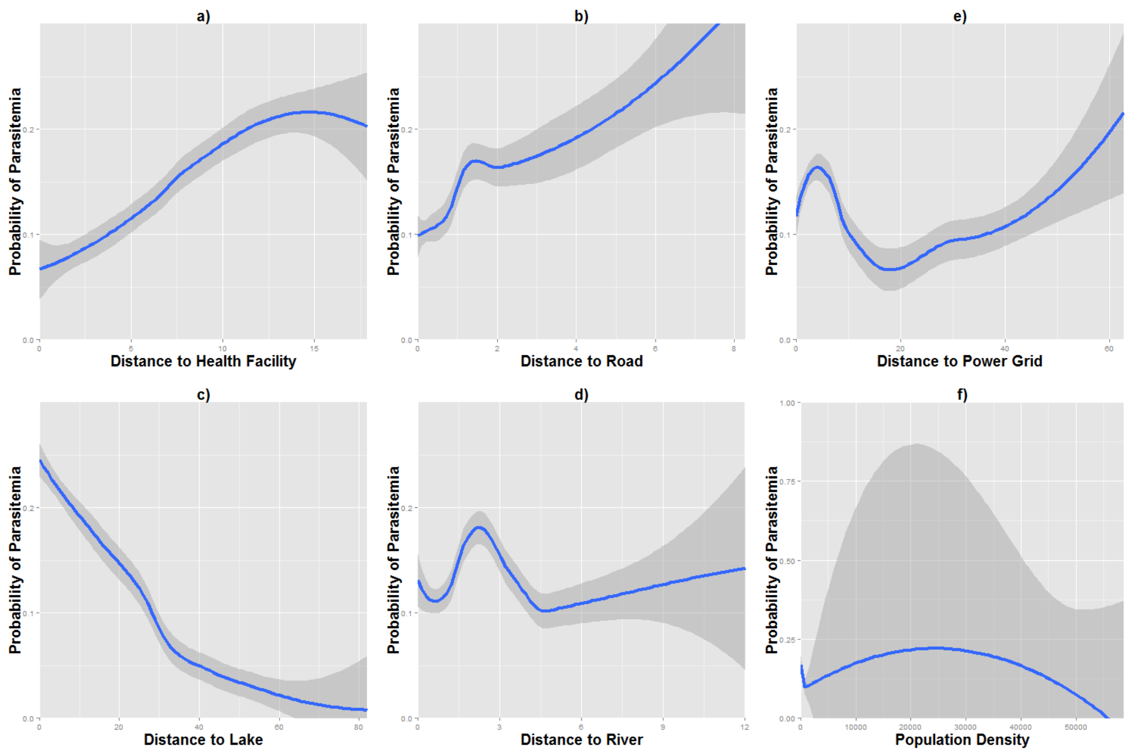

Figure 2.5: Distance to geographic features and parasitemia status. Lines are drawn using a local regression methodology (loess). a) Probability (percent) parasitemia by distance to nearest health facility, b) by distance to nearest road, c) distance to the power grid d) by distance to nearest lake, e) distance to nearest river and f) population density.

density were significantly associated with parasitemia, but distance to river was not.

To evaluate relationships further, all covariates were included in a single multivariate model. Again, gender and distance to river were not significantly associated with parasitemia risk. ITN use was again protective against parasitemia, although at a reduced magnitude. When accounting for other spatial indicators, SES effects for the bottom quintiles disappeared. Younger age, increased distance to HFs and roads, decreased distance to lake, and increased population density were all associated with an elevated risk of parasitemia. A model including only the composite measure indicated that increased levels of urbanicity were associated with decreased risks of being parasitemic.

Generalized additive models of parasitemia including smoothed estimates of all terms, confirmed that patterns remained unchanged compared with the smoothed bivariate versions shown previously (see Figure 2.6). As parameter estimates for smoothed terms of generalized additive models do not exist, we present only the graphical results.

2.4.6 Interactions between predictive covariates

Visualization of potential interactions among hypothesized predictors and parasitemia risk was accomplished through chloropleth maps using the multivariate GAM model presented in the previous section. Though interactions between all covariates were assessed, we present results of only four that were of theoretical and analytic interest (Figure 4). Distance to nearest HF showed significant interactions with household material wealth.

Households in the highest material wealth categories were at lower risk for childhood parasitemia, a relationship that was weaker with distance to HFs. Indeed, regardless of their SES, households were at high risk for parasitemia when they were

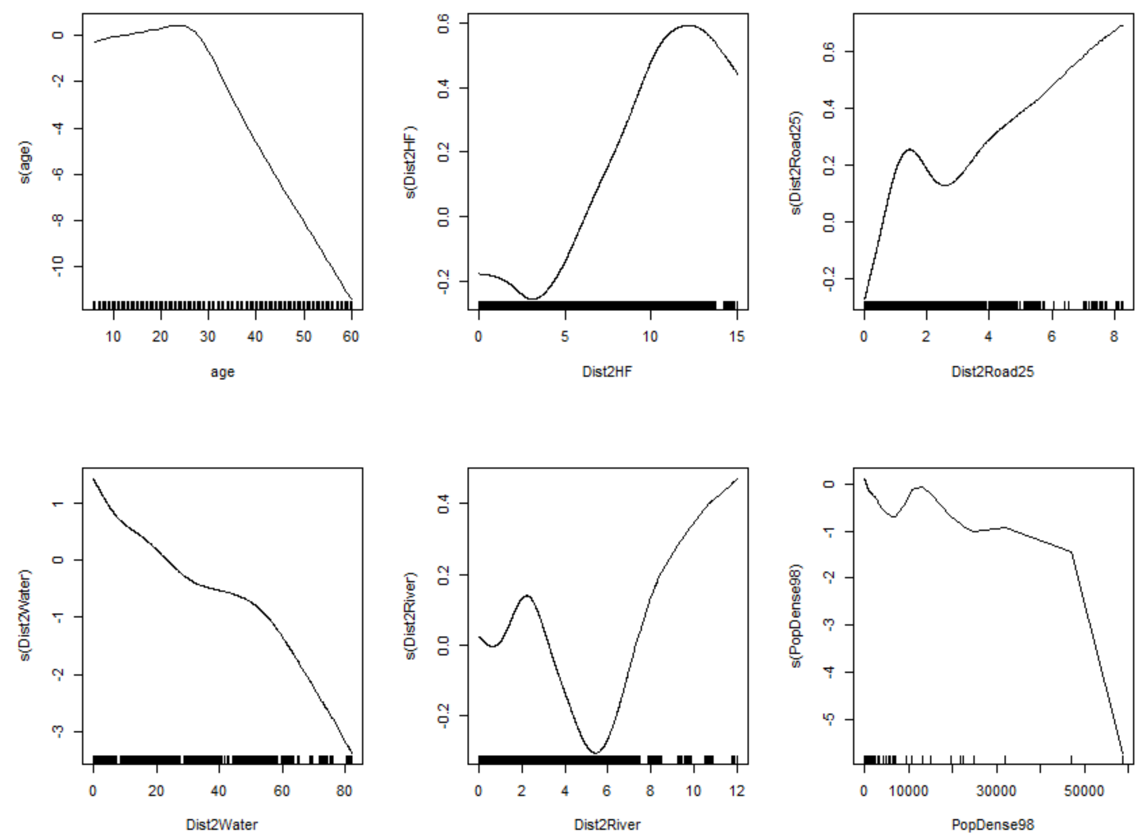

Figure 2.6: Patterns of parasitemia by smoothed continuous covariates against the log odds of having parasitemia in multivariate model: Age, distance to health facility, distance to road, distance to lake, distance to river and population density.

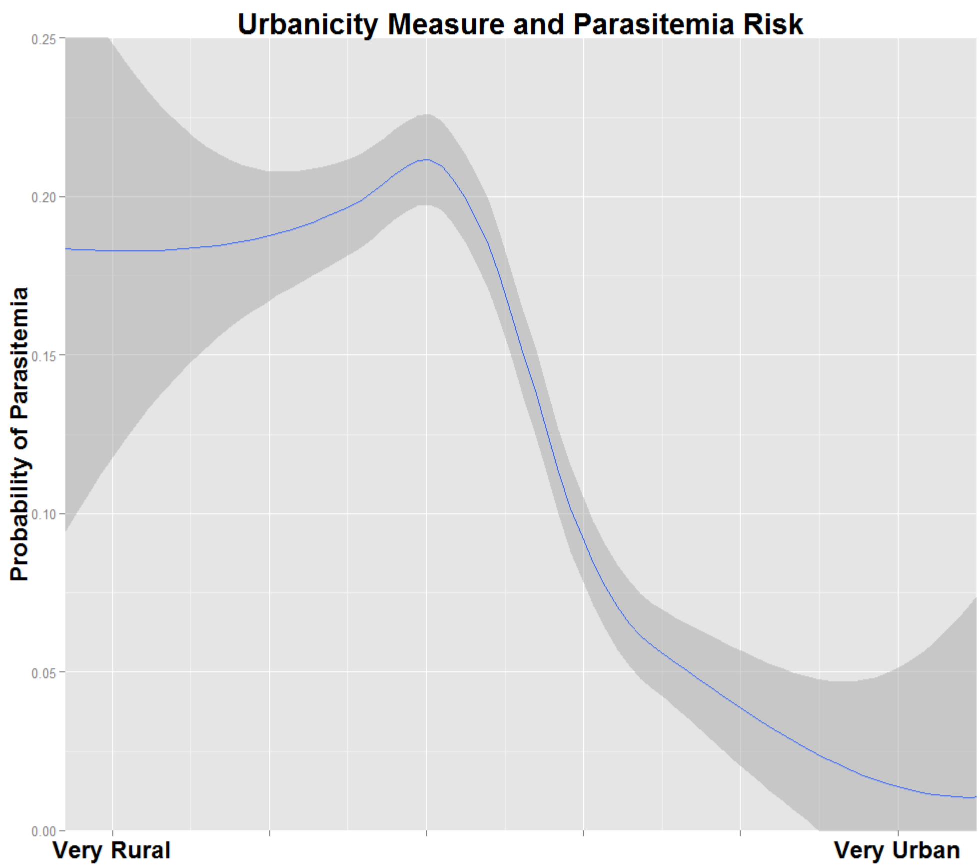

Figure 2.7: Probability of parasitemia by level of urbanicity.

at greater distances to HFs. Similarly, greater distance to roads influenced parasitemia risk, even for more affluent households. The pattern indicated that the relationship of the two covariates was purely additive. There was no evidence of multiplicative interaction between the two.

Material wealth had protective effects solely for households that were located very close to roads. Households located ¿4 km from a road appeared to receive little protective benefit from increased material possessions. Very close proximity to both roads and HFs was associated with low parasitemia risk, even though all households located very close to HFs were well protected. Households very distant from both roads and HFs were at higher risk for parasitemia. Sparsely populated areas at any distance from roads also were at high risk for parasitemia, while high population density areas were at very low risk for parasitemia.

2.5 Discussion

This investigation has shown that features associated with urbanicity are predictive of malaria risk in Malawian children whose households are located in a variety of different ecological contexts. Living closer to lakes and other water bodies increased the probability of Plasmodium infection, while higher population density, proximity to roads and to health services reduced risk, even when including potential confounders. We found that these relationships were graded, calling into question the utility of simple categorizations of ”urban” vs. ”rural” when assessing malaria transmission.

In studies of urban/rural impacts on health, two definitions are common. Urbanization refers to changes over time of human settlements in geographic size, population density and economic profile. Urbanicity, however, broadly refers to a set of

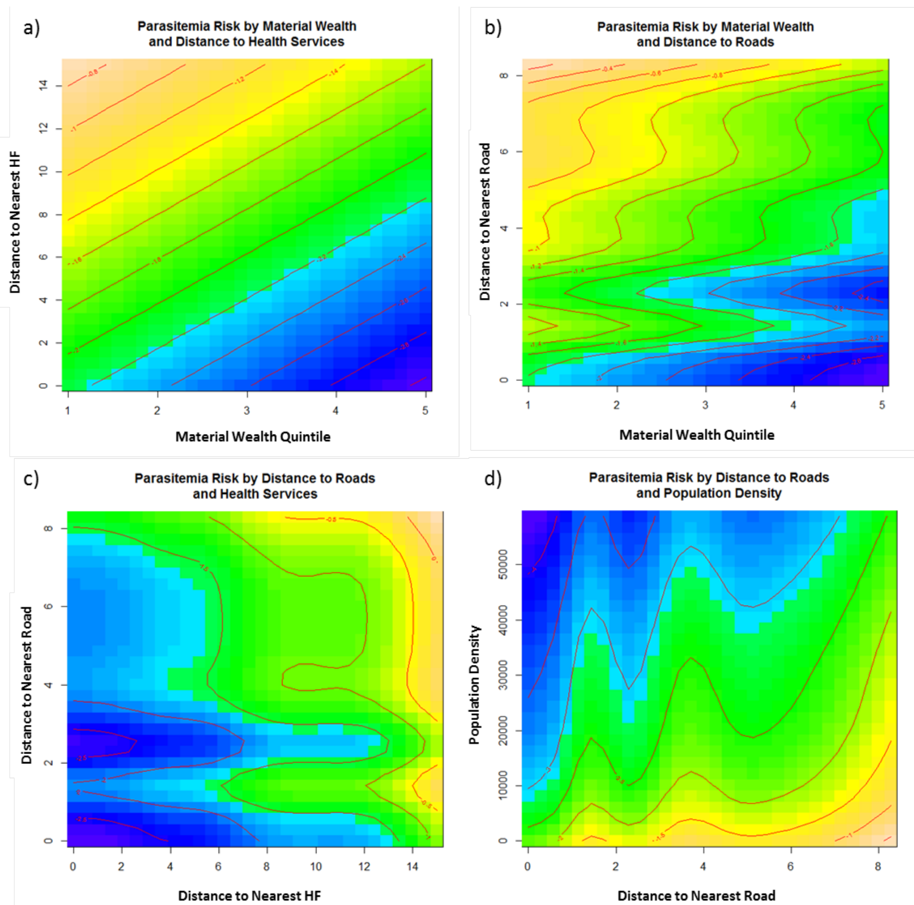

Figure 2.8: Interactions of predictive covariates on parasitemia risk. X and Y axes represent predictive covariates. Colors represent gradients of parasitemia risk (blue =low risk, yellow=high risk). Results are produced from trivariate generalized additive logistic regression models, smoothing the predictive covariates. a) Material wealth (low to high) against distance to health services on parasitemia risk b) Material wealth (low to high) against distance to road on parasitemia risk c) distance to health services against distance to roads on parasitemia risk and d) distance to road against population density on parasitemia risk.

characteristics which distinguish urban spaces from rural spaces and their impacts on residents[Dahly and Adair, 2007]. In our study, rather than accepting or creating categorical measures of "urban" or "rural," we sought to determine whether specific markers of urbanicity (population density, proximity to health care, malaria risk factors, SES, decreased proximity to wet areas) were associated with Plasmodium infection in children. We evaluated whether these factors interacted with one another, and with potential household-level determinants of malaria. We found that rough, politically determined designations of "urban" and "rural" were insufficient to describe conditions amenable to malaria transmission both without and within "urban" and "rural" areas

Urban and rural environments represent a wide variety of geographic, economic and socio-political contexts that are not carefully or consistently defined across the countries of SSA. As we have seen, in Malawi where only a limited number of areas are classified as "urban", many people might be considered to reside in rural areas though communities located in these areas have some of the same indicators of urbanness. As other authors have noted, independent of population density or remoteness, some communities may experience better standards of living, increased economic opportunities, and city-like services involving health care and schools[Vlahov and Galea, 2002]. Naturally, we would expect communities with access to resources to have better health profiles than those which are extremely isolated and underserved.

In targeting malaria interventions, if no simple division between urban and rural areas can be found, then strategies that rely on exclusively on ill-defined categories will produce shortfalls in some parts of the continuum. Some communities within "rural" areas may be at low risk for disease yet receive an unnecessary amount of attention, leading to a waste of resources that could be better targeted elsewhere.

Likewise, rural-like areas proximate to large human settlements may be overlooked when designing intervention strategies. Uneven distribution of malaria transmission intensities and only rough knowledge of the location of transmission foci have been recognized as challenges to the spatial targeting of malaria control[Carter et al., 2000] and that malaria transmission is heterogeneous over space [Kreuels et al., 2008]. Our results confirm that the transmission profile throughout a holoendemic country like Malawi varies over space, but offer measurable and easily obtained markers that could potentially be used to aid in efficient targeting of interventions.

Though we used the case of malaria as a test to see if there were heterogeneities of disease in developing countries as a function of markers associated with development, we also found important results that may be specific to malaria. Household factors such as increased material wealth, or SES, and the use of ITNs were found to mitigate malaria risk in children. Although these factors were important to individual risk at the household level, community-level risk in the form of proximity to health services and roads was found to compromise or exacerbate individual risk. Appreciating the community context and identifying specific areas at higher potential risk will be important to developing more focused prevention. A better understanding of the causal mechanics of these underlying factors, such as what we demonstrated in our study, may unveil previously unknown associations of human ecology and malaria. For example, the exact manner in which proximity to features such as health services and roads mitigate against Plasmodium infection in children remains unknown, though we have shown it to be an important indicator of decreased risk. Access to prompt health care and interventions such as ITNs are two possibilities, though broader access to transportation and thus economic markets may be part of the developmental mechanism that reduces malaria incidence. We found the effects of material wealth and urbanicity acted independently to increase or decrease malaria risk so that the key may not merely improved housing conditions, as is often posited. We offer that considerably more work needs to be done to untangle the relationship of economic development and malaria. This issue will become ever salient as Africa continues to develop.

Our study suffered from a number of important limitations. First, though one of our goals was to create a measure based on data that could be easily obtained for any developing country, we were hampered by the lack of more specific markers of urbanicity and development. Data on the locations of school or markets might have helped to make our results more robust. Second, the low level of internal reliability of the measures chosen was cause for concern. Given our experiences in Malawi, though, we feel as though the composite measure is a reasonable representation of the gradient of urbanicity in Malawi. Third, the cross-sectional nature of the malaria data may be ignoring important temporal effects of seasonal malaria transmission. Data was collected to assess prevalence at a time of peak transmission. We may find, though, that not only is prevalence and malaria risk impacted by urbanicity, but that the nature of seasonal patterns of transmission may also differ by developmental context.

2.6 Conclusions

In this research, we have shown that, given a set of measures associated with urbanicity, there exists is gradient across the map of Malawi. Urban-like areas exists in those areas traditionally classified as "rural" and and rural-like areas exist within and in close proximity to area traditionally classified as "urban." We have also shown that a common developing world disease such as malaria has a graded association with the level of urbanicity. We then suggest that policy makers who wish to deliver interventions to target malaria should take these heterogenities in to account so as to prevent wastage and deliver scarce resources to the areas with the greatest need.

Table 2.1: Correlations of urbanicity factors

	Dist to HF	**Dist to River**	**Dist to Lake**	**Dist to Elec**	**Dist to Road**	**Pop. Density**
Dist to HF	1	0.08	-0.08	0.26	0.5	-0.15
Dist to River	0.08	1	-0.11	0.24	0.16	0
Dist to Lake	-0.08	-0.11	1	-0.19	-0.1	0.04
Dist to Elec	0.26	0.24	-0.19	1	0.17	-0.08
Dist to Road	0.5	0.16	-0.1	0.17	1	-0.13
Pop. Density	-0.15	0	0.04	-0.08	-0.13	1

Table 2.2: Loadings of first two principal components of urbanicity measures. Note that the first component contains weights for all six measures.

Loadings:		
	Comp.1	**Comp.2**
Distance to HF	-0.546	-0.345
Distance to River	-0.309	0.534
Distance to Lake	0.264	-0.461
Distance to Power Grid	-0.443	0.351
Distance to Road	-0.536	-0.295
Population Density	0.231	0.416
	Comp.1	Comp.2
SS Loadings	1	1
Proportion Variance	0.167	0.167
Cumulative Variance	0.167	0.333

Table 2.3: Reliability Analysis: Cronbach's alpha and Guttmans lambda 6 are calculated to measure the internal reliability of urbanicity factors.

Reliability analysis				
	Raw α	**Stand. α**	**Guttman's λ 6**	**Average r**
	0.00022	0.52	0.51	0.15
Reliability if an item is dropped:				
Dist to HF	0.00017	0.41	0.37	0.12
Dist to River	0.00023	0.51	0.49	0.17
Dist to Lake	0.00019	0.52	0.5	0.18
Dist to Elec	0.00013	0.44	0.43	0.13
Dist to Road	0.0002	0.41	0.37	0.12
Pop. Density	0.36014	0.54	0.52	0.19

Table 2.4: Survey demographics, household characteristics and associations with parasitemia for households and children in eight Districts of Malawi, 2007. Means of continuous variables are compared through t-tests. Categorical associations are tested using chi-square tests.

		Plasmodium Parasitemia		
	Total	**Positive**	**Negative**	**p**
N	6094	822 (13.48%)	5272 (86.51%)	$\leq$**.0001**
Parasitemia				
Under ITN	3127 (51.31%)	346 (42.09%)	2781 (52.75%)	$\leq$**.0001**
Age	24.69 (.00%)	18.03 (.00%)	26.15 (.00%)	$\leq$**.0001**
Gender (Male)	2978 (48.87%)	387 (47.08%)	2591 (49.14%)	0.28
Water Source				$\leq$**.0001**
Piped Water	356 (5.84%)	39 (4.74%)	317 (6.01%)	
Protected/Borehole	3479 (57.09%)	502 (61.07%)	2977 (56.47%)	
Public Faucet	670 (10.99%)	34 (4.14%)	636 (12.06%)	
Trad. Public Well	590 (9.68%)	129 (15.69%)	461 (8.74%)	
Piped into Yard	699 (11.47%)	79 (9.61%)	620 (11.76%)	
River/Canal/Stream	300 (4.92%)	39 (4.74%)	261 (4.95%)	
Toilet				$\leq$**.0001**
Flush Toilet	181 (29.70%)	29 (3.53%)	152 (2.88%)	
Pit Latrine	4519 (74.15%)	541 (65.82%)	3978 (75.46%)	
VIP Latrine	25 (.41%)	3 (.36%)	22 (.42%)	
Bush	39 (.63%)	13 (1.58%)	26 (.49%)	
Other	1330 (21.82%)	236 (28.71%)	1094 (20.75%)	
Roof Type				$\leq$**.0001**
Natural Material	4491 (73.69%)	696 (84.67%)	3795 (71.98%)	
Iron Sheets	1603 (26.30%)	126 (15.32%)	1477 (28.01%)	
Floor				$\leq$**.0001**
Dirt	4824 (79.15%)	713 (86.73%)	4111 (77.97%)	
Wood	1270 (20.84%)	109 (13.26%)	1161 (22.02%)	
Distance to				
Road	0.96	1.26	0.92	$\leq$**.0001**
HF	6.50	7.80	6.30	$\leq$**.0001**
Lake	26.89	13.49	28.98	$\leq$**.0001**
River	2.33	2.34	2.33	0.85
Power Grid	12.55	11.16	12.77	$\leq$**.0001**
Population Density	7,961	3,915	8,589	$\leq$**.0001**

Table 2.5: Add caption

	Bivariate Models		Multivariate Model		Model with Urbanicity Var.	
Intercept			**1.74(1.28, 2.37)**	**≤.0001**	1.04(.83, 1.30)	.76
Gender	1.09(.94, 1.26)	.27	1.09(.92, 1.28)	.31	1.07(.92, 1.25)	.37
Slept under ITN last night	**.65(.56, .76)**	**≤.0001**	**.50(.43, .59)**	**≤.0001**	**.64(.55, .75)**	**≤.0001**
SES Quintile						
1 (Poorest)	ref					
2	**.75(.62, .92)**	**≤.0001**	.84(.67, 1.04)	.10	**.79(.64, .96)**	**.02**
3	**.64(.52, .79)**	**≤.0001**	.85(.68, 1.08)	.18	**.68(.55, .85)**	**≤.0001**
4	**.41(.32, .52)**	**≤.0001**	**.58(.44, .76)**	**≤.0001**	**.50(.39, .65)**	**≤.0001**
5 (Least Poor)	**.42(.32, .55)**	**≤.0001**	**.54(.40, .73)**	**≤.0001**	**.64(.48, .85)**	**≤.0001**
Age (in months)	**.95(.94, .96)**	**≤.0001**	**.94(.94, .95)**	**≤.0001**	**.95(.94, .96)**	**≤.0001**
Distance to						
HF	**1.06(1.05, 1.08)**	**≤.0001**	**1.03(1.01, 1.04)**	**≤.0001**		
Road	**1.21(1.15, 1.27)**	**≤.0001**	**1.15(1.08, 1.22)**	**≤.0001**		
Lake	**.96(.96, .96)**	**≤.0001**	**.96(.95, .96)**	**≤.0001**		
River	1.00(.97, 1.04)	.85	1.03(.99, 1.07)	.14		
Power grid	**.99(.99, 1.00)**	**≤.0001**	**.99(.99, 1.00)**	**≤.0001**		
Population Density	**1.00(1.00, 1.00)**	**≤.0001**	**1.00(1.00, 1.00)**	**.02**		
Urbanicity	**.71(.66, .77)**	**≤.0001**			**.76(.70, .82)**	**≤.0001**

CHAPTER III

DISTANCE TO HEALTH SERVICES INFLUENCES INSECTICIDE-TREATED NET POSSESSION AND USE AMONG SIX TO 59 MONTH-OLD CHILDREN IN MALAWI

3.1 Abstract

Background Health ministries and providers are rapidly scaling up insecticide treated nets (ITN) distribution to control malaria, yet possession and proper use typically remain below targeted levels. In Malawi, health facilities (HFs) are currently the principal points of ITN distribution, making it important to understand how access to these ITN sources affects ownership, possession, and use. The authors evaluated the association between proximity to HFs and ITN possession or use among Malawian children six to 59 months of age.

Methods A household malaria survey undertaken in eight districts of Malawi during 2007 was used to characterize ITN possession and use. The location of each respondent's household was geocoded as was those of Ministry of Health (MoH) HFs and other health centers. Euclidean distance from each household to the nearest HF was calculated. The authors then analyzed the significance of distance and ITN possession/use through standard statistical tests, including logistic regression. Continuous, composite measures of urban and rural are compared with dichotomous classifications according to political boundaries.

Results Median distance to HFs was greater among households that did not possess ITNs and did not use an ITN the previous evening. Descriptive statistical methods confirmed a pattern of decreasing ITN possession and use with increasing distance from HFs. Logistic regression showed the same statistically significant association of distance to HFs, even when controlling for age and gender of the child, ratio of nets to children in household, community net possession and use, and household material wealth.

Conclusions Strategies that exclusively distribute ITNs through HFs are likely to be less effective in increasing possession and use in communities that are more distant from those health services. Health providers should look towards community-based distribution services that take ITNs directly to community members to more effectively scale up ITN possession and regular use aimed at protecting children from malaria.

3.2 Background

Insecticide-treated mosquito nets (ITNs) have reduced all-cause childhood deaths by 15-20 % according to diverse research evidence [Gamble et al., 2006, D'Alessandro et al., 1995, Lengeler, 2004, Eisele et al., 2011, Phillips-Howard et al., 2003, ter Kuile et al., 2003, Steketee and Campbell, 2010]. ITN program evaluations have also demonstrated substantial impacts against malaria [Mathanga and Bowie, 2007, Mathanga et al., 2006]. Greater coverage has produced enhanced reduction in malaria morbidity and mortality, even more so among those within a close proximity of households with treated nets [Hawley et al., 2003]. Given these benefits, as well as the low cost, safety and ease of ITN implementation, national malaria programs are now scaling up ITN distribution in attempting to achieve the Roll Back Malaria target of 80% coverage. In Malawi, nearly all residents live at some level of year-round risk of Plasmodium infection. The Malawi Ministry of Health (MOH) estimates that about six million malaria episodes occur each year[National Malaria Control Programme, 2010] among a 2010 population of 15 M people [United Nations Development Program, 2010]. To control malaria, the Government of Malawi is rapidly scaling up effective malaria interventions [Malawi Ministry of Health (MoH), 2005]. Since 1998, the ITN program in Malawi has distributed cost-subsidized ITNs to children under 5 years of age, and to pregnant women, through public Health Facilities (HFs) and short-term mass distribution campaigns. According to UNICEF's Multiple Indicator Cluster Survey (MICS) and the recent Malawi Malaria Indicator Survey (MIS), possession of at least one ITN has increased from 49.5% in 2006 to approximately 63% in 2010 with utilization for pregnant women and children under five increasing from 26% to 49% and from 23% to 59%, respectively /citenmcp, Mathanga2011. However, as has been shown in past studies, possession and use can vary significantly by district[Kadzandira, 2004]. Although ITNs are an effective means of preventing transmission, inequities exist both in use and distribution. [Schellenberg et al., 2003] and [Matovu et al., 2009] demonstrated that socioeconomic status (SES) was a major influence on knowledge of and access to health care, even in rural areas considered to be uniformly very poor. In countries where ITNs are partially subsidized and socially marketed, cost is the main factor which prevents the poorest of the poor from accessing and utilizing them [Bernard et al., 2009, Ruhago et al., 2011]. To reduce barriers to possessing an ITN, starting in 2007, the Government of Malawi has been providing free ITNs to pregnant women and children ¡ 5 years old (yo) attending a public HF [Skarbinski et al., 2011]. Although coverage has significantly increased since the implementation of facility-based free ITN distribution, the program remains inequitable. Coverage in urban areas is still much higher than that in rural areas [National Malaria Control Programme, 2010, Mathanga et al., 2011]. Although many health ministries and NGOs widely distribute ITNs for free or at low cost, their incorrect and inconsistent use remains problematic. Usage patterns differ among age groups [Noor et al., 2009a], house construction, sleeping configuration [Alaii et al., 2003, Iwashita et al., 2010], education level [Atieli et al., 2011]. This suggests that possession and distribution are only a first step towards reaching widespread household use of ITNs. This is particularly important for the rural poor, who often reside in areas of diminished public health infrastructure and challenging, vector-friendly topography. In addition, poor households often live in rudimentary conditions. Hence, the members of these households live under the highest risk of disease [Alaii et al., 2003]. Distance to health services impacts on health seeking behaviors [Rosero-Bixby, 2004, Gething et al., 2004]. Travel times, lack of access to transportation, and seasonally inaccessible roadways can present barriers to patient access to health facilities [Chayovan et al., 1984]. Areas of low access are often inhabited by people who need health care the most [Wang and Luo, 2005]. Ill residents in areas where access is difficult often under-utilize services or present to health facilities (HF) only when their condition is grave, sometimes missing opportunities to effectively treat health problems [Cambanis et al., 2005]. Distance to HFs may also negatively impact disease prevention. For malaria in particular, remoteness and proximity to HFs have been shown to be associated with ITN possession in Kenya [Prudhomme O'Meara et al., 2011]. Proximity to health services and ITN distribution points might also influence regular and proper use of ITNs. Accordingly, the authors examined household-level determinants of reported ITN possession and use among six to 59 month-old children in Malawi, using data gathered during a 2007 survey of malaria patterns. Associations between geographic distances to HFs and reported ITN possession and use were evaluated.

3.3 Materials and Methods

3.3.1 Parasitemia Survey

A population-based, cross-sectional survey was undertaken in eight of Malawi's 28 Districts during April/May 2007. Strategically conducted at the end of the rainy season when malaria-related morbidity is normally highest, the Districts were chosen from throughout the country. Surveys were conducted in Blantyre, Mwanza, Phalombe, and Chiradzulu Districts in the Southern Region, Lilongwe and Nkhotakhota in the Central Region, and Karonga and Rumphi in the Northern Region. The Institutional Review Boards at the College of Medicine, University of Malawi and the US Centers for Disease Control and Prevention (CDC) approved the study protocol. Household selection and sampling Households were selected for inclusion in the study using a modified EPI cluster survey method as described by Turner et al. [Turner et al., 1996]. The modified cluster survey method involved: a) selection of Enumeration Areas (EAs) from each of the eight Districts with probability proportional to size (PPS) of the population b) use of EA maps to create sub-clusters or segments of approximately equal population size c) the random selection of one segment d) an interview with all households in the selected segment e) the selection of one child 6 to 59 months old from each surveyed household. The survey was initially intended to determine the extent of Plasmodium infection in Malawi. Therefore, children under 6 months of age who are presumably protected from infection through the presence of maternal antibodies were excluded. There was a median number of 32 households per EA among 220 total EAs. The number of households per segment

Table 3.1: Summary of household surveyed by sample locations and demographic characteristics, and of ITNs per household

	Households	
	No.	%
All Districts	7,564	100.00%
District		
Phalombe	930	12.30%
Blantyre	520	6.90%
Chiradzulu	736	9.70%
Mwanza	1,052	13.90%
Lilongwe	792	10.50%
Rumphi	1,162	15.40%
Nkhotakhota	1,189	15.70%
Karonga	1,181	15.60%
SES Quintile		
1 (lowest)	1,758	23.20%
2	1,661	22.00%
3	1,513	20.00%
4	1,391	18.40%
5 (highest)	1,241	16.40%
Gender (Male)	3,839	50.70%
Age (Avg. months)	25.12	–
No. Children (per HH)	1.26	–
No. People (per HH)	4.26	
ITNs (Avg. per HH)	1.35	–
ITNs (Avg. per Child)	0.31	–

was indeterminate from the data. A total of 7,564 households were included in the final database. (See table 3.1)

3.3.2 Data collection and definitions

Trained interviewers administered structured questionnaires to consenting household heads and/or parents/guardians of selected households to gather information on household ITN possession and use by children six to 59 months old, SES of the household, house construction, and other potential risk factors. The questionnaire was originally developed in English and translated into two main languages spoken in the selected Districts (Chichewa and Chitumbuka). Latitude and longitude of the house was taken using a GPS unit. Data were recorded electronically using a PDA and downloaded every evening of the survey onto a secure digital card, then later added to a master Microsoft Access database. A household was defined as a family comprised of a male or female head, his or her husband or wife, as well as children and immediate family members who shared income. An ITN was defined as any bed net, regardless of treatment status, since for more than a decade treated nets only have been distributed in Malawi. Because the objective of this study was to evaluate health care access rather than net treatment practices, no attempt was made to distinguish between treated nets, time since re-treatment, or long-lasting insecticidal nets (LLINs).

3.3.3 Health facility data

All HFs in Malawi, both public and private, were comprehensively surveyed in 2000 by the Japan International Cooperation Agency (JICA). The geographic coordinates for each HF, in addition to facility type, possession, funding source, type of road leading to the facility and road condition, were all recorded. For the present analysis, only Malawi MoH hospitals, clinics, maternity clinics and dispensaries, and hospitals operated by religious groups (e.g. CHAM facilities) were considered (Figure 3.1). Although a small number of surveyed households of sufficient material means may have patronized private facilities, free net distribution and MoH health policies emanate from public HFs run by the MoH and cooperating religious organizations. Thus, as private clinics operate independently of MoH influence and policies with regard to malaria treatment and prevention, private clinics were excluded from this analysis.

Distance to health facility measurement Lacking individual data on travel methods, routes and travel times, distance to the nearest HF from each surveyed household was calculated using simple Euclidean distance calculated in ArcGIS 10.0. A more complex distance estimate with various assumptions about road use produced

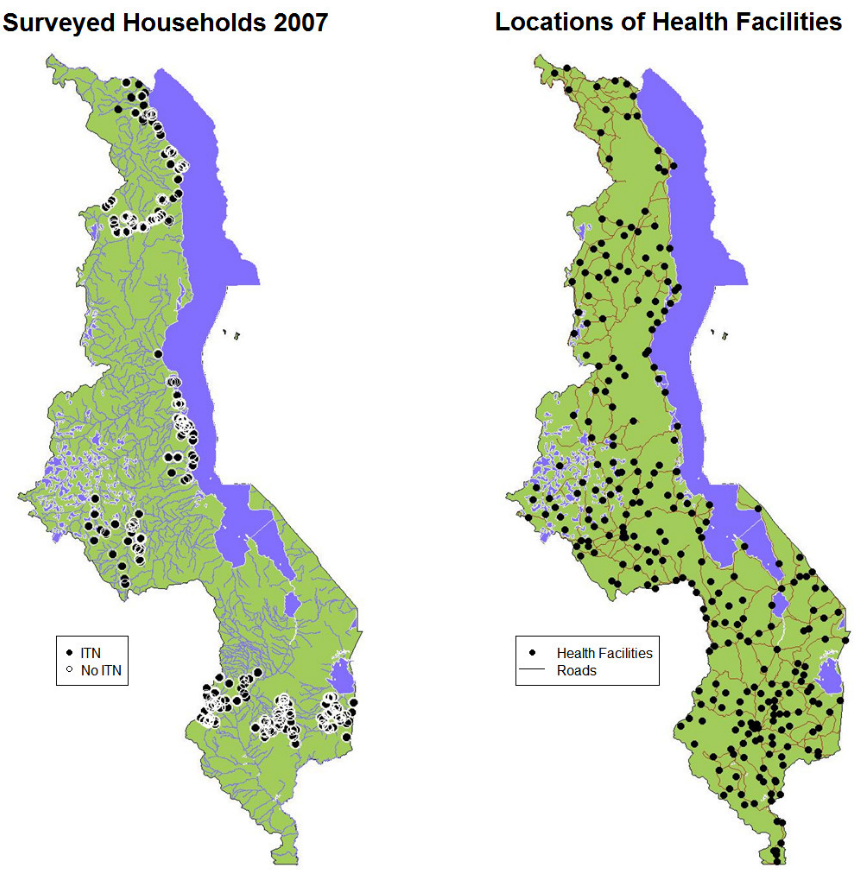

Figure 3.1: Maps of Malawi showing (a) locations of households in the Northern, Central and Southern Regions surveyed during the 2007 sampling period and (b) Health facilities and major roads throughout the country.

highly correlated values (data not shown). The HF located most proximate to each household may not always be the facility that households most consistently utilize. Data on preferred facilities, health seeking behaviors and health services were not available. In spite of this limitation, the facility of any type that was located closest to the surveyed household, was used assuming that the closest facility stands as an appropriate proxy for access to health services generally. Four types of HFs were considered: maternity/dispensaries, district hospitals, religious hospitals and primary health centers.

3.3.4 Statistical methods

Associations between distance to nearest HF and ITN possession or use in the previous 24 h were explored. First, median distances to the nearest HF for the both ITN possession and use were compared using Wilcoxon tests of difference in medians. To determine trends in ITN possession and use in relation to increasing distance to HF, the complete set of distances to nearest HFs from households was broken into 10 equal and ordered groups (deciles). Next, percentages of sampled children in each category were calculated within each decile. Visual representations of the percentages of households within each decile were produced and a non-parametric loess curve to demonstrate trend was fit Logistic regression was used to statistically test the relationship between increasing distance and ITN possession and ITN use. Linear and quadratic terms for distance to nearest health facility were included, suspecting that the relationship of distance to outcomes would not be linear. Tests for statistical significance in both bivariate and multivariate models were performed. Factors such as SES, gender, age and the ratio of nets to children in the household might confound the relationship of distance to outcomes, motivating a multivariate model. To account for possible contributions of surrounding households to the outcome of interest, a spatial covariate representing the percentage of the nearest five sampled children who reportedly possessed or used ITNs was included. The univariate (1) and multivariate (2) models were:

$$logit(\pi) = b_0 + b_1(DistancetoHF) + b_2(DistancetoHF2) \tag{3.1}$$

$$\begin{aligned} logit(\pi) = b_0 + b_1(DistancetoHF) + b_2(DistancetoHF2) + b_3Age + b_4Gender \\ + b_5NetRatio + b_6SESquintile + b_7(\%ofsurrounding5neighbors) \end{aligned} \tag{3.2}$$

Associations between the type of HF nearest the household and net, ITN possession, and ITN use were evaluated. Since differing levels of ITN distribution occur at the different facilities, patterns of association with net possession, ITN possession and ITN use were tested using logistic regression and a categorical predictor of the four health facility types of interest: maternity/dispensaries, district hospitals, religious hospitals and primary health centers. All statistical analyses were performed in R, version 10.1.1 (CRAN.org).

3.4 Results

Overall, 75.8% of surveyed households reported owning an ITN. Of all households surveyed, 69.5% stated that the child chosen for the survey slept under a net the previous night. ITN possession and ITN use varied among districts, with Karonga reporting the highest levels of use (88.1%) and possession (85.3%). Households in Mwanza District had the lowest levels of ITN possession (76.0%), while Chiradzulu had the lowest level of ITN use by children within the previous 24 h (45.1%) (See table 3.2).

Table 3.2: Percentages of households reporting possession of at least one ITN and use of ITNs by the surveyed child in the previous 24 hours by district and wealth quintile.

	Possesses	**1 ITN**	**Child Slept**	**Under ITN**
	No.	%	No.	%
All Districts	5738	75.80%	5195	69.50%
District				
Phalombe	768	82.60%	688	74.50%
Blantyre	338	65.00%	281	54.20%
Chiradzulu	492	66.80%	332	45.10%
Mwanza	800	76.00%	724	68.80%
Lilongwe	573	72.30%	499	63.60%
Rumphi	840	72.20%	803	69.70%
Nkhotakhota	919	77.20%	868	73.10%
Karonga	1008	85.30%	1000	88.10%
SES Quintile				
1 (lowest)	1239	70.40%	1127	64.10%
2	1249	75.20%	1144	68.80%
3	1188	78.50%	1099	72.60%
4	1060	76.20%	948	68.10%
5 (highest)	1002	80.70%	941	75.80%

ITN possession and use followed similar patterns among SES groups. Households in the lowest quintile of material wealth reported the lowest levels of ITN possession and use, while possession and use were highest among the wealthiest of households. The middle three SES quintiles did not vary appreciably from one another

3.4.1 Distance, possession and ITN use

Wilcoxon tests statistically confirmed differences between distances to nearest HF and ITN possession and use. Households that did not possess ITNs and which reported that children did not sleep under one the previous night were located further away than households that possessed and used ITNs. Households that reported possessing an ITN were located on average 3.87 km from the nearest HF, whereas households that did not possess one were located 4.65 km away. Households reporting that the surveyed child slept under an ITN the previous night were located 3.85 km

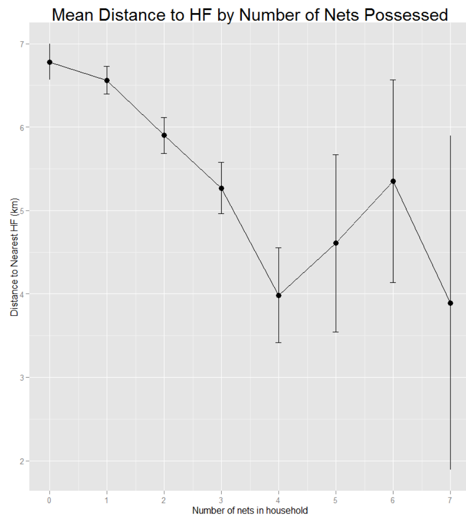

Figure 3.2: Mean distance (with error bars) to nearest health facility by the number of nets possessed in the household.
Households that possess few nets are located farther away from health services than households which possess many nets. There were few households with more than four nets.

away from the nearest facility, while households that reported that the child did not sleep under an ITN were more distant, being located 4.24 km away. Both differences were statistically significant (p ¡ 0.0001). The distance to the nearest HF also varied by the number of nets within the home. Households that possessed more nets were located closer to a HF than households which possessed very few. (See figure 3.2)

Household possession and use of ITNs in the previous 24 h followed similar trends with increasing distance. Both possession and use were highest in households most proximate to health services and lowest among those farthest away from HFs. The trend in declining ITNs with distance to the nearest HF was not linear, rather dropped sharply for households within 5-7 km, then leveled off for the remaining households further away (Figure 3.3). Patterns of ITN use given possession of at least one ITN showed the same distance-decay pattern as that for possession only. ”Hockey stick” regression was used to determine an optimal breakpoint in the associative trend of distance on ITN possession and use, noting that the trend of decay

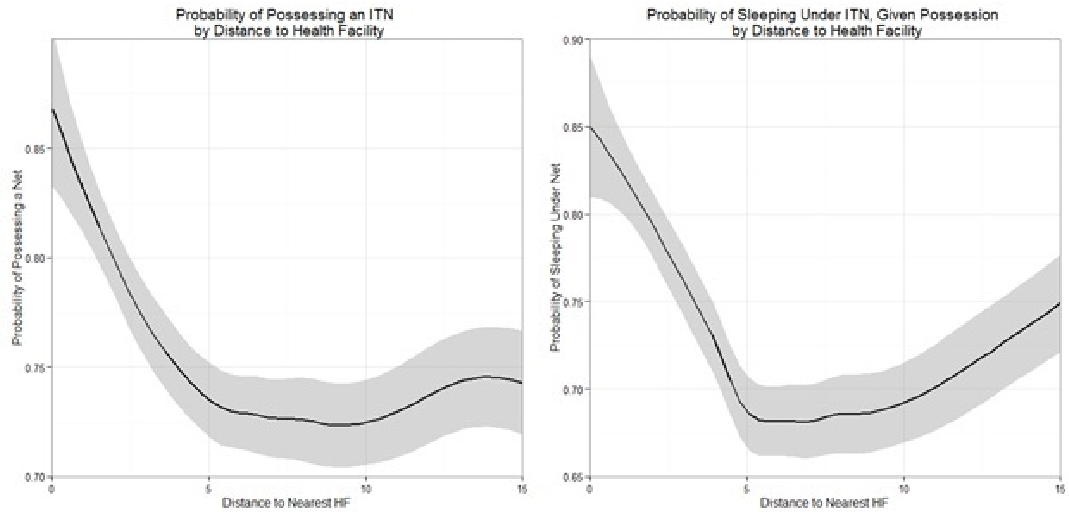

Figure 3.3: Possession of any type of net and possession of ITNs by quantile of household distance to nearest health facility (left) along with use of any type of net in the previous 24 h by quantile of household distant to nearest health facility for 7,564 households. Lines represent loess (locally weighted scatterplot smoothing) curve fits to illustrate trends.
Trends illustrated using loess (locally weighted scatterplot smoothing) line fitting.

in the loess interpolation appears to change strikingly at 5-7 km. There was a breakpoint in distance and ITN possession at 5.2 km, where possession stops declining with distance and becomes constant. There was also a breakpoint of 6.4 km for ITN use given possession. The increase in use for very remote households was worth noting. This study only includes known HFs and does not take into account the locations of community-based health services which could be driving this phenomenon.

Logistic regression models confirmed statistical significance of distance to nearest HF for ITN possession and ITN use given possession in the previous 24 h in both bivariate models and multivariate models with possible confounding covariates. Linear and quadratic terms for distance were significant in all models. While use of ITNs by neighboring households was the most important predictor of both net possession and net use given possession among surveyed children, the effect of distance upon net use remained unchanged, both in magnitude of effect and pattern (Table 3.3). Interestingly, SES was not significantly associated with ITN possession or use. However, age was significantly associated with ITN use, implying that households may prioritize ITN use for very young children who sleep alongside mothers.

Table 3.3: Results of logistic regression models of possession of any kind of net, ITN possession and reported ITN use in the previous 24 hours

	Net Possession		Slept Under ITN	
	OR	**p-value**	**OR**	**p-value**
Intercept	5.23 (4.56, 6)	¡ 0.0001**	17.58 (15.33, 20.16)	¡ 0.0001**
Distance	0.82 (0.78, 0.87)	¡ 0.0001**	0.75 (0.72, 0.79)	¡ 0.0001**
Distance2	1.01 (1.01, 1.02)	¡ 0.0001**	1.02 (1.02, 1.03)	¡ 0.0001**
Intercept	0.36 (0.26, 0.5)	¡ .0001**	2.17 (1.28, 3.69)	0.004*
Distance	0.92 (0.87, 0.97)	0.002*	0.87 (0.78, 0.96)	¡ 0.005*
Distance2	1.01 (1, 1.01)	¡ 0.015*	1.01 (1, 1.02)	¡ 0.002*
Age	1 (1, 1.01)	0.531	0.98 (0.97, 0.99)	¡ 0.0001**
Gender	0.97 (0.87, 1.09)	0.662	1.02 (0.85, 1.24)	0.806
SES	1 (0.96, 1.05)	0.88	0.95 (0.88, 1.02)	0.157
Neighbors	28.83 (23.28, 35.7)	¡ 0.0001**	33.07 (24.05, 45.46)	¡ 0.0001**
Net Ratio		NA	1.36 (0.88, 2.1)	0.173

Both bivariate and multivariate are included
* = p ¡ .01, ** = p ¡ .0001

The covariate representing ITN possession and use among proximal neighbors was intended to account for spatial dependencies in the data which could negatively affect the estimation process. Households which are located in communities where ITN possession is high are, of course, more likely to own nets themselves. In terms of possession, for example, community ITN coverage will be related to distance to the nearest health services as a point of distribution and to the outcome of household ownership. Thus, this variable was introduced in the multivariate models as a potential confounder to be controlled for. The very high contribution of proximate ITN possession on household possession in the multivariate logistic model confirms this assumption (OR 28.83). However, as households do not receive nets from one another, further exploration of this covariate was deemed unnecessary although the authors recognize that neighbors may influence one another in procuring ITNs from health facilities. Conversely, the neighbor covariate for ITN use among possessing households was of interest since household behavior may be influenced by the behavior of one's neighbors. The odds of ITN use among households which were located in communities where there is universal coverage among proximate neighbors were 33 times higher than households located in communities where no people use ITNs. An assessment of spatial auto-correlation in ITN use produced a Moran's I statistic of 0.30 (p ¡ 0.001), indicating that households proximate to one another were more likely to exhibit similar ITN use behaviors. Despite the presence of the neighbor variable in models of both ITN possession and ITN use, the variable for distance to nearest health services remained significant. The association of distance to health services on ITN possession and use appears small, but not so small when considering the cumulative effects of distance. The OR for ownership of ITNs for households 5 km away from the nearest health services was 0.45 in the bivariate model and 0.84 in the multivariate model. Similarly, the OR for use given possession for households located 5 km from the nearest HF was 0.38 for the bivariate model and 0.63 for the multivariate model.

3.4.2 Health facility type

Households that were located closest to a district hospital had elevated odds (OR 2.64 (2.19, 3.19)) of possessing at least one ITN compared with those located close to dispensary/maternity clinics. However, ITN possession in households located near religious hospitals (OR 1.13 (0.83, 1.53)) and primary health centers (OR 1.07 (0.91, 1.24)) was not significantly different from that in households close to dispensary/maternity clinics. The odds of sleeping under an ITN were significantly higher among households that were closest to district hospitals (OR 2.67 (1.93, 3.69)) than those closest to dispensary/maternity clinics. Religious hospitals (OR 1.14 (0.68, 1.89)) and primary health centers (OR 1.08 (0.84, 1.4)) did not differ significantly from dispensary/maternity clinics in ITN use. (See table 3.4)

Table 3.4: Results of logistic regression modelling ITN possession and reported ITN use within the previous 24 hours by type of nearest health facility

	Facility Type	**OR**	**p-value**
ITN Possession	**Intercept**	**2.77 (2.60, 2.94)**	**¡ 0.0001**
	Dispensary/Maternity		
	District Hospital	**2.64 (2.19, 3.19)**	**¡ 0.0001**
	Religious Hospital	1.13 (0.83, 1.53)	0.43
	Primary Health center	1.07 (0.91, 1.24)	0.42
Slept Under ITN	**Intercept**	**8.33 (7.52, 9.23)**	**¡ 0.0001**
	Dispensary/Maternity		
	District Hospital	**2.67 (1.93, 3.69)**	**¡ 0.0001**
	Religious Hospital	1.14 (0.68, 1.89)	0.62
	Primary Health center	1.08 (0.84, 1.40)	0.55

3.5 Conclusions

Using simple methodologies, the authors have shown that distance to health services is associated with ITN possession. Interestingly, this analysis uncovered the same relation with reported household use of any type of nets, even among those households who possess at least one. This finding provides further evidence to suggest that health services may play an important role in providing not only material resources, but also promoting use of health interventions within the home. Although data on maternal attitudes toward local health workers and preferred sources of health information were not available in this study, the results support the inference that regular contact between citizens and health workers or health intervention distribution sites help promote and reinforce beneficial household health behaviors. In Malawi, present strategies of ITN distribution center on antenatal and under-five clinics. Given the results of this study, which suggest that possession of ITNs decreases with increasing distance from health facilities, there may be a need to enhance community-centered ITN distribution models, to achieve the same level of coverage as existing community-based vaccination strategies. ITNs could be distributed widely within communities, utilizing present community health workers to deliver them directly to households. Information on appropriate use should then be disseminated directly to caregivers, reinforcing proper protective behaviors. Other studies have shown that community based malaria education programs result in more consistent patterns of households ITN use [Rickard et al., 2011]. An emphasis on a community-based model over facility-based distribution strategies could address the problem of low ITN possession particularly among communities distant from health services, but could also serve to encourage consistent levels of use within households in isolated communities that have little access to malaria educational programs. The mechanisms of household-level decision-making as they relate to HF access are largely unknown. More frequent trips to HFs might result in more opportunities for health messages to reach households, reinforcing pro-active efforts to protect the health of family members and increasing awareness of the causes and prevention of malaria. This study lacked a quantified measure of education of female household heads, preventing formal examination of this possibility. Other studies have indicated that knowledge and perceptions of malaria sources varied among education levels [Alaii et al., 2003], with better educated mothers having greater malaria knowledge than those who were less educated. In addition, Dyke, et al [Dike et al., 2006] demonstrated in Nigeria that higher levels of education are not only associated with malaria knowledge, but also with actual ITN use. Health services tend to be located near markets, schools and other important areas of infrastructure. Thus, households near HFs are also likely to be of greater SES through participation in market economic activities, better educational opportunities and greater chances for employment. Residents living further away from health services, and thus from market centers, may tend to be less educated, less likely to participate in cash-based economic activities, and less prone to taking advantage of health services and interventions. However, because education level and SES are intertwined, the lack of significance of SES (wealth quintiles) in the regression model for household ITN use suggests that education plays less of a role in ITN use than health messages and access to services than might be assumed. While the insignificance of SES in the multivariate possession model may be the result of ITN distribution programs that specifically target low SES households, the lack of significance in a model of ITN use given possession suggests the need for further exploration of determinants of ITN use beyond material wealth. The authors recognize that there may have been systematic over-reporting of ITN use or variability in reports of ITN use among SES groups, for example. Respondents may have been concerned about self-implicating themselves if they believed that they neglected to protect their children from disease. Similarly, no clear attempt was made to disentangle actual practices from reported habits through structured verification of responses and the data prevented validation of responses of ITN use. However, misreporting of ITN use was probably unrelated to distance to nearest HF, suggesting no systematic bias that would influence statistical estimates of ITN use and health facility proximity associations. While absolute percentages of ITN use may be overestimated in the present survey, the reported patterns with proximity to health services are valid and representative. Equitable distribution of ITNs with strategies that maximize coverage of high risk areas should be of uppermost priority among health officials. The authors recommend that health workers take proactive steps to help communities that are remotely situated (particularly those beyond 5 km) from health services. Although nothing in these results allows one to test the hypothesis that direct, community-based health initiatives reinforce health behaviors, future research should attempt to measure the public health impact of community workers. Studies that assess community attitudes toward those workers could direct policy makers to upgrade current strategies which could, in turn, help improve the level of trust in the information and services that they deliver. Clearly, though, community based malaria programs should not be limited to ITNs, but should include other methods such as indoor residual spraying (IRS) and home-based treatment methods. Promoting a comprehensive approach in the fight against malaria should be of the utmost importance to both researchers and policy makers [Wilson et al., 2011]. IRS initiatives may obviate the need for regular, nightly use of ITNs and home treatment strategies for isolated areas may mitigate transmission levels. To this end, future research efforts should include other intervention methods, access to which may also be associated with distance to health services. Future research could utilize the methods presented here, to assess the potential role that access to health services can play in an interdependent system of interventions and work to target underserved geographic areas of significant risk for malaria. It is possible that within this system of interventions, some may be more effective than others and the correct 'recipe' for a sustainable strategy balanced with logistical costs may be geographically dependent on access to health services.

CHAPTER IV

INSECTICIDE TREATED NET USE BEFORE AND AFTER A MASS DISTRIBUTION IN A FISHING COMMUNITY ALONG LAKE VICTORIA, KENYA

4.1 Abstract

Introduction Insecticide treated nets (ITNs) have proven instrumental in the fight against malaria in holoendemic regions. As distribution of ITNs throughout sub-Saharan Africa (SSA) is being scaled up, however, maintaining coverage over time will be important to sustain current gains. The effectiveness of mass distribution of ITNs, and particularly the duration of effective use, is likely to contribute to the extent of long-term impacts.

Methods Mass distribution of ITNs to a rural Kenyan community along Lake Victoria was performed in early 2011. Surveyors collected data on ITN use both before and one year following this distribution. At both times, household representatives were asked to provide a complete accounting of ITNs within the home, where the nets were located and the ages and genders of the persons who slept under them the previous evening. Other data on household material possessions, education levels, occupations and community group membership were recorded. The presence of ceiling nets to prevent entry to the dwelling by vector mosquitoes and past participation in indoor residual spraying (IRS) campaigns was noted. Basic information

on malaria knowledge and health seeking behaviors were also collected. Patterns of ITN use before and one year following distribution were compared using spatial and multi-variable statistical methods. Associations of ITN use with various individual, household, demographic and malaria related factors were tested using logistic regression. A classification and regression tree methodology was employed to test for the relative contribution of various factors to ITN use.

Results Less than 50% of residents reported using ITNs at the time of distribution. One year following mass distribution, 92% of ¿5,000 individuals representing 2,000 households reported sleeping under an ITN the previous evening. However, ITN use varied by age, following a similar pattern both pre- and post-distribution. After infancy, ITN use sharply declined until the late teenage years then began to rise again, plateauing at 30 years of age. Males were less likely to use ITNs than females. Prior to distribution, socio-economic factors such as parental education and occupation were associated with ITN use. Following distribution, ITN use was even across social groups. Household factors such as availability of nets and sleeping arrangement still present a barrier to consistent use, however.

Conclusions Mass distributions of ITNs was effective in rapidly scaling up coverage, with use being maintained at a high level at least one year following. Free distribution of ITNs using a direct to household distribution method can eliminate socio-economic and spatial heterogeneities in ITN possession and use. Age is an important factor in determining consistent ITN use but problems of sleeping arrangement and ITN leakage will present a challenge to effective intervention campaigns.

4.2 Introduction

Insecticide treated bed nets (ITNs) have proven instrumental in the fight against malaria in sub-Saharan Africa (SSA) [Lengeler, 2004][Lim et al., 2011]. The World Health Organization has recommended that all health ministries and donor agencies scale up the distribution of ITNs, specifically to target populations of small children and pregnant women[World Health Organization, 2007]. ITNs have been shown to be associated with an average 20% reduction in overall parasite prevalence across a number of geographic contexts[2] accompanied by precipitous drops in certain Anopheline vector species in Kenya[Bayoh et al., 2010]. However, despite massive scale-up of ITN distribution all over SSA, shortfalls and inequities exist[Noor et al., 2009b], which might compromise long term elimination or control programs.

Possession of ITNs has been shown to be associated with factors such as proximity to distribution sites, cost, socio-economic status and the method of distribution [Larson et al., 2012][Cohen and Dupas, 2010][Skarbinski et al., 2011][Mathanga and Bowie, 2007][Noor et al., 2007]. ITN distribution programs can rapidly increase ownership and bolster household use. In Sierra Leone, for example, a mass distribution campaign increased household use 137% within six months[Bennett et al., 2012]. Possession, however, does not necessarily imply compliance. The decision of whether or not to use ITNs for the prevention of malaria results from a complex set of factors. In one Ghana study, people used ITNs to mosquito nuisance and not to prevent malaria [Adongo et al., 2005]. Seasonal patterns of precipitation and vector density along with education were associated with ITN use in the western Kenyan highlands[Atieli et al., 2011]. Sleeping arrangements, such as sleeping on the floor (as opposed to a bed) and availability of areas amenable to hanging nets also have been shown to be associated with ITN use[Iwashita et al., 2010]. Comprehensive knowledge of malaria and education in the purpose of ITNs has increased use among pregnant women in Nigeria[Ankomah et al., 2012].

Challenges to maintaining consistent coverage and compliance following scale-ups have been presented in various investigations. One study in Burkina Faso noted declines in motivation less than a year following widespread distribution, citing problems of convenience and the perception that malaria is multi-factorial[Toe et al., 2009]. Leakage (loss or disappearance of ITNs following distribution) of freely distributed nets was seen in a Senegal study, with nearly 10% of nets provided to the community being absent from target households 6 months later [Thwing et al., 2011]. Leakage has also been shown to compromise the cost-effectiveness of distribution campaigns[Pulkki-Brnnstrm et al., 2012]. To confront challenges that ensure widespread compliance, research has suggested that providing even minimal education can effectively increase household use compared with other methods [Rickard et al., 2011][Deribew et al., 2010].

The current project investigated patterns of ITN use before and one year following a mass distribution campaign associated with a separate trial. We explored determinants of use at the individual, household and community level in order to uncover factors that may compromise future efforts to increase ITN ownership and use.

4.3 Methods

(Figure 4.1).

The Gembe East area of Mbita District in Nyanza Province (Fig. 1) was targeted for a randomized trial of two different types of Olyset nets in Jan/Feb 2011. Teams of community members were employed to visit all households in the distribution area

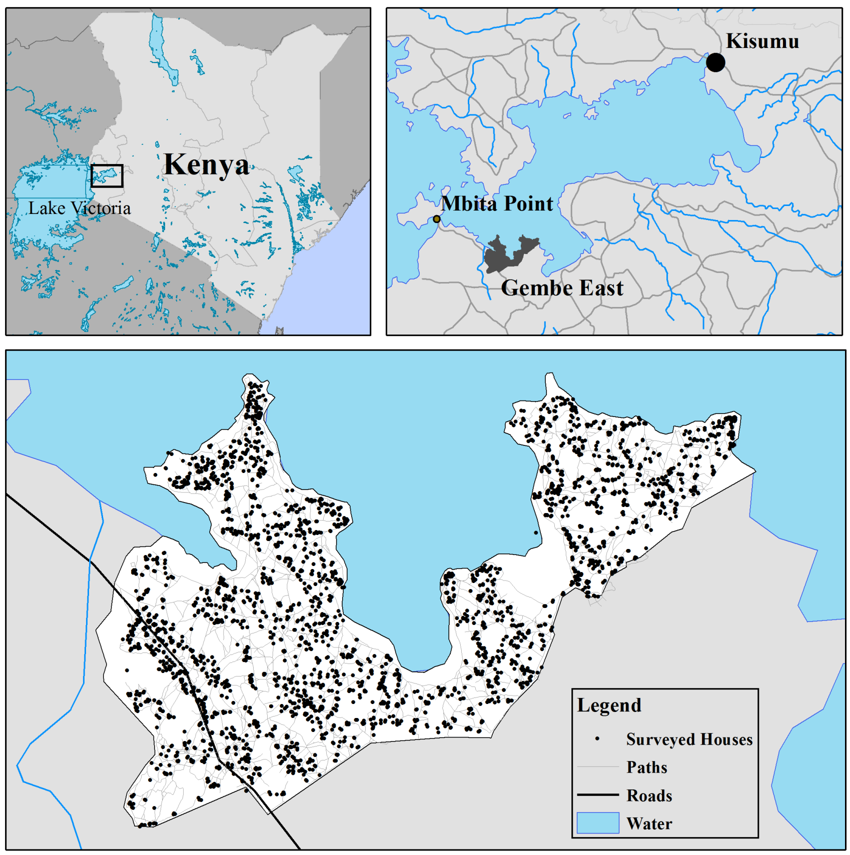

Figure 4.1: Study area and locations of households

(4,000), collect old nets (with homeowner consent) and provide each household with new ITNs. Survey teams explained to goals and purpose of the study to adult household representatives and obtained consent. Each household received a number of nets in relation to the number of people reported to regularly sleep in the home, following WHO standards. At the time of distribution, the ages and genders were noted. For each individual person, survey teams noted whether they reported sleeping under a net the previous evening. Sleeping arrangements were also noted.

Between January 2012 and August 2012, field workers revisited all households in the area with the aim of assessing the condition of the nets that were distributed roughly one year prior. Permission was again requested from an available adult household representative and the survey was conducted for those households agreeing to participate. For the post-distribution round of data collection, a comprehensive survey was created which included demographic questions, educational level achieved, and the occupations of male and female household heads. The survey teams recorded the presence of material goods such as radios, electricity and various types of livestock and noted types of roof and wall construction. From this, a composite household material wealth index was created using a principal components analysis methodology common to analyses of socioeconomic status or households in developing countries [21]. Membership in community groups such as churches and school attendance of children were recorded. Questions about malaria and ITN knowledge, along with general questions on health seeking and malaria-related health behaviors were asked.

Survey workers made a complete accounting of all nets in the household. Type and condition of each net, and the age and gender of the person(s) sleeping under each, was recorded. Nets that had been previously given out in the mass distribution were identifiable through a known code written on the brand tag of the ITN, but other nets were also recorded. Field workers also noted whether or not dwellings had closed or open eaves, a ceiling net was present, and any IRS in the past. All data were recorded on paper and entered later into Excel. GPS coordinates for each household were recorded using a Garmin GPS 60 device.

4.4 Statistical Analyses

Spatial patterns of ITN use before and after distribution, as well as other factors, were assessed visually. All maps were produced using ArcGIS version 10.1. GIS layers were obtained from DIVA-GIS[22]. Spatial autocorrelation was assessed using Morans I statistics.

Patterns of association of age and ITN use were graphically assessed using a local regression smoothing methodology. Bivariate associations were tested and odds ratios and confidence intervals produced using logistic regression. After testing individual bivariate associations, a backwards selection procedure was used to create an optimal multivariate model.

We employed classification and regression trees (CARTs), which are analytical tools that can be used to explore relationships between determinants and outcomes where associations are not necessarily linear and which may include interactions[23]. In this particular study, we were interested in the nature of associations between potentially explanatory variables and a binary outcome of ITN use. Not only did we wish to test for significance, but we also sought to determine the hierarchy of determinants. Thus, associations were graphically assessed through a decision tree, and variables were ranked by their relative importance in explaining the outcome. Classification and regression trees are a good way of finding groups of individuals with certain characteristics which may have a particularly low probability of ITN use that may not be found in parametric regression analyses. All statistical analyses were performed in R version 2.15.2.

4.5 Results

At the time of mass ITN distribution, 3,348 households representing 12,098 people were given nets and enrolled in the study. One year following, surveyors returned to the area and interviews were conducted with representatives from 2,083 households comprising 5,175 people. Households were located in all areas of Gembe East (Fig. 1). The mean age at the time of distribution was 13.X years and 15.X years one year post. Ages in both phases ranged from ≤1 to 99 years of age. In both phases, approximately 48% of people surveyed were male (Table 1).

Table 4.1: Survey characteristics of households and people during pre-distribution and post-distribution of ITNs in Mbita District, Kenya.

Characteristic	Pre	Post	P-value
Number of Individuals	12,098	5,175	–
Number of Households	3,348	2,083	–
Total percentage people who slept under an ITN previous evening	43.49%	91.98%	≤.0001
Percentage household members who slept under ITN previous evening	40.70%	74.87%	≤.0001
Median number of nets per household	1	2	≤.0001
Average number of nets per person in household	0.24	0.41	≤.0001
Percent of household members who were male	48.20%	48.32%	0.88
Mean age of household members	13	15	≤.0001
Number of people per household	3	4	0.002

Individual ITN use more than doubled from the time of distribution to one year following, from 43% in 2011 to 92% in 2012. Within households, the mean percentage of household members reporting sleeping under an ITN the previous evening increased from 40% to 75%. The median number of nets increased from 1 net per household to 2. Likewise, the number of nets per person present within each household also doubled (Table 1).

(Figure 4.2).

The spatial distribution of the percentage of household members reporting using ITNs the previous evening differed between the two periods (Fig. 2). Before distribution, use was low, though apparently slightly elevated in the low lying areas close to the water. One year following distribution, over all use had increased greatly, with some regions showing nearly 100% compliance among household members. Because certain parts of the study area were not resampled, it is difficult to compare the two maps. Statistical tests confirmed the presence of spatial autocorrelation prior to distribution. One year after ITNs were provided, spatial clustering was not evident (Moran's I statistic: Pre: .158, $p \leq .0001$, Post: .013, $p = .21$).

4.5.1 Condition and Number of ITNs Following Distribution

The majority (97%) of the nets found during the second survey in the households was Olyset nets that had been marked at the time of distribution, with 99% of these being found inside the dwelling (as opposed to outdoors) in current use. Nearly 20% of nets, the vast majority of which were in new condition one year previously, had visible holes (Table 2). Survey teams were asked to assess possible diversion of nets for other uses and stored nets, but assessment proved difficult. Many nets used for purposes other than malaria prevention are likely located far from the home. Regardless, some ITNs were found to be used for diverse purposes such as drying fish, covering plants and animal pens.

ITNs were initially distributed in a manner that would provide sufficient to allow all household members the opportunity to sleep under a net and thereby cover the entire community. Households of 1 or 2 members were given a single net, 3- or 4-member households were given two, etc. However, it was found that the ratio of net possession to the number of household members was not as would be expected (Fig.

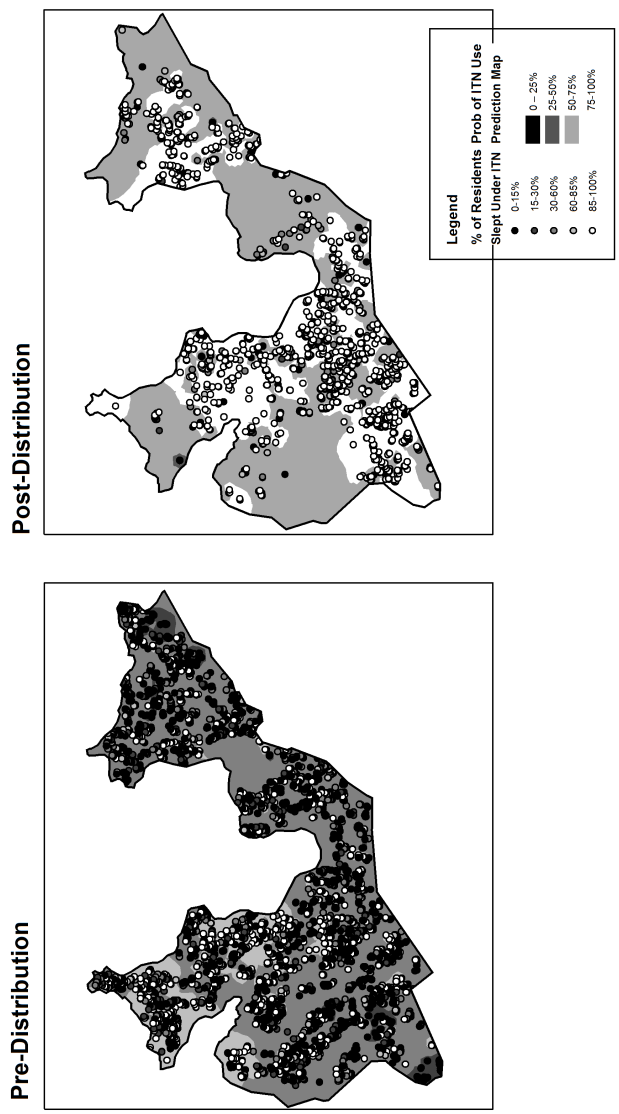

Figure 4.2: Spatial distribution of ITN use before and after distribution with non-parametric inverse distance weighting interpolation to illustrate trend.

3). In fact, very few households had the exact number of ITNs that would have been given to them at the time of distribution. On average, households had fewer ITNs than they were given. Small households of one or two people had slightly more, on average.

(Figure 4.3).

4.5.2 Determinants of ITN Use

At the time of distribution, ITN use overall was reported by less than half of surveyed people, but heterogeneous among age groups (Fig. 4). Reported use of an ITN averaged high starting after birth, declined to very low in the late teen years, then rose again until approximately age 30, and then dropped again among the elderly. Increasing use among males in their 20s occurred later than that among females, perhaps reflecting the tendency for men to be older than women in couples of reproductive age. Though coverage of ITNs one year post-distribution was nearly universal, the same pattern of age as associated with ITN use, overall and between genders, was apparent . Females tended to use ITNs more than males (F: 93% vs. M: 90%, $p \leq .0001$).

(Figure 4.4).

4.5.3 Household Survey

About half of individuals reported sleeping on the floor as opposed to a bed, and 40% reported sleeping in open rooms rather than a formal bedroom (Table 3). More than 90% of all houses surveyed were observed to have open eaves, which could give mosquitoes access to humans at night. Ceiling nets which are intended to cover open eaves and prevent mosquitoes from entering the home were present in some area. 22% of surveyed households were observed to have them. The Kenyan Ministry of

Table 4.2: Types and condition of nets found in home one year following mass distribution

Characteristic		N	%
Total No. of Nets		**2,328**	**100**
Type of Net	**Olyset**	2,256	96.91
	Parmanet	70	3.01
	Other	2	0.09
How obtained	**Bought**	87	3.87
	Free Distribution	1,980	88.12
	Other	180	8.01
In the house	**Yes**	2,233	99.33
	No	15	0.67
In use	**Yes**	2,178	98.06
	No	43	1.94
Holes	**Yes**	405	18.11
	No	1,831	81.89

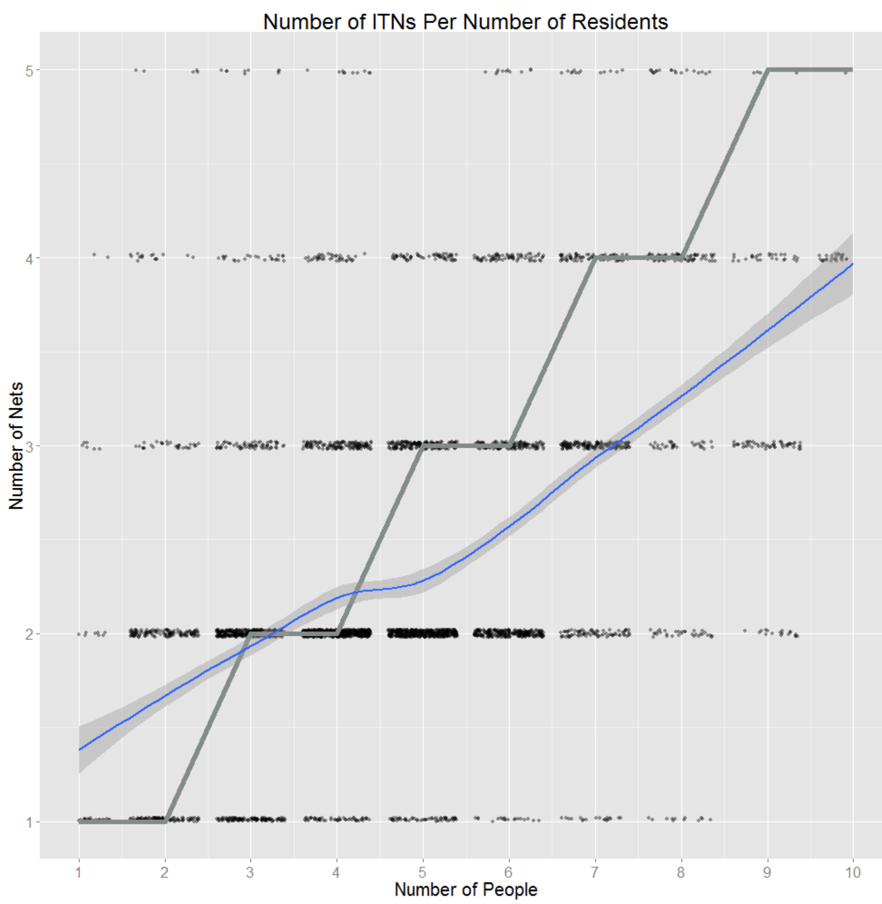

Figure 4.3: Number of ITNs per person in household. Expected ratio given distribution strategy and actual number of nets per person found one year post distribution.

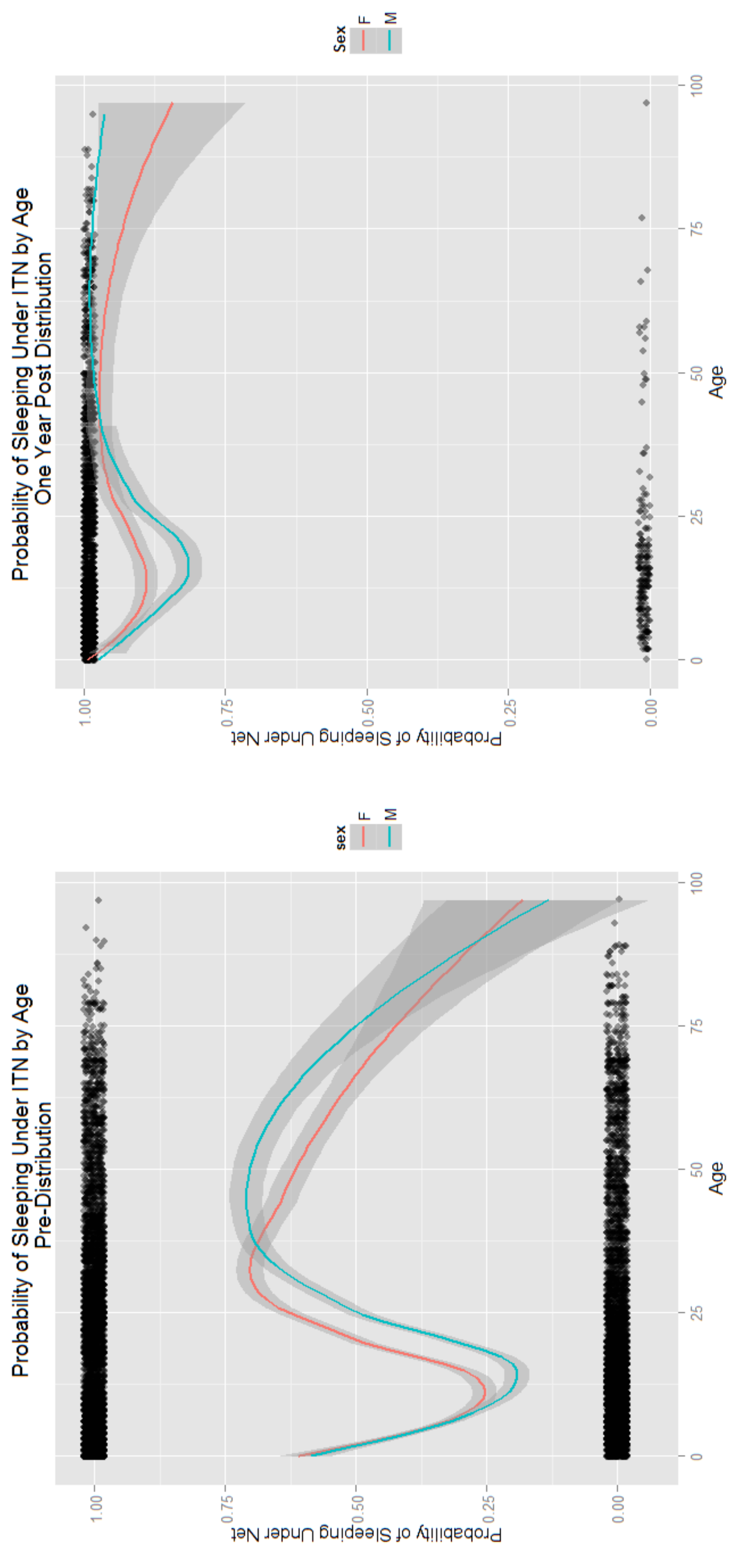

Figure 4.4: Patterns of age and ITN use pre and post distribution. Separate plots for males and females are presented.

Health had also performed indoor residual spraying within the year that nets were distributed. 62% of households had been sprayed. Surveyors noted that 2.5% of households were using nets for other purposes.

Fathers tended to be somewhat better educated than mothers, and occupational activities differed slightly. Though farming was commonly reported as a means of obtaining money, more men than women reported that they were involved in fishing activities and more women considered themselves merchants than men. We recorded church membership of respondents and grouped them by religious affiliation. Half identified as belonging to a formal religion such as Catholicism, Anglicanism and Islam, but nearly a third identified belonging to one of many Pentecostal churches. 16% identified as belonging to Roho, a local mix of Christian and indigenous beliefs (Table 3).

4.5.4 Determinants of ITN Use Pre and Post Distribution

Given very high net use among all groups following distribution, data analysis was restricted to young persons. Net use post-distribution by age groups indicated similar and nearly universal for both sexes after age 35 (TABLE OR FIG.). To make comparisons the same restriction was applied to the 2011 pre-distribution data. As age was associated with ITN use within this window follows a parabolic pattern, a quadratic term for age was used instead of a linear term .

Results of bivariate logistic regression models for all variables pre and post distribution can be seen in Table 4. Prior to distribution, there were no significant differences between the sexes, in the number of household residents and in the number of rooms in terms of ITN use. Age was a significant predictor of ITN use pre-distribution (though the continuous nature of age makes interpretation of the OR difficult). Sleeping on the floor was associated with a decreased odds of using an

Table 4.3: Results of the household survey

Characteristic		N	%
Sleeping Area (ind.)	Floor	1,808	41.29
	Bed	2,571	58.71
Sleeping Room (ind.)	Open room	1,764	39.91
	Bed room	2,656	60.09
Eaves	Open	1,768	93
	Covered	133	7
No. of rooms- median (min, max)		2 (1,15)	
Ceiling Net	Yes	467	22.42
	No	1,616	77.58
IRS	Yes	922	62.51
	No	553	37.49
Alternative ITN use	Yes	18	2.49
	No	704	97.51
Purpose of ITN	Prevent malaria	123	16.71
	Stop mosquitoes	613	83.28
Husband Education	Never (ref)	25	5.3
	Primary	313	66.31
	Secondary	81	17.16
	College	53	11.23
Husband Occupation	Farming (ref)	137	27.85
	Fishing	133	27.03
	Merchant	90	18.29
	None	27	5.49
	Other	56	11.38
	Teacher	49	9.96
Mother Education	Never	124	18.4
	Primary	465	68.99
	Secondary	66	9.79
	College	19	2.82
Mother Occupation	Farmer	96	14.61
	Merchant	281	42.77
	None	239	36.38
	Other	20	3.04
	Teacher	20	3.04
	Fishing	1	0.15
Church Membership	Formal (Cath, etc)	237	52.55
	Pentecostal	139	30.82

ITN (OR .24 (.21, .28)) along with sleeping in an open room (OR .20 (.17, .24)) and having been sprayed (IRS) in the past (OR: .77 (.65, .92)). Decreased ITN use was also significantly associated with reported use of ITNs for other purposes (OR .84 (.72, .98)). Increased levels of paternal education were associated with an increased odds of using an ITN the previous night but ITN use was elevated only in households where the mother had a college education, compared with no education at all (OR 2.26 (1.15,4.49)). There was suggestive evidence that young people in households where the father was involved with fishing were less likely to use ITNs (OR .64 (.40, 1.02)) than households where the father was involved with other occupations, though young people in households headed by teachers were very likely to use them (OR 1.95 (1.14, 3.37)). Similarly, compared to households where the maternal head reported farmer as an occupation, households of teachers (OR 3.51 (1.73, 7.29)) and merchants (OR 1.6 (1.04, 2.51)) had an elevated odds of using ITNs.

Following ITN distribution, the factors which characterized net use in people under the age of 35 changed. Males were less likely to sleep under ITNs than females (OR .64, (.50, .80)). As before, sleeping on the floor (OR .37 (.28, .48)) and sleeping in an open room (OR .42 (.33, .54)) were both associated with decreased odds of ITN use. The number of rooms and the number of people per household both became positively associated with ITN use. In contrast to pre-distribution, having been sprayed in the past was associated with elevated odds of using an ITN (OR 2.03 (1.54, 2.66)). The presence of a ceiling net was associated with decreased odds of using an ITN (OR .58 (.45, .75)). Paternal education and both maternal and paternal occupation were no longer associated with ITN use among young household members . The odds of a young person using an ITN in households headed by mothers having any level of education were higher than those households where the mother had no education at all. Compared with those linked to formal religions, being affiliated with a Pentecostal church was predictive of ITN compliance. There was no evidence for associations of material wealth with ITN use.

As these measures may be correlated, an optimal multivariate regression model was produced. Tests indicated that members of households were correlated with one another (Fig. 5) and that the inclusion of a random intercept for household was appropriate. Thus, backwards selection was used to produce a final model based on Akaikes Information Criterion (AIC). The final model included age (continuous), a non-significant term for gender, sleeping on the floor, and the ratio of nets to people living in the home. Interactions were tested for and none were found. Only the final model is presented.

(Figure 4.5).

4.5.5 Ranking of Measures/ CART Analysis

CART analysis to explore interactions between and to determine the relative importance of variables in predicting ITN use was performed for both pre- and post-distribution data. As was the case in the bivariate regression models, the determinants of ITN use differed between the two periods. Before ITNs were provided to households, the number of rooms, the ratio of nets to people and the number of people within the home were highly associated with ITN use in young people. ITN use differed between one and multi-room structures . Houses with multiple nets were more likely to use them. Within single room structures, the next split occurred between household which had ITN to resident ratios of greater than and less than approximately .5 (two persons per net). Oddly, households which had higher net to person ratios were less likely to use ITNs. Within these net ratio groups, however, the number of people was an important determinant of ITN use. The least likely to

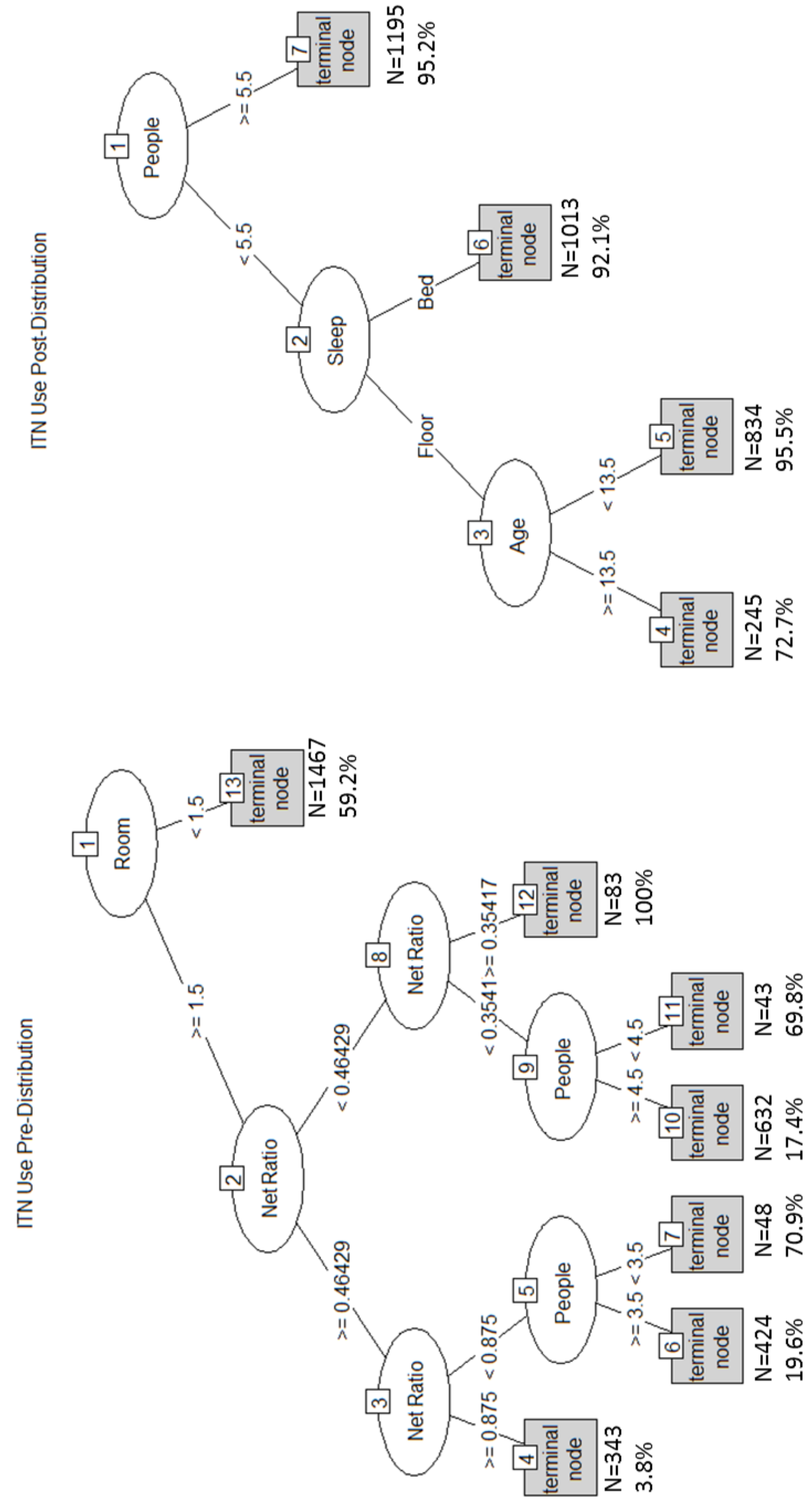

Figure 4.5: Classification and regression tree results of ITN use before and following mass distribution of ITNs. Data restricted to people less than 35 years of age.

Table 4.4: Bivariate associations of ITN use and covariates before and after mass distribution of ITNs.

	Pre-Distribution		Post-Distribution	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
Intercept				
Age (quadratic)	**1.00 (1.00 ,1.00)**	**≤.0001**	1.00 (1.00 ,1.00)	0.10
Male vs. Female	.86 (.36 ,1.99)	0.74	**.64 (.50 ,.80)**	**≤.0001**
Number of people	.99 (.95 ,1.03)	0.64	**1.07 (1.03 ,1.11)**	**0.003**
Floor vs. Bed	**.24 (.21 ,.28)**	**≤.0001**	**.37 (.28 ,.48)**	**≤.0001**
Open room vs. Bed room	**.20 (.17 ,.24)**	**≤.0001**	**.42 (.33 ,.54)**	**≤.0001**
Open eaves	**1.53 (1.03 ,2.34)**	**0.04**	1.06 (.66 ,1.62)	0.80
Number of rooms	1.04 (.96 ,1.13)	0.31	**1.15 (1.01 ,1.32)**	**0.04**
Ratio of nets to people				
Ceiling Net	.97 (.84 ,1.13)	0.70	**.58 (.45 ,.75)**	**≤.0001**
IRS	**.77 (.65 ,.92)**	**0.003**	**2.03 (1.54 ,2.66)**	**≤.0001**
Alternative ITN use	**.84 (.72 ,.98)**	**0.02**	.89 (.71 ,1.12)	0.33
Husband Education				
Never	ref		ref	
Primary	**.57 (.34 ,.98)**	**0.04**	.48 (.17 ,1.39)	0.16
Secondary	**.37 (.19 ,.71)**	**0.003**	1.26 (.59 ,2.43)	0.52
College	**1.09 (.56 ,2.15)**	**0.77**	.63 (.28 ,1.32)	0.23
Husband Occupation				
Farming	ref		ref	
Fishing	.64 (.40 ,1.02)	0.06	1.44 (.83 ,2.51)	0.19
Merchant	1.06 (.67 ,1.68)	0.79	1.15 (.64 ,2.15)	0.64
None	1.18 (.60 ,2.28)	0.62	1.09 (.41 ,3.78)	0.88
Other	1.56 (.93 ,2.61)	0.09	1.31 (.67 ,2.72)	0.44
Teacher	**1.95 (1.14 ,3.37)**	**0.02**	1.35 (.63 ,3.24)	0.46
Wife Education				
Never	ref		ref	
Primary	.89 (.64 ,1.23)	0.49	**2.99 (2.01 ,4.38)**	**≤.0001**
Secondary	.67 (.37 ,1.16)	0.16	**3.14 (1.74 ,5.93)**	**≤.0001**
College	2.26 (1.15 ,4.49)	0.02	3.24 (1.10 ,13.86)	0.06
Wife Occupation				
Farmer	ref		ref	
Merchant	**1.60 (1.04 ,2.51)**	**0.04**	1.13 (.67 ,1.86)	0.62
None	1.16 (.74 ,1.85)	0.52	.92 (.54 ,1.51)	0.74
Other	.62 (.17 ,1.87)	0.43	.49 (.22 ,1.17)	0.09
Teacher	**3.51 (1.73 ,7.29)**	**≤.0001**	.57 (.24 ,1.51)	0.22
Church Membership				
Formal (Catholic, etc)	ref		ref	
Pentacostal	.92 (.67 ,1.26)	0.60	**2.46 (1.55 ,4.05)**	**≤.0001**
Roho	.94 (.58 ,1.49)	0.79	1.12 (.71 ,1.82)	0.64
Wealth Quintile				
Lowest	ref		ref	
2	**.74 (.56 ,.99)**	**0.04**	1.03 (.73 ,1.46)	0.86
3	**.72 (.53 ,.99)**	**0.04**	1.39 (.89 ,2.22)	0.16
4	.87 (.66 ,1.15)	0.32	1.22 (.83 ,1.78)	0.32
Highest	1.11 (.84 ,1.46)	0.46	1.07 (.74 ,1.57)	0.72

sleep under an ITN were people who lived in multi-room households where the net to person ratio was nearly 1:1.

One year following distribution, though ITN compliance was high overall, it was first split between households which had 5 or fewer residents and more than 5 residents. Households with five or fewer residents were then split between those who slept on the floor and those who slept in a bed. Within those who slept on the floor, ITN use was split between those over 13 years of age, and those 13 and under. The least likely to sleep under an ITN were those over 13, who slept on the floor and lived in households of 5 or fewer people.

4.6 Discussion

The results here suggest that obtaining high levels of coverage through a free, mass distribution of ITNs is possible and that compliance can be rapidly increased and maintained even one year following. Problems of inequities of coverage between socio-economic, educational and occupational groups are erased through no cost, comprehensive provision of ITNs. Furthermore, problems of spatial heterogeneities in ITN possession can be mitigated through a direct-to-household delivery strategy.

However, there is evidence that suggest that even when sufficient numbers of nets is proactively provided to household to cover all residents, shortfalls continue to persist. Specifically, despite dramatically increased levels of ITN compliance overall,

Table 4.5: Optimal multi-variate model of ITN use. Model selected through backward selection procedure using AIC to choose best model.

	OR	**CiL**	**CiU**	**p**
Intercept	2804.38	899.6	8742.26	$\leq$.0001
Age (quadratic)	1	1	1	0
Male vs. Female	0.86	0.49	1.51	0.6
Floor vs. Bed	0.04	0.02	0.11	$\leq$.0001
Ratio of nets to people	0.31	0.13	0.74	0.01

relative patterns of ITN use along age groups remain unchanged. Practical issues of household sleeping arrangement and home construction continue to present barriers to full coverage of ITNs and appear related to age patterns. Problems of where and how to hang nets in common areas, a hurdle noted in other studies [Iwashita et al., 2010][Alaii et al., 2003][Ng'ang'a et al., 2009], are not, however, easily rectified. Heterogeneous age effects in ITN use have been noted by other researchers in a variety of contexts, including Kenya[Noor et al., 2009a]. However, it has been thought that distribution strategies which target children and pregnant women are responsible for such heterogeneities. Our study, where nets were provided to all members of the community, provides evidence to counter that assumption.

Of concern is the problem of ITN leakage that was discovered. Though ITNs were given to households in sufficient numbers to cover all household members, the actual number of nets found one year later was significantly lower than that which would have been expected. During related research activities, the authors have found that freely distributed ITNs can often be found in households other than that to which they were initially given. Furthermore, though nets are provided with the message that ITNs are specifically for the prevention of malaria, household economic needs cause nets to be diverted to remunerable activities such as fishing agriculture, particularly in the region of the study site [Minakawa et al., 2008]. It is obviously unreasonable to expect household heads, weighing numerous and sometimes conflicting pressures will follow the dictates of malaria researchers. Thus, the possibility of leakage, which has been noted in other studies[Tami et al., 2005][Beiersmann et al., 2010][Willey et al., 2012], should be taken into account prior to mass distribution. More research into optimal strategies which account for leakage and alternative uses of ITNs is needed. We do not wish to overstate the "problems" of alternative uses of

ITNs for fear of stoking unfounded alarmism that may damage distribution activities that provide wide benefits to human health [Eisele et al., 2011]. We would point out that despite uses of nets for fishing activities, that more than 90% of people slept under one, and that more than 97% of the nets found in the households were from Nagasaki. From a distributional point of view, this might be considered to be a success.

The extent of ITN increased coverage and use in this study provides reason for encouragement. We would expect that malaria transmission may be reduced, incidence of disease lessened, and mortality averted. However, given that this particular region is known to be an area of very intense transmission [Bousema et al., 2004][Munyekenye et al., 2005], the persistence of ITN use within specific age groups should be cause for great concern. Like all African countries, Kenyas age distribution is bottom heavy. This particular study region was no exception. If large numbers of young people are not using nets, even in the context of high compliance, the numbers of people could be more than enough to sustain transmission. Increased coverage of ITNs has been noted to have diminishing returns on mitigating parasite prevalence in high transmission areas (find this paper). If there are systematic shortfalls in coverage that occur in other contexts as well, the results from this paper could provide a partial explanation for that phenomenon.

Or course, our study suffers from a number of limitations. First, the nature of the question of use is based on a self-reported measure, often given by a proxy member of the household and sometimes from a person who does not reside in the structure being surveyed. We note that in the pre-distribution survey, households may have been incentivized to under-report use of ITNs with the aim of obtaining a free net. However, the age patterns follow a trend which agreed with other studies. If household representatives were understating true use, the understatement have been merely shifted the curve downward and not differentially. That reported use following distribution was nearly universal, though, would counter claims of underreporting of ITN use as households. It might be said that household representatives would over-report to satisfy surveyors but would rationally see no benefit from this. Teams visually confirmed whether nets were hanging in the home or not and noted who was sleeping under nets on two different portions of the survey further countering claims of inaccuracy. Second, data has only been collected at two time points. We do not know the extent of use in very dry or very wet seasons. As the data was collected over the course of several months, temporal effects could compromise internal reliability of ITN use measures. When testing for spatial patterns of ITN use, however, no patterns were apparent that might coincide with the movements of survey teams. As we have only sampled at two time points one year apart, we may also see use decline over time in the future.

Finally, data problems such as misreported information and missing data presented significant challenges to analysis. Problems of data recording and entry are naturally common to all studies, but every attempt was made to maximize data quality. Despite the challenges, we felt that the results were intuitive and agreed with existing research, though offer new insights.

CHAPTER V

DIFFUSION OF SUBSIDIZED ACTS IN ACCREDITED DRUG SHOPS IN TANZANIA: DETERMINANTS OF STOCKING AND CHARACTERISTICS OF EARLY AND LATE ADOPTERS

5.1 Abstract

Introduction: Many households in sub-Saharan Africa utilize the private sector as a primary source of treatment for malaria episodes. Expanding access to effective treatment in private drug shops may help reduce the incidence of severe disease and mortality. However, little is known about the market level factors that influence the stocking of new medicinal products in private drug shops in developing countries. A longitudinal survey of Accredited Drug Dispensing Outlets (ADDOs) in two regions of Tanzania to evaluate the effectiveness of the Affordable Medicines Facility malaria (AMFm) provided us with a unique opportunity to explore the determinants of health product diffusion over time and characteristics of early and late adopters.

Methods: 356 ADDOs in the Rukwa and Mtwara regions of Tanzania were surveyed at seven points between Feb 2011 and May 2012. Shop level audits were used to measure the availability of subsidized ACTs at each shop. Data on market and shop level factors were collected during the survey and also extracted from GIS layers. Potential determinants were contextualized within three categories: customer demand, market competition and shop level characteristics including supply, stocking and staff qualifications. Customer demand was assessed using population data and reported daily customer traffic. Factors of market competition were derived using locations of proximal shops and clinics, and reported names of competing shops. Shop representatives were also asked to provide information on frequency and amount of stocking, location of regular suppliers and staff qualifications. Associations of all determinants with ACT stocking were tested using regression methods. Early and late adopters of ACTs were compared.

Results: Following the introduction of a subsidy for ACTs, stocking increased from 12% to nearly 80% over the seven survey rounds. There were some regional differences in the stocking behavior. Fewer shops in Rukwa stocked ACTs than in Mtwara over all of the survey rounds. Stocking was influenced by higher number of proximal shops and clinics, larger customer traffic and the presence of a licensed pharmacist. High profile and well-connected shops were more likely to stock ACTs than isolated shops. Early adopters were characterized by a larger percentage of their customers seeking care for malaria like symptoms and a large surrounding population. Early adoption of ACTs was also associated with sourcing from specific wholesalers/suppliers.

Conclusions: Decisions to stock new pharmaceutical products in Tanzanian ADDOs are influence by a combination of factors related to both market competition and customer demand for drugs to address specific conditions. Early adoption of new products, which presumably set the stage for the product adoption for rest of the market, may be associated with specific types of customers. Wholesalers/suppliers from which the retail shop sources its product appear to be an important determinant in introducing new drugs into the market. Efforts to expand access to new pharma-

ceutical products in developing country markets could benefit from initial targeting of shops in competitive markets to encourage faster product diffusion across all drug retailers.

Keywords Malaria, ACT, Drug shops, Tanzania, Marketing, Product diffusion

5.2 Introduction

Despite the successful development of effective medications to treat health conditions such as malaria, diarrheal disease, HIV and tuberculosis, access to these medications remains highly constrained in most developing countries[Cameron et al.,]. Crowded public health facilities, drug stock outs and lengthy travel times have all been noted as barriers to improving access to effective medications in public sector health facilities[O'Connell et al., 2011, Buabeng et al., 2008, Chuma et al., 2009, Cohen et al., 2010]. It is no wonder, then, that the private sector is typically the first choice in treating common health conditions such as malaria and diarrhea[Littrell et al., 2011]. A major problem, though, is that the latest and most effective medications are often unavailable at private drug shops. This could be due to high retail prices, regulation that prohibits stocking some products in private drug shops, or simply because patients, caregivers and drug shop owners are unaware that there exist more effective drugs than those which are commonly sold. Expanding access to safe and effective medications in private drug shops might allow households to receive proper treatment for life threatening disease earlier, reducing the chance of severe disease and mortality.

Diffusion, – the spread of new products within a social or market system upon introduction– has been studied extensively in developed country markets[Duval and Biere, 2002]. In his theory of the diffusion of innovations, Rogers[Rogers, 2003] introduces the concept of new adopters. Early adopters make use of technologies and subsequently encourage the late majority and laggards to adopt until the new technology or product spreads through the entire market. Rogers model assumed that first adopters of new products differed from people who adopt at later times. Bass[Bass, 1969], however, expanded up Rogers work by hypothesizing that innovators lead the introduction of new products, while imitators are inspired to purchase new goods following the example of those around them. He created a mathematical model of adoption and applied it to a range of durable consumer goods. The interpretation of Bass innovators vs. imitators has been since generalized to address marketing mechanisms of broad advertising vs. social contagion. Since that time, the Bass model has been applied extensively to determine how internal and external factors, such as within group market competition vs. broad media messages, influence product diffusion [Meade and Islam, 2006, Van den Bulte and Joshi, 2007, Desiraju et al., 2004]. Bass basic ideas work well with current social network theory, where high profile and well-connected individuals influence proximate contacts, who in turn imitate one another [Watts and Dodds, 2007, Katona et al., 2011]. See figure 5.1 for a graphical representation of both the Rogers and Bass models of product diffusion. Where the Rogers model divides adopters on the basis of timing alone, the Bass model assumes that adopters are intrinsically different and may adopt new technologies at any time, but in distinct ways. Innovators will choose to adopt new technologies independently of other individuals within the same group, while imitators will accept the new products or technologies in response to others around them.

To date, little is known about how health products diffuse through retail markets Sub-Saharan Africa. One study, though, indicated that developing countries are

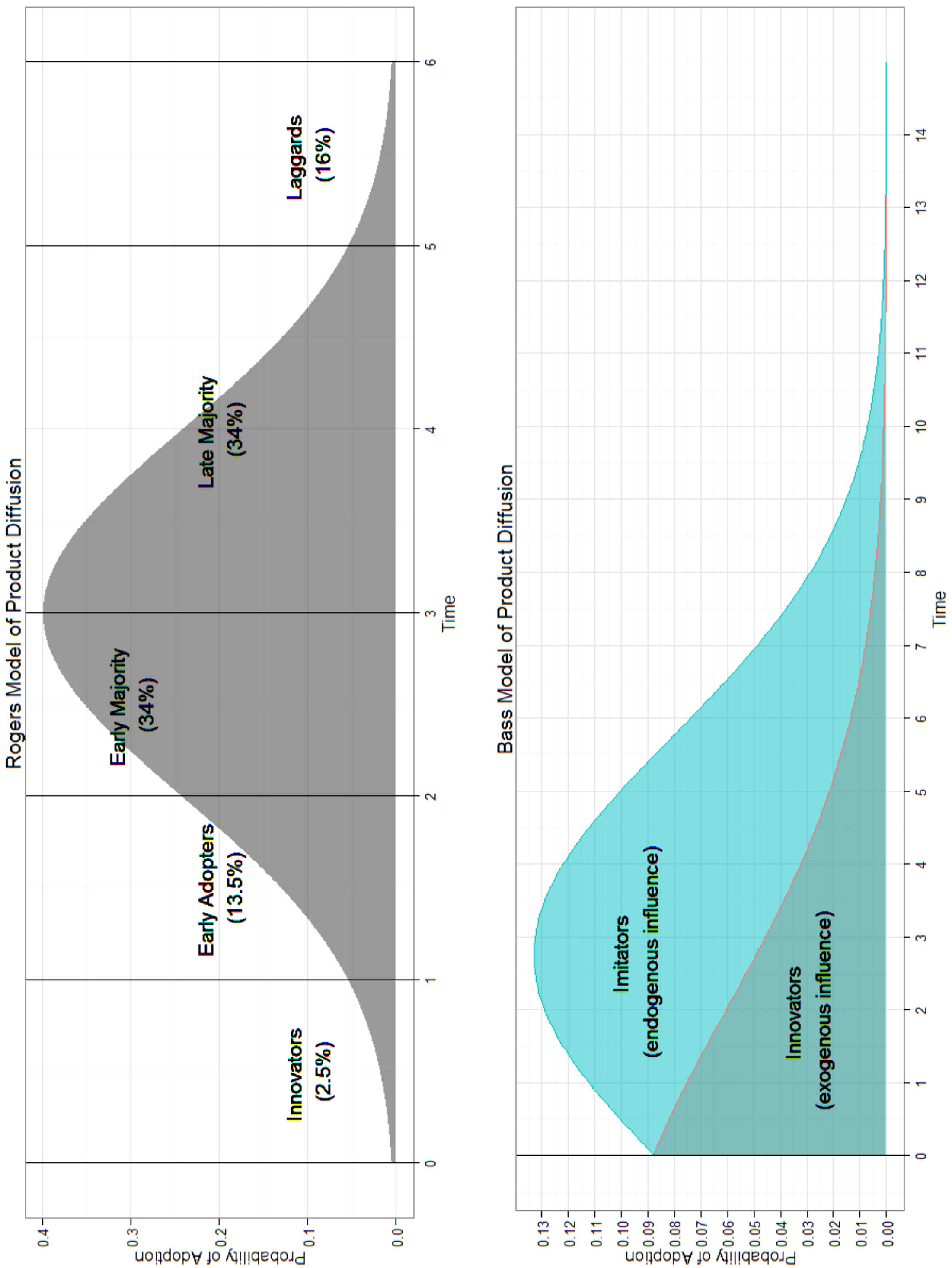

Figure 5.1: Models of product diffusion: a) Rogers original model of early to late adopters of new technologies and products b) The classic Bass model of product diffusion. Innovators spearhead new products at any time, while imitators follow the example of others within the group.

known to adopt new technologies more slowly than developed countries once available, but that diffusion of products within countries occurs quickly[Sarvary et al., 2000]. Other studies found, however, that average penetration potential in developing countries is one third as that of developed countries, that peak sales in developing countries takes longer than in developed countries, and that delayed product introduction tends to not have positive effects on the overall adoption rate[Talukdar et al., 2002]. High prices have been associated with a reduced rate of diffusion of prescription medications in developing countries [Desiraju et al., 2004]. Studies of pharmaceutical product diffusion in developed country settings indicated that large health facilities tend to lead the market in adopting new drugs [Wen et al., 2011].

Of secondary interest to the authors of this paper is how products are diffused through networks of shops, connected either through perceived mutual competition, or through common suppliers. A network based approach similar to techniques used in social network analyses was used to analyze competition between shops in the study areas. Network analysis has recently been extensively used to study problems of social networks, such as friend networks for information sharing or large and intricate assemblages of partnerships as applied to the study of sexually transmitted diseases [Bell et al., 1999, Rice et al., 2012, De et al., 2004, Rothenberg et al., 1995]. Some work has been done applying network methodologies to economic questions [Al-Laham and Amburgey, 2010, Timberlake and Shin, 2000, Landherr et al., 2010]. We are unaware of any work that has been done that analyzes network based competition to understand stocking behavior of certain goods and/or pricing.

Knowing how and whether existing models of product diffusion can be applied to drug shops and private markets in sub-Saharan Africa could help public health groups more effectively expand access to essential medications. By identifying specific characteristics of early adopters, new drugs may be introduced more efficiently into the market, thus maximizing availability and minimizing time to universal adoption. We hypothesize that stocking of new products will be the result of a combination of factors which include both local demand for effective products, and a desire for shops to remain competitive in the market by emulating the behavior of peer shops.

In this paper, we leveraged data from a study which longitudinally tracked the adoption of ACTs in Tanzanian Accredited Drug Dispensing Outlets (ADDOs) over seven time points. The study was conducted as a part of an operational research project to assess the Affordable Medicines Facility Malaria (AMFm), an ACT subsidy program hosted by the Global Fund to Fight Tuberculosis, HIV and Malaria. The AMFm provided a supply side subsidy to decrease the price of artemisinin combination therapies (ACTs) to reduce prices and to increase availability and use of ACTs in private drug shops in eight pilot countries. As data was collected from the start of when AMFm subsidized ACTs first arrived in Tanzania, this data-set provided a unique opportunity to follow a pharmaceutical product from the first point of introduction.

This paper will be structured as follows. First, we will describe patterns of ACT stocking over time. Second, we will test associations of competition and demand variables with ACT stocking over the study period. Third, we will characterize shops as early and late adopters and test associations of possible determinants with adopter status. Finally, we will measure and test the contributions of internal and external influence using a mixed influence model. A broad goal of this paper will be to discover whether new product adoption in ADDOs is the result of a shop level motivation to stock ACTs due to actual or yet to be realized customer demand (innovator), or whether shops stock new products due to influence by market competitors.

5.3 Methods

5.3.1 Ethical approval

The study was approved by the Institutional Review Board of Harvard University School of Public Health (Protocol #19372-102) and the National Institute of Medical Research of Tanzania (NIMR/HQ /R.8a/Vol. IX/1017).

5.3.2 Data

A comprehensive survey of 356 Tanzanian Accredited Drug Dispensing Outlets (ADDOs) was conducted in two regions (see figure 5.2) from February 2011 to May 2012 over seven survey periods (see table 5.1). Surveyors noted whether subsidized ACTs were being stocked and recorded retail prices. Comprehensive retail audits, where all anti-malarial products were noted, were performed twice. At each comprehensive audit, shop attendants were asked a set of questions regarding sources of supply, stocking frequency and restock amounts.

Table 5.1: Data collection schedule.

	2011				2012		
	mid Feb to end Mar 2011	end Mar to mid Apr 2011	end Apr to mid May 2011	Aug-11	Jan-12	end Mar-mid Apr, 2012	May-12
Retail Audits	R1	R2	R3	R4	R5	R6	R7

(Figure 5.2).

5.3.3 Measurement

Shop level characteristics were assessed using characteristics related to demand, competition, and shop staffing, sourcing and ordering.

5.3.4 Demand Measures

Demand side characteristics were assessed through a combination of methods. The size of shops customer base and possible catchment populations were estimated using data from the survey and available GIS layers. AfriPop has created interpolated grid maps of population for nearly all sub-Saharan African countries using available census data, and satellite imagery [AfriPop Project, 2011]. To estimate catchment populations of each ADDO, a radius of 5 km was drawn around the known location of each shop. Total population within 5 km was extrapolated from the AfriPop population raster for Tanzania and added to the database. In addition to population based demand estimates the shop attendants were asked to provide an estimate the number of customers that visited their shop on the previous day, the number of customers that presented with malaria like symptoms, and the number of customers on busy and slow days.

5.3.5 Competition Measures

Retail competition was analyzed using two methods. First, we utilized a spatial methodology assuming that proximity to other shops implies competition for customers in overlapping catchments[Cohen et al., 2010]. For each shop in the survey, using the exact locations, we calculated the distance to nearest ADDO and the number of ADDOs within 3 km. We performed the same procedure using the locations of known public health facilities offering reproductive and child health (RCH) services.

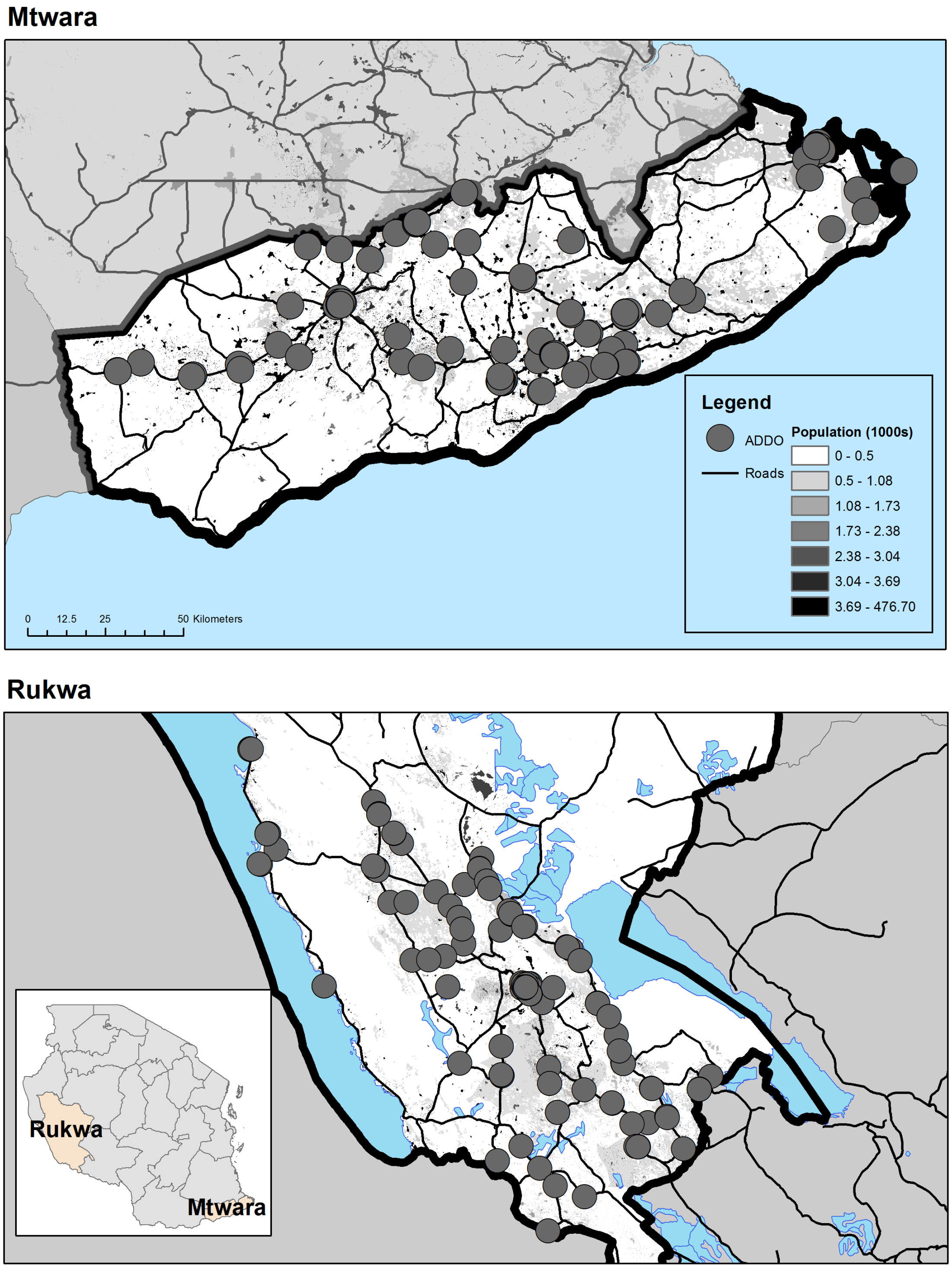

Figure 5.2: Locations of surveyed ADDOs and target regions.

ADDO representatives were asked to provide the names of up to three other drug shops which they regarded as their competitors. The names were compared with the master list of participating ADDOs in this study and numerical shop keys were assigned for consistency. We constructed a competition network of all shops, graphically illustrating the connections between shops. Certain shops may maintain a high level of prominence within the market through having a large market share, the ability to sell products for considerably lower prices than other shops or other factors. Thus, these shops will be more likely to be identified by shops as competitors than other shops, even when distant. Similarly, two shops may be connected to one another through a mutual intermediary, but may be unaware that they are identifying a common competitor.

Two basic measures of network centrality are applied in this case: degree centrality and betweenness. For each shop, the degree is the number of other shops that identify that shop as a market competitor. Betweenness is a measure of whether a specific shop acts as a bridge between otherwise disconnected shops in the network. Calculation of the network measures is performed using UCINET ver. 6[Borgatti et al., 2002].

5.3.6 Shop Staff and Stocking Habits

Shops were asked to report the qualifications of dispensers, their level of health training and the number of employees in the shop Shops were also asked to report the quantity and frequency of replenishment, and the source of obtaining supplies (location of wholesaler).

5.3.7 Product Diffusion under the AMFm

Using Rogers (8) methodology, shops were classified into the broad categories of early adopters and late adopters. This was done through visual inspection of stocking trends. Finer classifications (e.g. mid to late adopters and laggards) would have been ideal, but it was thought that the small number of survey rounds would not accommodate them. Coefficients of innovation (internal influence) and imitation (external influence) were produced using a form of the classic Bass diffusion model??. The version of the Bass model to describe sales of new products used in this paper is:

$$S(t) = e^{-(p+q)t}/((1 + q/pe^{-(p+q)t})^2) \tag{5.1}$$

where S(t) is the rate of change of adoption (at time t) p and q are the coefficients of innovation (the propensity for shops to stock products independent of other shops) and imitation (the propensity for shops to stock products in response to the behavior of peer shops). Parameters were estimated using a non-linear regression methodology[Srinivasan and Mason, 1986]. Through these estimates, we hope to quantify the potential roles of shops which independently assume risks of stocking new and untested retail products (innovation) and those which stock as a result of a need to imitate other shops (imitation or social contagion[Van den Bulte and Stremersch, 2004]). If p/q ratio, for example, were larger than 1, we might conclude that shops stock ACTs due to endogenous market imitation and a desire to remain competitive, rather than broad messages sent through either exogenous advertising avenues, messages from common wholesale suppliers or customer demand. The small number of time points prevented the implementation of more rigorous forms of diffusion modeling (e.g. a hazard model with predictive covariates).

5.3.8 Regression Methods/Tests of Association

Tests for associations of all variables with ACT stocking over the seven survey rounds were performed using a logistic regression model including covariates for survey round and region to account for trend and differences between the two survey areas. We conducted tests for associations of all variables with ACT stocking, and with early/late adopter status. As ACT stocking is likely the result of a combination of factors, some of which may be correlated with one another, a multivariate model of ACT stocking was produced. Backwards selection (based on AIC) was used to select an optimal set of covariates. Variables were eliminated one by one, until a final set of significant covariates was reached. Associations of potentially predictive covariates and adopter status were testes using chi-square tests for categorical variables and t-tests for continuous variables. All statistical analyses were performed using R version 2.12.0[R Core Team, 2012].

5.4 Results

5.4.1 Descriptive Results

Customer Demand

See table 5.2 for full descriptive results. There was an average of approximately 12,000 people living around each ADDO, though catchment populations varied widely. Shop representatives were asked to estimate how many customers came to the shop the previous day, how many of those customers presented for malaria related concerns, and for estimates of the number of customers on the busiest and slowest days. Shops reported a mean number of 25 customers the previous day, 4.5 of which appeared for malaria. Out of all customers seen the previous day, an average of 20%

of them appeared with malaria like symptoms.

Market Competition

Distances between shops ranged from .1 km to nearly 40km between each shop, with a mean distance of approximately 3 km. There number of shops located within a 3 km radius around each shop ranged from zero to a maximum of 36 shops. Similarly, ADDOs were located proximate to public RCH clinics, with distances ranging from less than 30 meters to nearly 130 km away.

Shops were asked to name up to three other shops that were seen as market competitors. Not all shops named a total of three competitors. Many shops reported three competitors as requested, though some reported less. 89% of shops identified at least one competitor. 67% identified at least two, whereas only 44% reported three. From this we were able to construct the network of competing shops and common suppliers (See figure 5.3). The mean network degree, or the number of times each shop was named by another, was 2.37 and the average betweenness centrality, a measure of network connectivity, was 7.62. The most highly connected shop had 11 connections and the lowest was 0.

Shop Level Ordering Practices

Most shops (43%) reported restocking medicinal supplies once a month. Another 30% order stock biweekly and 12% of shops order stocks once every two months. Few shops ordered stocks weekly and even fewer ordered once every 3 or more months. Upon restocking, most shops reported ordering a months supply of drugs or less. Shops generally ordered from proximal wholesalers in nearby mid-sized towns, though nearly 10% reported ordering stocks from distant Dar Es Salaam. There was a nurse/midwife present at nearly two thirds of the shops. A few reported having a

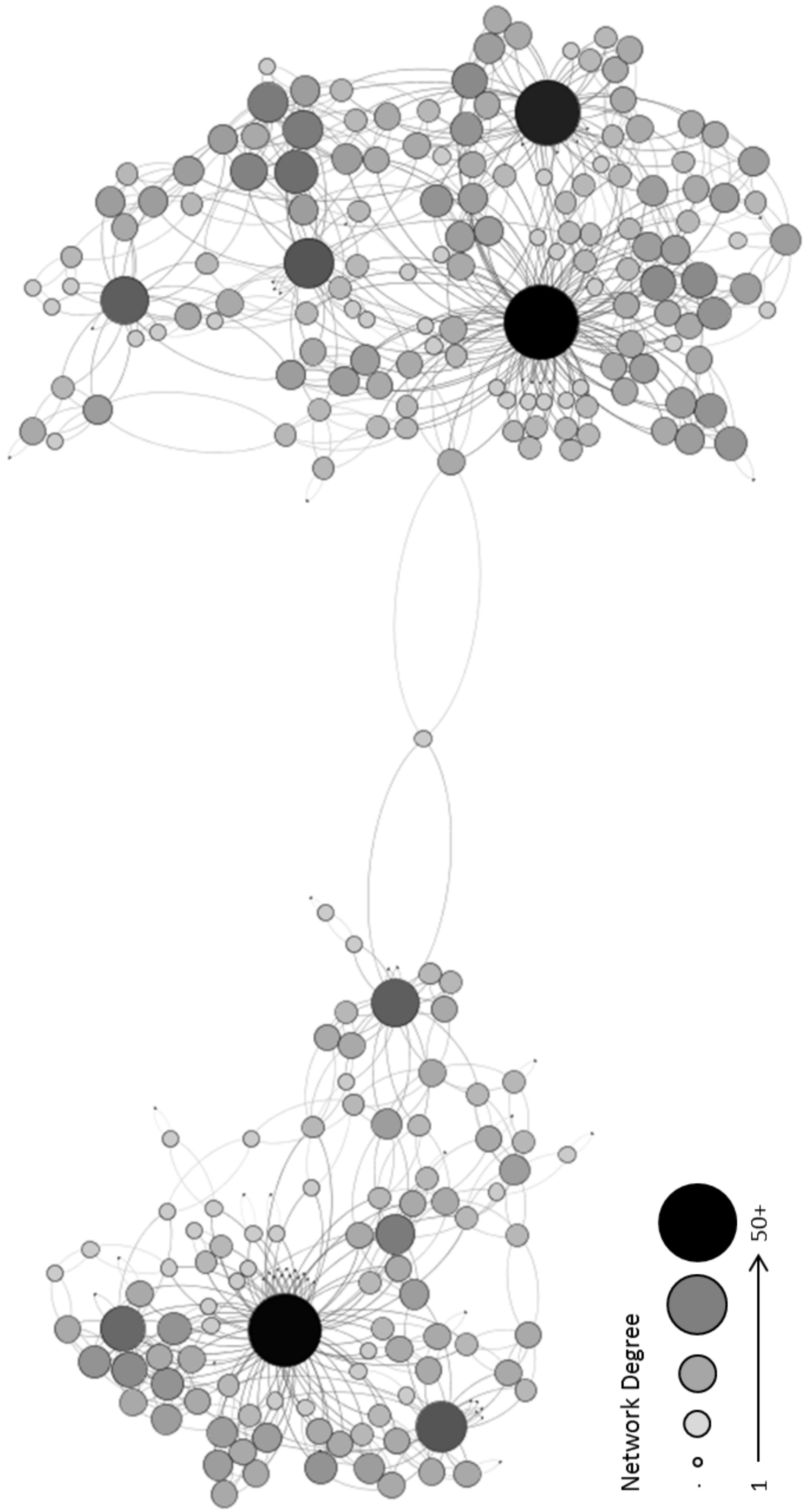

Figure 5.3: Competition network. Sizes of nodes are proportional to network degree. Nodes are colored by common wholesale suppliers.

doctor or a pharmacist on duty.

5.4.2 Diffusion of ACTs under the AMFm

Stocking of AMFm subsidized ACTs increased rapidly over the seven survey rounds. 12% of shops were reported to have ACTs in stock in the first round. By the final round, more than 80% of shops were stocking ACTs. Patterns of stocking over time were similar between Rukwa and Mtwara, but shops in Mtwara were more likely to stock ACTs overall. (See figure 5.4 and table 5.3).

(Figure 5.4).

5.4.3 Determinants of ACT Stocking

Logistic regression models controlling for survey round and region indicated that the number of ADDOs (OR 1.02 (1.01, 1.03)) and RCH clinics within a 3 km radius (OR 1.06 (1.00, 1.12)) were both associated with increased odds of stocking ACTs over the seven survey rounds. Spatial proximity to other ADDOs (OR 1.00 (0.99, 1.00)) and RCH clinics (OR 1.00 (0.98, 1.01)) was not associated with ACT stocking.

While the association of increased population with ACT stocking was not significant (OR 1.01 (0.99,1.02)), increased numbers of customers appearing on the previous day (OR 1.02 (1.00,1.03)) and increased numbers of customers presenting for malaria concerns (OR 1.07 (1.04,1.09)) were both predictive of ACT stocking in any round. The fraction of customers presenting for malaria concerns was highly predictive of ACT stocking (OR 3.01 (1.41, 6.46)). Frequency of ordering and supplier location was found not to be associated with ACT stocking. The odds of ACT stocking in shops which employed a pharmacist were more than three time higher than those which did not. See table 5.4 for complete results.

Shops were asked to list up to three of their perceived competitors. Increasing

Table 5.2: Descriptive results of ADDO survey: shop level characteristics. Mean are presented for ordinal and continuous variables. Percentages are presented for categorical variables.

	Mean/%
N	356
Distance to Nearest ADDO	3.17 (Range:.10,38.89)
No. of ADDOs Within 3km	8.58 (Range:.0, 35)
Distance to Nearest RCH Clinic	2.23 (Range: .02, 130.4)
No. of RCH Clinics Within 5km	1.85 (Range: 0, 7)
Degree	2.37
Betweenness	7.62
Population Within 5km	12090
No. of Customers on Previous Day	25.05
No. of Customers Presenting for Malaria on Previous Day	4.56
% Cust. Presenting for Malaria	19.79%
Frequency of Ordering	
Every Week	5.60%
Once a month	43.40%
Twice a month	29.90%
Every Two Months	11.20%
Every Three Months	7.90%
Don't Know/No Set Schedule	2.00%
Amount Ordered	
1 week	3.60%
2 weeks	28.70%
1 month	45.00%
2 months	12.40%
3 months	6.80%
Don't Know	3.60%
Supplier Location	
Dar Es Salaam	9.20%
Masasi town	5.60%
Mbeya	10.40%
Mtwara town	25.10%
Sumbawanga	49.80%
Qualifications	
Doctor Present	12.20%
Pharmacist Present	1.65%
Nurse or Midwife Present	65.02%

Table 5.3: Percent of shops stocking ACTs by survey round and region.

	R1	R2	R3	R4	R5	R6	R7
Both Regions	12.55%	26.09%	37.55%	66.67%	73.25%	78.14%	80.08%
Rukwa	3.45%	7.64%	19.26%	51.82%	62.41%	70.14%	73.38%
Mtwara	24.55%	50.46%	61.76%	87.63%	88.24%	89.32%	88.78%

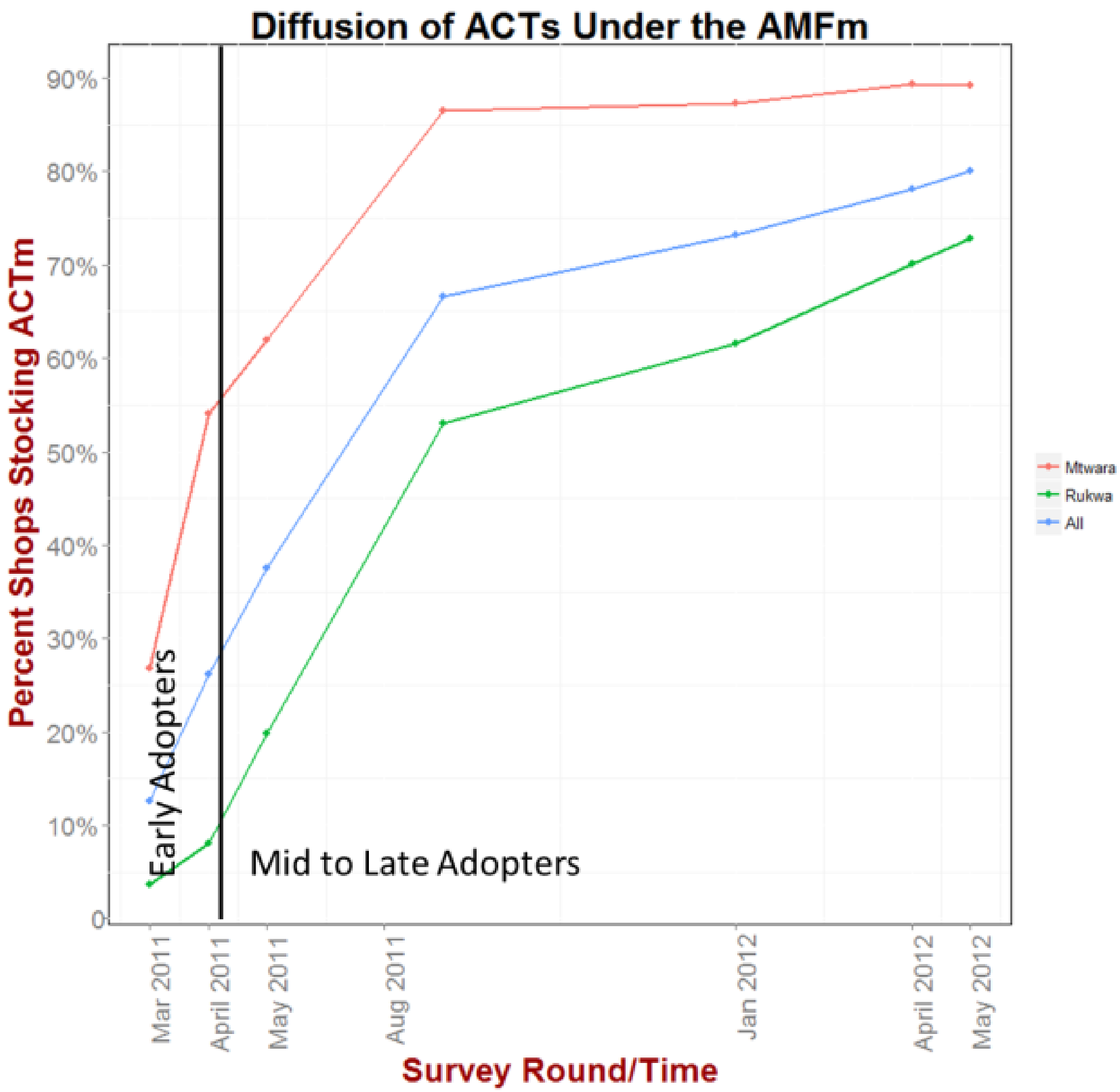

Figure 5.4: ACT product diffusion over the seven survey round under the AMFm. Trends by the two survey regions (Rukwa and Mtwara) along with overall trends are plotted. Early adopters are designated as those shops which stocked ACTs in the first two survey periods. All other are classified as mid-to-late adopters.

Table 5.4: Odds ratios and confidence intervals for bivariate associations of shop level characteristics with ACT stocking controlling for trend over the seven survey rounds and survey region.

	OR (95% CI)	p
Distance to Nearest ADDO	1.00 (0.99,1.00)	0.23
No. of ADDOs Within 3km	1.02 (1.01,1.03)	0.001
Distance to Nearest RCH Clinic	1.00 (0.98,1.01)	0.90
No. of RCH Clinics Within 3km	1.06 (1.00,1.12)	0.04
Degree	1.16 (1.08,1.25)	≤.0001
Betweenness	1.01 (1.00,1.01)	0.01
Population Within 5km	1.01 (0.99,1.02)	0.31
No. of Cust. on Previous Day	1.02 (1.00,1.03)	≤.0001
No. of Customers Presenting for Malaria on Previous Day	1.07 (1.04,1.09)	≤.0001
% Customers Presenting for Malaria	3.01 (1.41,6.46)	0.004
Frequency of Ordering		
Every Week		
Once a month	1.01 (0.59,1.73)	0.96
Twice a month	1.13 (0.65,1.96)	0.66
Every Two Months	0.89 (0.48,1.65)	0.70
Every Three Months	0.65 (0.33,1.28)	0.21
Don't Know/No Set Schedule	1.85 (0.72,4.77)	0.20
Amount Ordered		
1 week		
2 weeks	0.71 (0.37,1.38)	0.31
1 month	0.69 (0.36,1.32)	0.26
2 months	0.70 (0.35,1.43)	0.33
3 months	0.33 (0.15,0.74)	0.01
Don't Know	0.59 (0.25,1.40)	0.23
Supplier Location		
Dar Es Salaam		
Masasi town	0.88 (0.45,1.74)	0.71
Mbeya	1.93 (0.92,4.06)	0.08
Mtwara town	1.54 (0.93,2.53)	0.09
Sumbawanga	1.22 (0.64,2.33)	0.55
Qualifications		
Doctor Present	1.06 (0.76,1.48)	0.74
Pharmacist Present	3.12 (1.29,7.53)	0.01
Nurse or Midwife Present	1.20 (0.91,1.60)	0.20

network degree of shops was highly associated with increased odds of ACT stocking (OR 1.16 (1.08, 1.25)). Betweenness centrality was also associated with ACT stocking (OR 1.01 (1.00, 1.01)), though not as strongly. Though not included in the table, the hypothesis that shops may be influenced by competing shops was tested by noting whether at least one of the reported competing shops stocked ACTs. This was done for each of the survey rounds. A logistic regression model for ACT stocking was produced testing associations with the stocking status of perceived competitors while controlling for survey round and region. Tests indicated that the odds of stocking ACTs for shops whose competitors also stocked them were 1.4 (CI: 1.14, 1.93) times higher than shops whose competitors did not.

As the relationship between predictors and outcomes may not be entirely linear, patterns of association of predictors on ACT stocking were explored graphically. Smoothed estimates of predictive covariates controlling for survey round and region can be seen in figure 5.5. Population, percent of customers presenting for malaria concerns, number of shops within 3km, and total customers on the day of survey were all positively and mostly linearly associated with ACT stocking. Distance to nearest shop was inversely associated with ACT stocking for shops which were very proximate to one another (under 10 km), but not associated at all for very isolated shops. Network degree showed positive associations with ACT stocking.

5.4.4 Multivariate Model of ACT Stocking

The final model is presented in table 5.5. Controlling for region and the survey round, the increased customer numbers and the fraction of customers appearing for malaria concerns were both positively associated with ACT stocking. Increased numbers of proximal shops was associated with a slight though statistically significant increase in the likelihood of stocking ACTs. Larger numbers of proximate RCH clinics was associated with a decreased likelihood of stocking ACTs. In short, ACT stocking appeared to be associated with a combination of shop traffic and the presence of proximate competitors.

Table 5.5: Results of optimal multivariate model based on a backward selection procedure. All variables were included in the model, and then removed one by one until an optimal set of significant variables was reached.

	OR (95% CI)	**p**
(Intercept)	0.14 (0.09, 0.24)	≤.0001
Total number of customers on previous day	1.02 (1.01, 1.02)	≤.0002
Percentage of customers appearing for malaria concerns (per 10% increase)	1.19 (0.52, 2.70)	≤.0003
Number of ADDOs within 3km radius	1.04 (1.02, 1.07)	0.001
Number of RCH clinics within 3 km	0.89 (0.78, 1.01)	0.065
Round 1	ref	
Round 2	2.72 (1.61, 4.61)	≤.0001
Round 3	4.99 (2.96, 8.43)	≤.0001
Round 4	22.55 (13.07, 38.90)	≤.0001
Round 5	28.41 (16.40, 49.21)	≤.0001
Round 5	41.73 (23.78, 73.24)	≤.0001
Round 7	49.06 (27.58, 87.26)	≤.0001
Mtwara	ref	
Rukwa	0.15 (0.11, 0.20)	≤.0001

5.4.5 Early/Late Adopters

Shops which first stocked ACTs in any of the first two survey rounds were considered early adopters while all other shops were classified as late adopters. Though there was evidence that some measure were associated with the probability of stocking in any round, very few of our measures were associated with early vs. late adopter status. Early adopters, however, tended to be located in areas of higher population than that of late adopters. The fraction of customers presenting for malaria concerns was also slightly higher in early adopting shops compared to shops which started stocking ACTs at a later time (24% vs. 18%). The location of the wholesale supplier was significantly associated early adoption of ACTs. More than half of shops which first stocked ACTs within the first three rounds reported buying their supplies from a

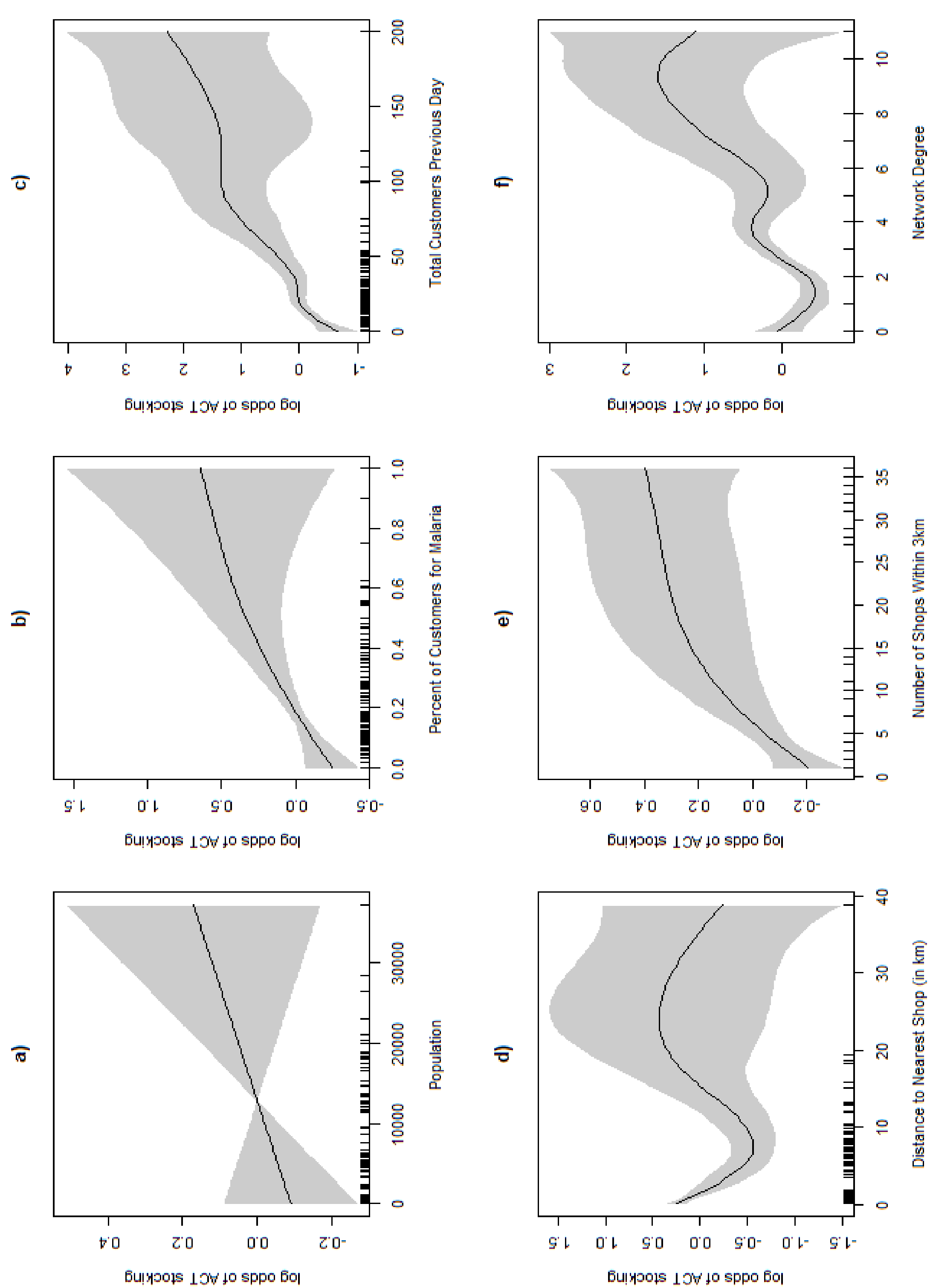

Figure 5.5: Plots of smoothed estimates of predictive covariates on the log odds of stocking ACTs controlling for survey round and region: a) population, b) percent of customers presenting for malaria concerns, c) total customers the previous day, d) distance to nearest shop, e) number of shops within a 3km radius and f) network degree

wholesale supplier in Mtwara perhaps indicating that this particular supplier offered subsidized ACTs ahead of other wholesalers. Full results can be seen in table 5.6.

Graphically, we sought to characterize adopter status by population, distance to nearest competing shop, and the number of shops within a 3km radius (see figure 5.6). Increasing population and increased fraction of customers appearing for malaria concerns was associated with an increased probability of being an early adopter. Distance to nearest competing shops was only relevant for shops where the closest shop was within 5km. Past 5km, there appeared to be no association with adopter status. Increased numbers of proximate shops (within a 3km radius) was associated with an increased probability of being an early adopter. However, shops located within very dense and competitive areas appeared to have the lowest probability of stocking ACTs under this program.

5.4.6 Internal vs. External Influence

Again, the small number of time points constrained our ability to estimate coefficients of internal and external influence through more complex models. However, using the previously presented model form, parameters estimates for the Bass model were p=.01, q=.53 yielding a p/q ratio of 53. Shops may be responding to broader market trends (imitative behavior) when making decisions to stock ACTs, as opposed to a desire to satisfy local demand.

5.5 Conclusions

An operational research study of the AMFm provided us with an opportunity to track the diffusion of a health product in the private market in a developing country from its introduction to widespread availability. We know of no other study which has focused on the question of how pharmaceutical products diffuse in developing

Table 5.6: Associations of shop level characteristics with early and late adopters of ACTs with tests for statistical differences.

	Early Adopter	Mid/Late Adopters	p
Distance to Nearest ADDO	2.65	5.43	0.23
No. of ADDOs Within 3km	7.76	9.41	0.22
Distance to Nearest RCH Clinic	1.55	2.79	0.18
No. of RCH Clinics Within 3km	1.57	1.95	0.16
Degree	2.38	2.42	0.86
Betweenness	9.36	7.21	0.57
Population Within 5km*	15238.84	11984.37	0.02*
No. of Customers on Previous Day	28.36	24.76	0.41
No. of Customers Presenting for Malaria on Previous Day	5.38	4.38	0.19
Percent Customers Presenting for Malaria	0.24	0.18	0.01
Frequency of Ordering			0.68
Every Week	4.05%	6.85%	
Once a month	47.30%	38.36%	
Twice a month	29.73%	30.14%	
Every Two Months	8.11%	13.01%	
Every Three Months	9.46%	8.90%	
Don't Know/No Set Schedule	1.35%	2.74%	
Amount Ordered			0.3
1 week	1.35%	4.79%	
2 weeks	28.38%	26.71%	
1 month	52.70%	41.10%	
2 months	9.46%	13.70%	
3 months	6.76%	8.22%	
Don't Know	1.35%	5.48%	
Supplier Location			≤.0001
Dar Es Salaam	10.81%	8.90%	
Masasi town	9.46%	4.79%	
Mbeya	4.05%	13.70%	
Mtwara town	54.05%	12.33%	
Sumbawanga	21.62%	60.27%	
Qualifications			
Doctor Present	9.09%	17.30%	0.14
Pharmacist Present	1.29%	2.56%	0.88
Nurse Present	77.92%	72.43%	0.45

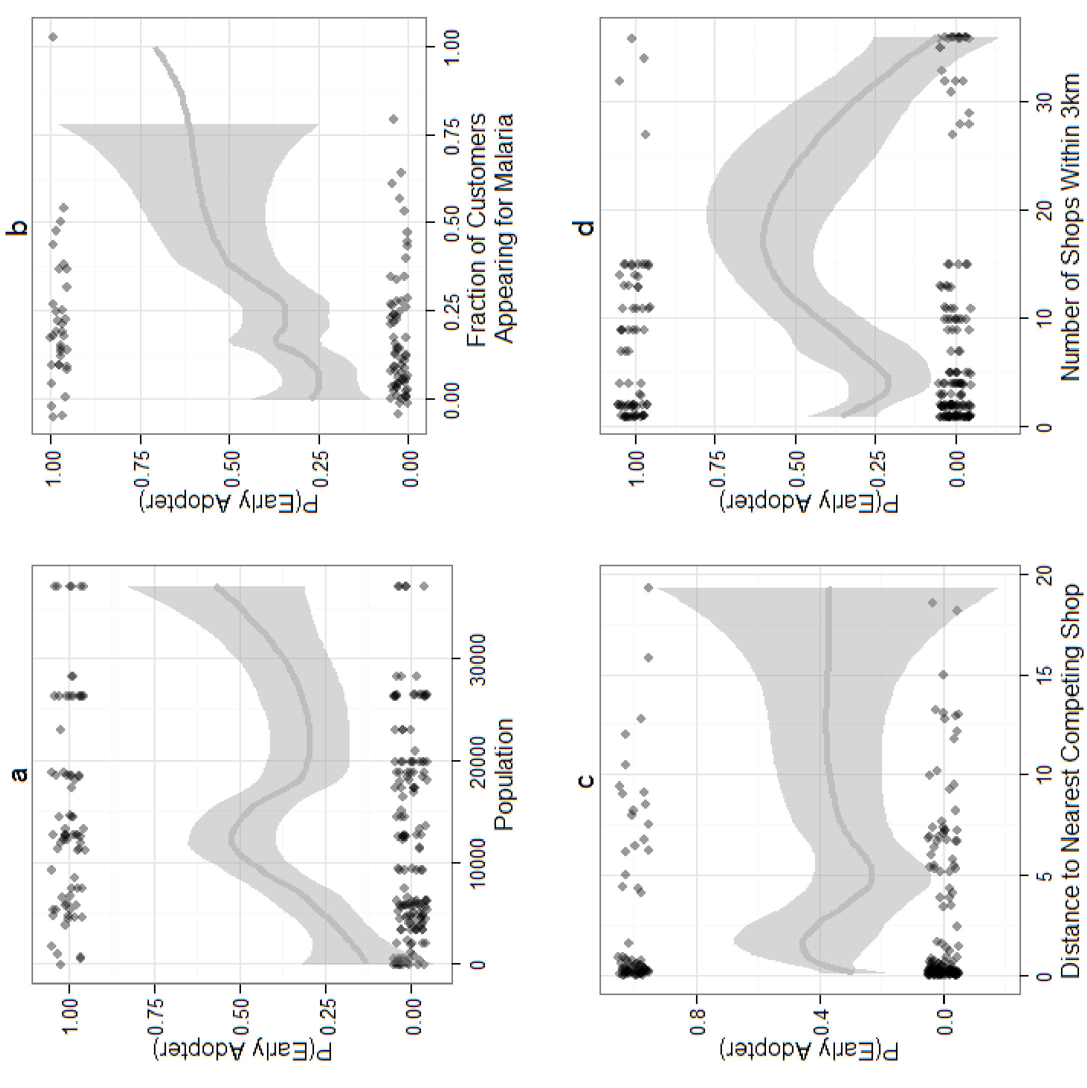

Figure 5.6: Probability of being an early adopter of ACTs under the AMFm by a) population, b) network degree, c) distance to nearest competing shops and d) the number of shops within a 3km radius. Trend lines are produced using loess fitting. Points represent adopter status of shops.

world markets using a comprehensive longitudinal series of surveys. Understanding the specific characteristics of shops which stock new products and shops which adopt new products earlier than others could help inform targeting and design of future campaigns to increase availability.

Through our study, we found that busier, more prominent shops in direct competition with others in densely populated areas were more likely to stock ACTs than isolated shops which served fewer customers. We also found evidence that might suggest that shops which have a higher fraction of their customers presenting for malaria concerns are more likely to stock anti-malarial medications overall and are more likely to adopt new products targeting malaria more quickly. We noted that a specific wholesaler location (Mtwara) was associated with early product availability in small shops suggesting that wholesalers also may play an important role in expanding product availability. Though the limited number of time points prevented more rigorous analysis using a mixed influence model, the parameters estimates from the Bass model used suggest that shops predominantly imitate one another when stocking ACTs, rather than respond exclusively to customer demands. This result is to be expected if shops are responding to suggestions from wholesalers to stock new products. An optimal multivariate model included a combination of increased customer demand, both overall and for malaria, and increased numbers of proximate sources of pharmaceutical. This could imply that decisions to stock new products are the result of a complex mix of factors related to both a need to imitate and thus remain competitive in the market and satisfy the potential demands of customers.

Our study suffered from many limitations. First, though we feel that the regions selected are representative of much of Tanzania, the presence of the shop accreditation system in Tanzania might limit the generalizability to other African countries.

Though private, the ADDOs are licensed and accountable to the central regulatory body which in partnership with local health authorities and development partners attempts to ensure standards of shop keeper knowledge and product quality. The private pharmaceutical sector in other Sub Saharan African countries might not be as formalized. New products introduced to the market might diffuse in a manner different from what we experience in Tanzania.

Second, though we had access to detailed data such as shop locations, names of competing shops and customer numbers, we lacked more detailed knowledge of the attitudes and experiences of the shop proprietors themselves. Informal interviews while study teams were in Tanzania indicated that business knowledge and attitudes were heterogeneous among shops. Future studies might seek to collect more detailed data on how shop owners strategize their businesses, assuming they do at all. Knowing more information about what criteria shop owners use to determine which new products will they start stocking might help create efficient strategies for the launch and faster adoption of new health technologies in private markets. There is evidence that educational strategies that seek to improve the knowledge and thus efficiency of small drug providers has been shown to be effective in some contexts[Wafula and Goodman, 2010].

Third, the unique nature of the AMFm might have produced a case of product diffusion that may not always be applicable to other contexts. New products that lack such public support and deep price subsidies might not diffuse as quickly. The AMFm was widely publicized and ACTs were likely known to customers and shopkeepers. Shops may be reluctant to stock a product that is unfamiliar to them or has yet to be accepted by or is unknown to current customers.

5.6 Abbreviations

ACT, artimisinin combination therapy; ADDO, accredited drug dispensing outlet; AMFm, Affordable Medicines Facility Malaria; GIS, geographic information systems; RCH, reproductive and child health;

5.7 Endnotes

RCH clinics were used as a proxy in place of all public health facilities as we did not have GPS coordinates of all public health facilities. A large fraction of public health facilities offer RCH services so this was a reasonable approximation.

CHAPTER VI

CONCLUSIONS

When I was a child, my familys home in Jackson, MS was inundated in what was then known as the great Easter flood of 1979. It turns out, of course, that flooding was a regular occurrence in that particular area, as was confirmed by the old sharecroppers who farmed the land prior and just after World War II. Nearly all the homes in my particular neighborhood were ruined, and everyone displaced. In addition to a sudden spike in heart attacks among the elderly, the subsequent rise in alcoholism and economic disasters, drinking water also became contaminated, and soon hospitals were experiencing a flood of their own. I noted, however, that not all people were affected by the flood. In fact, the extent of the damage seemed to be graded on socio-economic lines. Wealthier people, with greater access to cash resources were able to weather the damage better than their poor counterparts.

Even in my 10 year old brain, I took notice of a few very important points. Given the proper resources and equitable access to high altitude areas far from water, the rains would pose little threat. I noticed that the best areas of Jackson were always on hills and had the fewest houses on the largest pieces of land. And I noticed that when relief efforts came and the power started to come back on, the neighborhoods closer to town and with the best resources would be the first to return to normality.

Thus, my conclusion was that this disaster was not natural, but entirely man made, a combination of ecological, economic, social and infrastructural factors that could not be teased apart, but worked in concert to create the best or the worst of conditions.

In this respect, malaria, is no different from that flood in Mississippi which caused so much suffering. Malaria is multi-factorial health issue, the factors of which transcend simple biological interactions. The tools to prevent, cure, control and eliminate malaria exist, but a host of economic, structural, infrastructural, political, ecological and social factors dictate who has access to them and who does not. To this end, a whole systems approach is needed to analyze problems of malaria, i.e. an approach that asks questions large enough to accommodate an answer and recognizes that the complex social and economic context in which disease occurs is as much of a causal factor of disease as that of the direct transference of pathogen to host[Levins R, 1999]. In this dissertation, we have sought to uncover at least a small fraction of this set of questions.

6.1 SUMMARY OF MAJOR FINDINGS AND RESEARCH IMPLICATIONS

In chapter two, we found urban and rural spaces were not mutually exclusive entities, but rather that urban-like areas existed in "rural" areas and that rural-like areas existed in or proximate to "urban" areas. We applied these new classification to find that parasitemia prevalence varied inversely along a gradient of urbanicity. We found no sharp divides between what is traditionally considered "urban" and "rural." Proximity to markers of locations suitable for vector breeding such as lake fronts and rivers were found to be predictive of *Plasmodium* infection, though factors of urbanicity such as proximity to health services, roads and population were also informative. These relationships held even when controlling for potentially confounding factors such as ITN use and socio-economic status.

However, we were not able to answer the question of temporal causation. In an ideal world, we would be able to observe how malaria transmission changes, as areas urbanize. Learning about how small temporal changes in the social and economic landscape are associated with changes in malaria transmission over time may begin to uncover this question. Better understanding of how factors of urbanicity and urbanization work dynamically with malaria transmission will have important implications for development, a set of questions that will become ever more salient as economies in SSA urbanize.

In chapter three, we learned that in a context where ITNs are delivered using the existing public health delivery system, that ITN possession was inversely associated with proximity to public clinics and hospitals. We also found that ITN use within the home was associated with proximity, even when households already possess one or more nets. In chapter two, we found that households which are most distant from health facilities are at the highest risk for infection yet we found here that these populations were the least likely to possess and use nets. A strategy which centers on fixed locations may be insufficient to provide sufficient protection for populations at high risk. To account for spatial shortfalls in ITN possession and use, we recommended that the existing Community Health Worker (CHW) program be utilized to improve coverage.

In chapter four, we looked at ITN in precisely the opposite context as that of chapters two and three. We found that ITN use increased one year following a comprehensive, direct to household distribution of ITNs to a community along Lake Victoria in Kenya. We found that this strategy induced equity among socio-economic and educational groups. However, we also found that, even after coverage levels exceeded 90%, ITN use varied by age. Specifically, ITN use dropped with age following birth, reached a minimum at approximately 15 years of age, then increased again until approximately 35 years of age after which it remained consistent. As this pattern has been noted previously in other studies in other geographic contexts, we conclude that this shortfall may be an unavoidable.

As malaria elimination becomes an important focus for researchers and policy makers, more research needs to be done to determine the impacts of consistently vulnerable age groups on malaria transmission. Dynamic models of malaria transmission, some including age and immunity effects, already been experimented with[Mandal et al., 2011], though extensions of these models might include the presence of other interventions such as IRS and ceiling nets. We recommend that policy maker look to broad "multi-pronged" approaches which combine several types of interventions to combat malaria in areas of intense transmission. Modeling might also reveal an optimal combination of interventions which deliver consistently strong protection. Others have attempted dynamic models of malaria transmission and ITN coverage to find optimal levels of coverage and insecticidal strength[Gu and Novak, 2009].

Finally, in chapter five, we found that availability of anti-malarial medications under the AMFm in private shops was determined by broader market factors such as competition between shops and customer demand for medications. We found that shops which stocked malaria medications tended to be located in high population, market centers, but which were also located proximate to other shops and reproductive health clinics. Full penetration of new anti-malarial products to serve out of reach population using the private sector was shown to be possible. We note the results of chapter two, which showed that communities at the highest risk for disease reside the farthest away from health facilities, where medications are normally distributed. Tanzania's ADDO program is somewhat of a special case in SSA. Retail outlets, however, exist in nearly all communities, no matter how remote. Exploring shop level determinants of new health product adoption might help policy makers expand access to effective medications in areas which need them the most by leveraging the private sector.

6.2 Closing Statements

All of the chapters in this dissertation provide useful information which can assist policy makers in more effectively targeting anti-malarial interventions, particularly to remote populations. No intervention and no delivery strategy will ever produce perfect outcomes. However, the results of this dissertation suggest that careful consideration of spatial, logistic and market factors can improve access and potentially reduce wastage. Malaria, like floods in Mississippi, requires multi-faceted strategies to ensure that groups who suffer the most are the first to receive help. Comprehensive strategies which utilize multiple and diverse areas of expertise will be essential for control and eventual elimination.

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